

Surgery in Africa - Monthly Review

Prevention and Treatment of Cancer of the Cervix in Africa - I

(Editors' note: this important review will be published in two parts: Part I on epidemiology, screening, prevention and diagnosis of CIN in May 2010 and Part II on the treatment of CIN and invasive cervical carcinoma and the challenges in Africa later in 2010. A pdf of the entire review will be available with Part II).

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1.0 Introduction

Cancer of the uterine cervix is the most common cancer affecting women in Africa and in developing countries, and second only to breast cancer worldwide. (1) (2) This cancer kills approximately 270,000 women each year, with nearly 85% of those deaths in resource-poor settings. (3) In spite of this significant burden of disease most women in the world have been denied any form of screening which would lead to prevention of this disease. Kitchener in an article in Vaccine in 2006 noted the probability of an additional one million more deaths from cervical cancer over the "next five years." (4)

For a sense of perspective we can compare the number of maternal deaths per year, estimated to be 342,900 in 2008 (5) to the previously quoted number of 270,000 cervical cancer deaths per year. 99 per cent of the maternal deaths per year and 85 percent of the cervical cancer deaths per year occur in developing countries. The elderly, the economically disadvantaged and those who do not participate in screening programs are disproportionately represented among women who develop and die from this disease. (6) Approximately 500,000 new cases are reported each year. (7) Although effective and definitive treatment is technically possible in the pre-invasive stage of this cancer, treatment of frankly invasive cancer is difficult to impossible in developing countries. (8)

The introduction of the Papanicolaou smear during the late 1940's in the USA decreased the incidence of invasive cancer of the cervix by 70%. (9) Even though this cytology-based screening program greatly reduced the burden of cervical cancer in developed countries, this approach has not proven effective in resource-poor countries that lack the infrastructure to support these programs. (8) Recently new approaches to preventing cervical cancer have been proposed. Human papillomavirus (HPV) testing and visual inspection of the cervix with acetic acid (VIA) are two new screening tests being proposed to identify pre-cancerous conditions of the cervix. (10)

The field of cervical cancer prevention is rapidly evolving as a consequence of the positive identification of the cause of the disease: a limited number of viral types from the human papilloma virus (HPV) family. Professionals and institutions around the world have the opportunity to join together and inform and update themselves on the HPV and cervical cancer story. Experts recommend that educational efforts have to be made at all levels and with a sense of urgency. In order to achieve success a phenomenal worldwide effort is necessary. (11)

Cervical cancer is a preventable and curable disease, preventable by vaccination and screening and curable if identified at an early enough stage. It is gradually becoming a rare disease in many developed countries; this is not the case in most developing countries. In sub-Saharan Africa it accounts for 22.2% of all cancers in women. In the west the incidence has decreased markedly as a result of effective screening programs. In many parts of Africa (12) and Asia Oceania (13) on the other hand invasive cervical cancer is relatively common with most of the patients presenting in advanced stages.

The incidence of cervical cancer is still high in most developing countries. The rate can be 15 times higher in resource poor countries compared to high income countries ([Table 1](#)). The true incidence of cervical cancer in most African countries is unknown and there is gross under reporting. Only a few countries have functional cancer registers and record keeping is minimal or non-existent. Some of the figures quoted in the literature are hospital-based which represents a small fraction of women dying of cancer of the cervix as most women cannot access hospital care and die at home. ([14](#))

Table 1 Cancer of the uterine cervix, incident cases, deaths, age-standardized incidence and mortality rates 2002 (adapted from sources [14, 15](#))

	North America	Western Europe	South America	South Central Asia	Eastern Africa	Southern Africa	Western Africa	Middle Africa	Northern Africa
Cases in 2002	14600	12700	48300	157700	33900	7600	20900	8200	8100
Deaths in 2002	5700	5600	21400	86700	27100	4400	16700	6600	6500
Age standardized Incidence /100,000	7.7	10.0	28.6	26.2	42.7	38.2	29.3	28.0	21.1
Age standardized Mortality /100,000	2.3	3.6	12.9	15.0	34.6	22.6	23.8	23.0	9.8

2.0 Epidemiology

2.1 Age

There is a similarity between the age-distribution of cancer of the cervix all over the world. The usual pattern in most countries is a rise that starts in the early 20's, shoots up sharply in the 30's and plateaus at 40-50years of age ([15](#)). The level of plateau may vary but the pattern is consistent. Data from cancer registers in developing countries indicate that approximately 80-90% of confirmed cases were among women 35years and older ([16](#)). In a major review in Ibadan Nigeria, the mean age of all cases was 51.8years ([17](#)). In Angola, Madagascar and Uganda more than 20% of patients with cervical cancer are younger than 35years. In most Asian countries, less than 10% are in women below 35years. ([18](#))

2.2 Sexual Activity

The association between sexual activity and the occurrence of cervical cancer has long been established. In the mid 19th century, Italian scholar, Domenico Rigoni-Stern, noted the extreme rarity of carcinoma of the cervix among nuns. Martin in 1967 ([19](#)) identified the following women as low risk group women for development of cervical cancer: Muslim women, Amish women, Jewish women, Seventh Day Adventist women, Irish immigrant women, Protestant and Catholic women who regularly attend religious services, women of high economic status and rural women. In the high risk group of women for cervical cancer development he included Puerto Rican women, Negro women, in mates of women's prisons, commercial sex workers, sexually transmitted disease patients, women of low socioeconomic status and urban women.

Rotkin and King in 1962 reported that the age at first intercourse is the variable of greatest clinical correlation ([20](#)). Patients who began coitus at 15-17 years have twice the incidence of cervical cancer as in the control groups. In matched controls, few cervical cancers developed in patients who began coitus after the age of 21. There were almost none in patients who had first coitus at age 37. It is well established that women who have multiple sexual partners have a higher frequency of cervical cancer than matched controls ([21](#)). Cervical cancer is more frequent in parous than in nulliparous women but the total number of pregnancies is not directly related to the frequency of cervical cancer ([22](#)).

These epidemiological factors correlate well with the current understanding of the pathogenesis of cervical neoplasia. It is now generally accepted that most of these factors are likely indicators of exposure to human papilloma virus (HPV) ([23](#)).

2.3. Male factor

The behavioral characteristics of the male partner are also contributory in development of cancer of the cervix. Kesler in 1967 observed that second and third wives of males whose first wives developed cervical cancer also had a higher than expected incidence of developing cervical cancer. There are also reports that female partners of patients with penile and prostate cancers more often than chance developed cervical cancer ([24-26](#)).

2.4. Genital infection

Genital infection as a primary etiologic agent of cervical cancer has been extensively studied over the years. Initially the searchlight was on cytomegalovirus (CMV) ([27](#)); later in the 70s and early 80s, Herpes Simplex Virus (HSV) ([28](#)) was suspected. Since the mid 80s there has been accumulating and convincing evidence that genital infection with human papilloma virus HPV is the primary etiologic factor ([29-32](#)).

2.5 Other risk factors - smoking

Several workers have reported a higher incidence among spouses of males in the low socioeconomic class ([33, 34](#)). Exposure to cigarette smoke has also been implicated as a risk factor ([35](#)). Carcinogens present in cigarette smoke are concentrated in cervical mucus and may interfere with local immunity ([35, 36](#)). Some studies show a reduced risk with use of barrier methods of contraception ([37](#)) and a few suggest possible increased risk with use of oral contraceptives ([38](#)). The role of nutritional elements is controversial some studies have shown reduced risk with higher intake of vitamins A, C, and E, carotenoids and folate, ([39](#)) while other studies show no effect.

2.6 HIV and carcinoma of the cervix

Infection with human immunodeficiency virus HIV may put a woman at higher risk of HPV infection and very probably puts her at higher risk of HPV induced carcinogenesis. In 1992 the US Centre for Disease Control and Prevention included cervical cancer and its precursors as one of the diseases that can be used to diagnose AIDS in women. Judson ([40](#)) has demonstrated an increased risk of invasive cancer in areas where infection with HIV-2 is common.

2.7 Reflection on risk factors

One useful way to classify risk factors for acquisition of HPV infection is based on either a biologically based risk or a behaviorally based risk as shown in [Table 2](#). Biologically based risk factors come into play mainly downstream from the exposure to HIV. Behaviorally based risk factors mainly affect the acquisition of HPV infection. [\(41\)](#)

Biologically based risk factors include age at first menarche, age at exposure to HPV, co-infection with other STIs, HIV infection, and immunosuppression, among others. Numerous studies have shown an increased risk of HPV infection at younger ages. The highest prevalence of HPV infection occurs in adolescents and young adults between the ages of 15 and 25, where it is believed that more than 75% of new HPV infections occur. [\(41\)](#)

Behaviorally based risk factors include number of sexual partners, characteristics of partners, contraceptive use, parity and use of alcohol, cigarettes, or illicit drugs. Consistently shown to be associated with an increased risk of HPV infection is a history of increasing number of lifetime sexual partners and having had a recent, new sexual partner. [\(41\)](#)

Table 2 Risk Factors known to be associated with HPV Infection (adapted from [41](#))

Biologically Based	Behaviorally Based
Immunosuppression	Lifetime number of sexual partners
HIV infection	Recent new sexual partner
Co-infection with other STIs	Older sexual partner
Micronutrient deficiencies	Oral contraceptive use
Genetic polymorphisms	Pattern of condom use
Age at exposure to HPV	Parity
Age at menarche	Number of partner's sexual partners
Type of HPV infection	Marital status
Co-infection with multiple HPV types	Heavy alcohol use
Viral load	Current or previous cigarette use
	Current or previous illicit drug use

3.0 Etiology

Infection with the human papilloma virus (HPV) as the cause of subsequent development of cervical cancer has been established beyond a reasonable doubt. Essentially all cervical cancers contain the DNA of an oncogenic HPV type. This association is present in virtually all cervical cancers worldwide. [\(42\)](#)

Infections caused by human papilloma viruses are very common and can cause warts, or papillomas, growing on skin throughout the body, particularly the hands and feet. There are over 100 types of HPV with about 40 types capable of being transmitted sexually and infecting the genital area. Genital HPV infection is one of the most common sexually transmitted diseases in the world. These infections rarely cause symptoms and therefore the majority of infections are not noticed by the person infected. [\(43\)](#)

Types of HPVs are divided into "low-risk" and "high-risk" depending on their ability to cause cancer. Both types of HPVs can cause the abnormal growth of cells, but only the high-risk types may lead to cancer. Sexually transmitted, high-risk HPV infections can cause cancers in both men and women. The most common types of high-risk HPV are 16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 68, and 69. These high-risk types of HPV cause growths that are usually flat, whereas low-risk types are associated with wart-like growths, which are not flat.

4.0 HPV Vaccines

Women in developing countries carry a heavier burden of risk of dying from cervical cancer. Cervical cancer is a tragic example of inequality in global health. Two effective prophylactic HPV vaccines give promise for a primary prevention strategy against HPV infection and cervical cancer. Both the quadrivalent HPV 16/18/6/11 vaccine (Gardasil®, Merck & Co., Inc.) and the bivalent HPV 16/18 vaccine (Cervarix™, GlaxoSmithKline Biologicals) have shown high safety, efficacy, and immunogenicity. HPV types 16 and 18 are responsible for 70% of the cases of cervical cancer worldwide. The three dose regimen required for vaccination with these vaccines costs \$360, the most expensive vaccine in history. When 80% of the cases of cervical cancer occur in developing countries, the expense of the vaccines becomes a difficult barrier. [\(44\)](#) (Louie, K, Cervical cancer prevention in Africa http://www.africa-health.com/back_issues.html)

The Global Alliance for Vaccines and Immunizations (The GAVI Alliance) provides technical assistance and financial support for immunization and vaccines in the world's poorest countries. Epidemiologic studies for 72 GAVI-eligible countries show that HPV 16/18 vaccinations could be very cost-effective even in the poorest countries. Cost-effectiveness would depend on high vaccination coverage of young, adolescent girls and the lowering of vaccine costs. Making this vaccine accessible and affordable to GAVI-eligible countries would be an investment in the future and could prevent the deaths of close to 5 million women vaccinated as young adolescent girls in the next two decades. [\(44-45\)](#)

Although the HPV 16/18 vaccine is being used extensively in developed countries, it is quite probable that widespread HPV vaccination against HPV 16/18 in poor countries is many years away. Girls need to be vaccinated before they become sexually active to prevent genital HPV infection. What beneficial effect HPV vaccination will have on those already infected with HPV 16 or 18 is unclear. Millions of women will remain at risk for developing cervical cancer for another 40 to 50 years, even if the vaccine becomes widely available in poor countries. In the meantime efforts to provide effective and affordable screening and early treatment programs in developing countries must continue if lives are to be saved. [\(46\)](#)

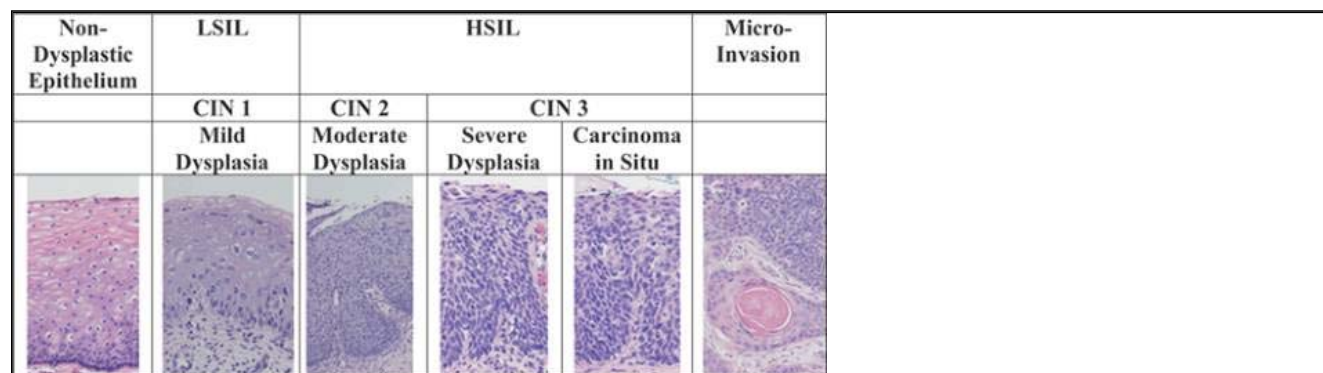
5.0 Cervical Intraepithelial Neoplasia (CIN)

5.1. Classification

The naming and classification of cervical precancerous lesions has changed many times over the 20th century. The term "cervical intraepithelial neoplasia" (CIN) replaced use of the term "dysplasia" to describe changes in the epithelial cells. CIN is divided into three classifications: CIN1, CIN2, and CIN3. In CIN1 only the lower third of the cells in the epithelial layer are abnormal. In CIN2 two-thirds of the cells are affected. In CIN3 there is involvement of the entire thickness of the epithelium. Full thickness involvement is also referred to as "carcinoma in situ."[\(47\)](#)

The most recent classification is the Bethesda System, which divides all cervical epithelial precursor lesions into two groups: Low-grade Squamous Intraepithelial Lesion (LSIL) and High-grade Squamous Intraepithelial Lesion (HSIL). LSIL corresponds to CIN1, and HSIL includes CIN2 and CIN3. More recently CIN2 and CIN3 have been combined into CIN2/3. (47)

Diagram 1 shows examples of various levels.



Images courtesy of Chisa Aoyama, MD, David Geffen School of Medicine at UCLA.

Diagram 1 – Histology of Cervical Intraepithelial Neoplasia (from Danforth's Obstetrics and Gynecology, 2008, Wolters Kluwer, Philadelphia, PA)

5.2. Natural History

The major steps in cervical carcinogenesis include infection of the metaplastic epithelium of the transformation zone of the cervix with one or more of the high-risk types of HPV, viral persistence, clonal progression of the infected epithelium to precancer, and invasion below the basement membrane. (47) **Diagram 2** shows these stages.

Metaplastic epithelium refers to areas of the body where one type of epithelium contacts and gradually replaces another type by literally transforming itself through a process known as metaplasia. A transformation zone on the cervix occurs naturally where columnar epithelium of the endocervical canal is transformed into squamous epithelium of the ectocervix. This process in children is relatively dormant, but it becomes quite active around puberty. Cervical carcinogenesis begins with infection with high-risk HPV types in areas of the cervix undergoing squamous metaplasia. It is likely that sexual contact explains the majority of HPV infections of the cervix. When infection with a high-risk type of HPV occurs, persists, and progresses, cancerous cells break through the basement membrane of the cervical epithelium and enter the stroma of the cervix. When cancerous cells cross the basement membrane and enter the stroma, a precancerous condition evolves into a cancerous one. (48)

Viral persistence can be defined as detection of the same HPV type two or more times within a given time interval between the examinations. Although time to clearance of the HPV virus varies between studies, almost all show that about 90% of all HPV infections are cleared from the cervix after two years. Long-term persistence of a viral type is not strictly correlated with carcinogenicity since some non-carcinogenic types show a long persistence as well. Virologists have come to the conclusion that the longer an HPV infection has persisted, the longer it is likely to persist. (48)

The presence of the histologic diagnosis of CIN3 is a good indicator of risk of the development of subsequent cancer. The time span between HPV infection and CIN3 has been calculated to be 7 – 15 years with most infections occurring in the later teens or early twenties and CIN3 diagnosis peaking around 25 – 30 years of age. The risk and timing of invasion below the basement membrane is impossible to predict. The median age of women with CIN3 is 27-30 years, while the median age of women with invasive cancer is much older, sometimes after a time span of ten years. (48)

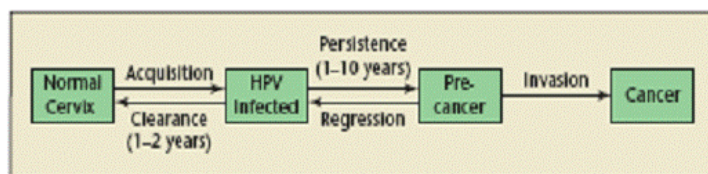


Figure 1. Stages in the development of cervical cancer. Acquisition of human papillomavirus (HPV) occurs via sexual contact. Most infections clear spontaneously, generally within 1 to 2 years. Persistent infections, which can last 10 or more years, lead to high-grade cervical lesions and eventually invasive cervical cancer if left untreated. Low-grade cervical lesions often regress spontaneously, but can also progress to higher grade lesions (pre-cancer) and cancer. Adapted from Burchell AN et al.⁴⁸

Diagram 2 – Stages in the Development of Cervical Cancer (from Dempsey, Review in Obstetrics and Gynecology, 2008; 1(3): 122-127)

5.3. Screening and Early Detection

In spite of knowledge of the cause and prevention of cancer of the cervix, successfully organized, population-based cervical cancer prevention programs have not yet been implemented in most developing countries. Denny states that contributing factors to this situation are poverty, lack of resources and infrastructure, and disenfranchisement of women. (49)

Reasons for the lack of attention to this cancer include the impressive burden of other diseases and the shrinking public health budgets in many developing countries. Communicable diseases and maternal or perinatal complications caused approximately 70% of all deaths in women in sub-Saharan Africa in 1995. The equivalent statistic for developed countries was 4.9%. (49)

Most countries in sub-Saharan Africa have very few specialists in obstetrics and gynecology, very limited laboratory facilities, very rare pathologists and cytotechnologists, and no facilities for cervical cancer screening or treatment. (49)

Women in developing countries are usually poorly educated, often illiterate, and lacking in economic power. This situation leads to difficulties in health-seeking behavior, access to health care, and understanding of women's health issues. (49)

Barriers to establishing effective cytology-based screening programs in developing countries include lack of the necessary infrastructure to obtain and transport the Pap smears to laboratories for processing and interpretation, lack of high-quality laboratories, and lack of specialists to perform follow-up tests and treatment. (49)

Denny suggests the following requirements for a successful screening program in low-resource settings: availability of screening, diagnosis, and treatment in accessible clinics; low-cost, low-technology screening tests, wide-coverage of target population, appropriate programs for public awareness, and built-in mechanisms for evaluation of the programs. The two most widely studied alternative approaches to cervical cancer prevention are visual inspection (with acetic acid or Lugol's iodine) and HPV-DNA testing. (49)

5.3.1. Visual inspection of the cervix with acetic acid (VIA)

Visual inspection of the cervix with acetic acid, also known as direct visual inspection (DVI), involves examining the cervix with the naked eye, using a bright light source, after the application of 3-5% dilute acetic acid using a cotton swab or a spray. The procedure involves waiting for one minute after the application of the dilute acetic acid. This strength of acetic acid is found in store bought vinegar. The ready availability of vinegar worldwide makes this method accessible in developing countries. The area of interest for inspection is the squamo-columnar junction (SCJ), or the area of the cervix where squamous epithelium meets columnar epithelium. This area is of interest because this is where squamous cell cervical cancer begins. (49)

Areas of epithelium that turn white after the application of acetic acid are referred to as "aceto-white". Finding a well-defined, aceto-white area close to the SCJ indicates a positive VIA test. A positive VIA test result means that a well-demarcated, intensely opaque area has been identified. Aceto-whitening can occur in immature squamous metaplasia and in inflamed and regenerating cervical epithelium, but this degree of whitening is less distinct and opaque. Early micro-invasive cancers can also turn white after application of acetic acid. A negative VIA test means that no well-demarcated, intensely opaque area near the SCJ has been identified after the application of acetic acid. (49)

Aceto-whitening is thought to be due to a reversible coagulation of intracellular proteins after the application of acetic acid. Neoplasia of the cervix is associated with higher concentrations of intracellular proteins, thus the dense aceto-whitening. (49) Unlike the Pap smear method which requires a series of steps and transfers to obtain a positive or negative answer, the VIA method yields an immediate result. Advantages to this approach include the possibility of offering treatment at the same visit where VIA was provided, reducing anxiety about waiting for a test result, and eliminating further diagnostic procedures. (49)

A recent field report from a Canadian family practice physician who worked for two years at a government district hospital in Malawi may clarify the state of cervical cancer prevention in one developing country. Dr. Ilona Hale writes, "I routinely saw women with late stage cancers and had nothing to offer but palliation. Pap smears are not feasible because of the lack of infrastructure but a system called "VIA" (visual inspection with acetic acid) is recommended as it has similar sensitivities, and lesions can be treated with cryotherapy in the same visit by nurses or clinical officers with relatively little training." <http://www.cmaj.ca/cgi/rapidpdf/cmaj.109-3125v1>

5.3.2. Visual inspection of the cervix with Lugol's iodine

Visual inspection of the cervix with Lugol's iodine is a visual screening method similar to VIA except that Lugol's iodine is used in the place of 3 – 5% vinegar. (46) Lugol's iodine, also known as Lugol's solution, consists of 5 g iodine and 10g potassium iodide mixed with 85 ml of distilled water. (50) When Lugol's iodine is applied to the cervix pre-cancerous areas appear as well-defined, thick, and mustard-yellow in color, while squamous epithelium stains brown or black, and columnar epithelium retains its normal pink color. Both VIA and VILI provide an immediate test result of either positive or negative. (51)

5.3.3. Liquid-based Cytology

Liquid-based cytology (LBC) relies on preserving collected cervical cells in a fluid medium rather than applying collected cells directly to a glass slide as in the collection procedure for a Pap smear. The suspension of cells is then processed at a laboratory to provide a uniform, thin layer of cervical cells without debris on a glass slide. Advantages of the LBC method include a more complete and uniform transfer of cervical cells from the sampling device to the slide. Other advantages include improved microscopic readability due to elimination of problems such as poor fixation, air-drying artifact, uneven thickness of cellular spread, overlapping of cells, and debris from blood and inflammatory cells. (52)

Reviews of published studies of LCB indicate an increased percentage of adequate samples, increased sensitivity and decreased specificity than the Pap smear. The impact of LBC on cancer incidence and mortality has not been established. The method is more expensive than Pap smears and requires additional instrumentation to process the samples. It is not feasible to implement in many low-resource settings. (52)

5.3.4. HPV Testing

Evidence from the mid-1990s using meticulous testing by polymerase chain reaction of a large international collection of specimens of cervical cancer has shown that HPV DNA was present in 99.7% of the specimens. (3) In 1999 Wallboomers et al. declared that HPV is a "necessary cause of invasive cervical cancer worldwide." (42) This is the first instance in which a specific virus and a causal relationship with a human cancer have been identified in cancer epidemiology. This knowledge has obvious implications for primary and secondary prevention of this disease. (50)

If infection with the HPV virus is an early precursor of cervical cancer, should HPV testing be used in screening for cervical cancer? On the opposing side to widespread HPV testing is the fact that HPV infection is highly prevalent among women of reproductive age and positive results of mass screening for HPV would be impractical if not impossible to follow up. In favor of HPV testing is the position that this would represent a scientifically sound approach for secondary prevention, particularly in developing countries, where cytology screening programs are difficult to implement. Consensus panels of the IARC and WHO have concluded that there is enough justification to evaluate HPV testing as an adjunct to Pap smear screening in cervical cancer. (3)

Sufficient evidence exists to recommend HPV testing in triage of women with atypical cytology. (53) However, as mentioned previously in this paper, up until now there has been no successful population-based cytology screening program in a developing country. (8)

Blumenthal et al in 2000 published their analysis of adjunctive testing for cervical cancer in low resource settings with VIA, HPV testing, and the Pap smear. (53) This analysis was based on 2199 women willing to be screened for cervical cancer in peri-urban clinics in Harare, Zimbabwe between

October 1995 and August 1997. Screening was performed with VIA, Pap smear, and HPV testing on all clients. The presence or absence of precancer was confirmed via colposcopy with biopsy as indicated for >97% of all women in the study. (53)

In the first phase of the Zimbabwe study, a trained, nurse-midwife performed a Pap smear followed by VIA testing on every woman at the first visit. Any woman with a positive VIA test was offered colposcopy during the first phase of the study. Appropriate treatment and follow-up was offered to all women who were VIA positive or who had a positive Pap smear in this first phase. (53)

The second phase of this study began about a year after the first phase and included HPV testing of all women in the study, whether they were screen-positive or screen-negative in the first phase. HPV testing was done to assess the sensitivity and specificity of this test as a single screening test in a developing country and also to assess the usefulness of HPV testing as an adjunct to VIA screening. (53)

In the Zimbabwe study using HSIL/CIN2-3 as the reference threshold of disease, the net sensitivity and specificity of VIA and HPV when used sequentially were 63.6% and 81.9%, respectively. The net sensitivity and specificity of Pap smears and HPV when used sequentially were 43.3% and 91%, respectively. VIA followed by the Pap smear yielded a net sensitivity of 37.5% and a net specificity of 94.3%.

The test qualities of HPV testing considered as a single test showed a sensitivity of 80.1%, a specificity of 61.1%. This lower specificity when compared to the sequential use of either VIA and HPV testing or the Pap smear and HPV testing shows a decrease in the number of women in the study who tested HPV negative who truly had normal cervixes.(53)

The authors concluded that in developing countries with limited resources for cervical cancer prevention but with the capacity for HPV testing, sequential testing involving the use of VIA followed by HPV testing could yield few false positives.(53)

5.3.5. Comparison of screening methods

The ultimate proof of success of a cervical cancer screening method is its ability to reduce the incidence of and number of deaths from cervical cancer in a cost-effective manner. The screening method must have adequate sensitivity and specificity for detection of precancerous lesions and must yield reproducible results. Such a method should be cheap, simple, and easy to apply; without side effects or complications; as painless as possible; and socio-culturally acceptable. (49)

Sankaranarayanan et al. reviewed statistics for cytology, VIA, and VILA in 2005. At that point in time, based on several published reviews, the sensitivity of cytology in detecting CIN2-3 ranged from 47% to 62%, and the specificity ranged from 60% to 95% in developing countries. In the same paper from 2005 sensitivity of VIA varied from 67% to 79% and specificity ranged from 49% to 86%. A review of ten cross-sectional studies done in six developing countries of the VILI method yielded a sensitivity range of 77% to 98% and a specificity range of 73% to 91%.(52)

Sankaranarayanan et al noted that screening with cytology was not a viable option in many developing countries because of an inability to meet requirements such as trained human resources, supplies, mechanisms for delivery of samples and results, laboratory infrastructure, and necessary financial resources. (52)

To be continued:

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