



November 18, 2010 Speaker: Michele Follen, MD, PhD (left) with Dr. Ellie Cantor

Report by Dr. Anita Gurnier-Hausser; photo by Dr. Sheryl Meyer

Dr. Michele Follen gave an informative and engaging presentation on November 18, 2010 entitled “Operation Stop Cervical Cancer in Africa.” Dr. Follen is the Director of the Center for Women’s Health Resources (IWHL), DUCOM Associate Dean for Research, and Professor of Obstetrics and Gynecology at Drexel University College of Medicine. She began her talk by first acknowledging the recent death of Britton Chance. Dr. Chance was an extremely accomplished Professor Emeritus of Physical Chemistry and Radiological Physics at the University of Pennsylvania, School of Medicine, known for his research on metabolic control phenomena in living tissues using noninvasive techniques such as optical spectroscopy and fluorometry in various tissues including breast tumors – technologies also employed by Dr. Follen in her cervical cancer research.

Before beginning her presentation, Dr. Follen distributed sheets of “learning objectives” which outlined various key points of her talk – ranging from new technologies used in cervical cancer screening to important life lessons she has learned through her research and experiences in Nigeria. To the tune of African drum beats, Dr. Follen then began her presentation with a photograph of a barefoot Nigerian woman carrying tree limbs and water buckets on her head. She explained that the incidence/mortality of cervical cancer in Nigeria directly correlates with poverty. Unfortunately few improvements have been made to the screening system, and many women get “missed” in diagnosis. Dr. Follen explained that she chose to work in Nigeria because it was the “toughest” place to start. In developing nations like Nigeria, the majority of women present with stage III or stage IV cervical cancer, when the disease has progressed beyond therapeutic support. As Nigeria is home to 25% of Africa’s population, this disease accounts for deaths of over 8000 Nigerian women each year. Clearly early detection methods are desperately needed in this region.

Dr. Follen pointed out that, ironically, much is known about cervical cancer, yet not enough is being done to prevent it. Glaxo-Smith-Kline and Merck have both recently introduced vaccines against human papillomavirus (HPV), a causal agent for cervical cancer. Although these vaccines will likely decrease the

incidence of cervical cancer in Europe, Canada and the United States over the next 10 to 20 years, unfortunately, no vaccine is currently available in Nigeria. Therefore, cervical cancer screening is vital for both the developed and the developing world until the effects of these vaccines are fully realized and widely available. The most common screening method, which involves cervical cytology studies, is the Papanicolaou smear. Pap smears are an efficient means of reducing both the incidence and mortality associated with cervical cancer. However, in developing countries, cytology-based screening followed by colposcopic detection is expensive and requires extensive laboratory infrastructure and trained personnel which are typically unavailable in these regions. Screening methods such as visual inspection with acetic acid (VIA) are less expensive and require less supplies and infrastructure; however, the specificity and reproducibility of this approach raises concerns.

Dr. Follen then shared some disturbing statistics. She explained that a Pap smear costs about \$8.00 (USD) in Nigeria, while the typical income there is less than \$1.00 per day. As 70% of the population of Nigeria lives below the poverty line, clearly the high cost of this screening method presents a huge problem. There is also a significant shortage of laboratory infrastructure in this region. Additionally, many health care professionals in Nigeria have fallen victim to the “Brain Drain” – defined as the departure of educated/professional people from one country/economy/field to another, usually for better pay or living conditions. As such, few health care workers are available to read cytology slides. As a result of these issues, only 2% of Nigerian women are ever screened for cervical cancer. However, Dr. Follen also mentioned a ‘bright side’ to this situation. Although only 2% of doctors/nurses stay in Nigeria, those that do remain are extremely committed, including Dr. Isaac Adewole, whom Dr. Follen described as her “counterpart” in Nigeria. Nonetheless, objective cervical cancer screening techniques which have high sensitivity and specificity, in addition to being easily interpreted, rapid, and less expensive, would greatly benefit developing nations such as Nigeria.

During her presentation, Dr. Follen discussed the use of four different technologies for cervical cancer screening to replace the traditional Pap smear. Two of these technologies involve fluorescence and/or reflectance spectroscopy, which take advantage of naturally occurring biological fluorophores. Dr. Follen began her explanation of this technology by pronouncing that “women glow”. For example, in normal cervical tissue, collagen crosslinks within the stroma and is strongly fluorescent. This fluorescence decreases with the development of neoplasms. In addition, in normal squamous epithelium, basal epithelial cells emit fluorescence associated with mitochondrial NADH and FAD. Malignancy is associated with a predictable change in the concentration of such fluorophores. As such, these biologically predictive features of cervical cancer (or cervical precancer) can be measured with various optical technologies. While point probes are used to interrogate specific cervical sites, multispectral imaging involves imaging the entire cervix. Recent technological advances have greatly reduced the costs associated with these technologies. As such, optical spectroscopic diagnosis could lower biopsy rates, improve patient selection for treatment and reduce costs. In addition, the specificity and sensitivity of these imaging techniques also renders them potentially clinically useful.

In addition to these spectroscopic methods, Dr. Follen also described the use of quantitative cytology and quantitative pathology for cervical cancer screening. These technologies involve acquiring and analyzing digital images of cervical cells for their size, shape, DNA content and chromatin distribution patterns. Using predictive models, abnormal cells (i.e. non-diploid cells) are identified using normal cells normalization standards. These methods provide objective and reproducible interpretation of cytological features and reduce the subjectivity associated with classical visual diagnostic procedures.

Dr. Follen emphasized many important life lessons she learned through her experiences with Nigeria. One lesson with particularly significance was that technologies which work “in our world” might not necessarily work elsewhere. For example, Dr. Follen’s group developed a multispectral digital colposcope (MDC) designed to rapidly image the cervix. The MDC adds the capability to measure fluorescence and polarized reflectance images as part of a commercially available colposcope, and automated image analysis algorithms provide realtime delineation of precancerous/cancerous areas. In collaboration with the University College Hospital (UCH) in Nigeria, Dr. Follen initiated a study to determine the feasibility of conducting future clinical trials using the MDC as a cervical cancer screening device. Despite the technological advances of the MDC, Dr. Follen described the multiple obstacles she encountered during this study, the most debilitating of which was the unstable supply of electricity in the hospital. She described the frequent and sometimes lengthy power outages in which she and others were forced to work in the dark as they attempted to switch to the hospital’s diesel power generators. In addition, the lack of available spare parts and tools also presented significant problems during this study. Although Dr. Follen and her group learned from these experiences and made appropriate adjustments/arrangements on future trips to Nigeria, it was ultimately decided that conducting future clinical trials with the current MDC device in Nigeria was simply not realistic or feasible, and also undesirable to her Nigerian collaborators.

After this initial study, it was determined that perhaps techniques such as quantitative cytology may be more appropriate screening approaches for use in Nigeria. Dr. Follen went on to describe another recent project involving collaboration between the M.D. Anderson Cancer Center, the British Columbia Cancer Research Centre, and the University of Ibadan, using seed funding provided by the ExxonMobile Foundation and the T. Boone Pickens Research Fund. A meeting to train health professionals in Nigeria, referred to as “Train the Trainers”, was designed to provide both training and equipment to personnel involved in the implementation of a cervical cancer control initiative in Nigeria using a specific training manual. Dr. Follen described the success of this initiative, namely that the training manual utilized was beneficial for both the trainers and the Nigerian health care professionals.

Dr. Follen’s impressive work has ultimately resulted in a 1.5 million dollar investment in cervical cancer research in Nigeria. She left us with this question – Will THIS country ever accept a less expensive, novel Pap smear alternative? Dr. Follen didn’t seem to think so – primarily because it might be a “source of litigation”. She ended by commending Nigeria for their efforts, for their willingness to learn and implement new diagnostic strategies, and for their focus on preventing cervical cancer, not just on building another health care unit.

http://www.awisphl.org/Nov2010meetingreport_Follen.pdf