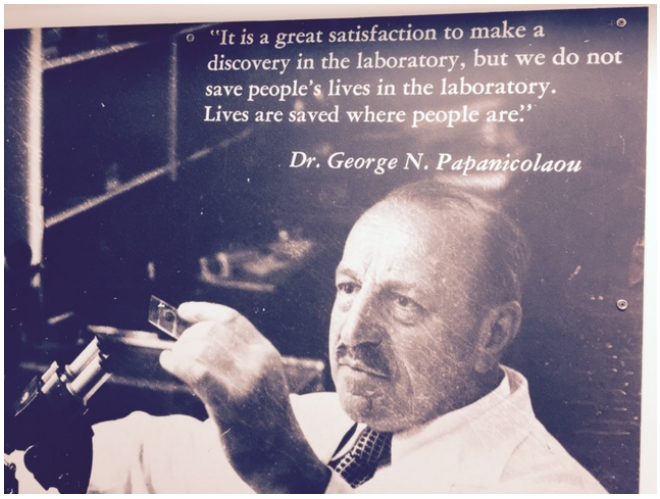
Cervical Cancer Screening Today



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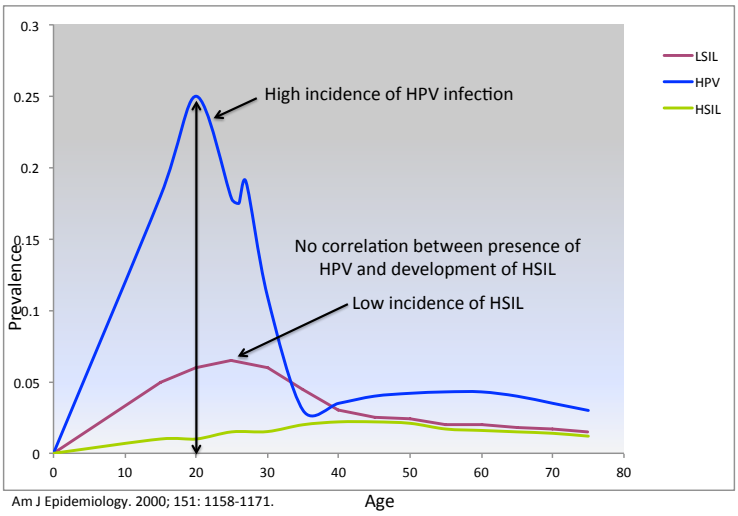
Father of the "Pap" Test

The current process for cervical cancer screening, the Pap test (methodology in use for the past 65 years), whether from a direct smear on a slide or a processed liquid specimen, relies on microscopic observation of abnormal epithelial cells identified in collected cervical specimens. The cytological processing is done in a laboratory and involves the analysis of the Pap smear under a microscope by highly trained cytologists (who are not readily available in developing countries). The analysis is very subjective and results in 8% to 30% false positives and 8% to 30% false negatives, (depending on country). Today, there are about 160 Million Pap smears done annually worldwide (cost $20.00 - $40.00) which represents only 10% - 14% of the global population that should be screened. And of those currently screened, poor sensitivity and specificity of the test results in nearly 16 million false positives and at least 16 million false negatives every year.

The false positives result in additional costs for further testing in addition to unnecessary emotional trauma to the patient. The false negatives have potentially clinically critical consequences to the patient. The process is also long and very labor intensive. Patients exhibiting positive results from Pap smears are followed by colposcopy with tissue biopsies to confirm a histological diagnosis of cervical cancer progression.

A major finding relating to the etiology of cervical cancer is that it generally develops from a persistent infection caused by a high-risk type HPV (Human Papilloma Virus), which infects epithelial cells. Fortunately, the majority of cases of HPV infection are cleared by the women's own immune system; however, in a small percentage (~10%) the virus integrates into the patient's genome, leading to measurable changes in specific protein production in cervical cells, and the development of dysplasia and neoplasia. It is for this reason that the American College of Obstetrics and Gynecology recently recommended a reduction in the number of screening tests in young women; it also highlights the problems with Pap and HPV test specificity (i.e., false positives).

Recently, an FDA Advisory committee unanimously recommended HPV Testing (Roche Cobas) as a primary screening tool for detection of cervical cancer in women. Although this announcement highlights a need for more objective and accurate molecular tests to replace the Pap test, it also raises significant problems with using HPV tests as a primary cervical cancer-screening tool. The major problem with the HPV test is that the HPV infection does not correlate with abnormal high-grade lesions (HSIL) as shown below. Furthermore, although over 80% of women in the US will have acquired HPV infection by the age of 50, the vast majority of these women will be free of HPV infection without any treatment. High-risk types of HPV, such as types 16 and 18, increase the probability of a patient's risk of developing a high-grade cervical lesion. Importantly, however the presence of this infection does not automatically mean that the patient has a cervical lesion that requires therapeutic intervention. Moreover, although the presence of high-risk type HPV in samples helps to identify patients at increased risk for development of disease, these **analytes do not comment on the presence or current state of cervical lesions since HPV infection can be a cause but is not necessarily always the cause of cervical cancer.**



An HPV vaccine is currently available to girls and young women in developed nations with the intent of eliminating HPV infections, and thereby ultimately reducing the number of deaths from cervical cancer. It is important to note that this practice is not a replacement for cervical screening; the FDA requires continued routine screening for cervical cancer even after vaccination since the vaccine is not 100% effective. Its adoption in many resource-limited areas are experiencing some compliance issues due to the inconvenience of sequential doses over extended periods of time and high cost of the vaccine. Furthermore, a recent Duke University study has shown that the HPV strains affecting African-American women differ from those treated with the vaccine (HPV subtypes 31, 35, 45 vs. HPV vaccine subtypes 16, 18, 56). With Africa having one of the highest occurrences of cervical cancer, vaccine use to curb the spread of HPV causing cervical lesions is not an option.