VOLUME XXVI NO. 10 / MAY 25, 2004

Publishing for 26 Years

ONCOLOGY TIMES

www.oncology-times.com

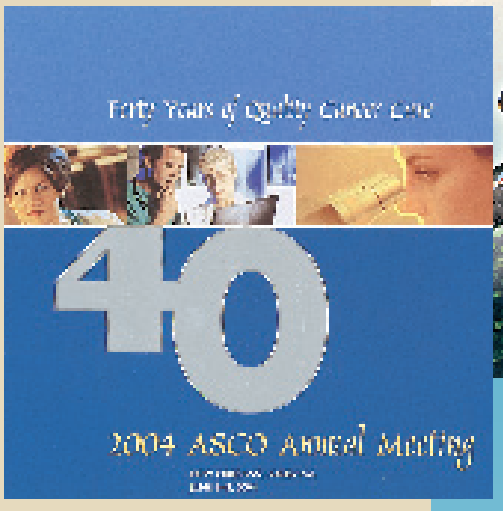
LIPPINCOTT WILLIAMS & WILKINS

THE NEWS CENTER FOR THE CANCER CARE TEAM

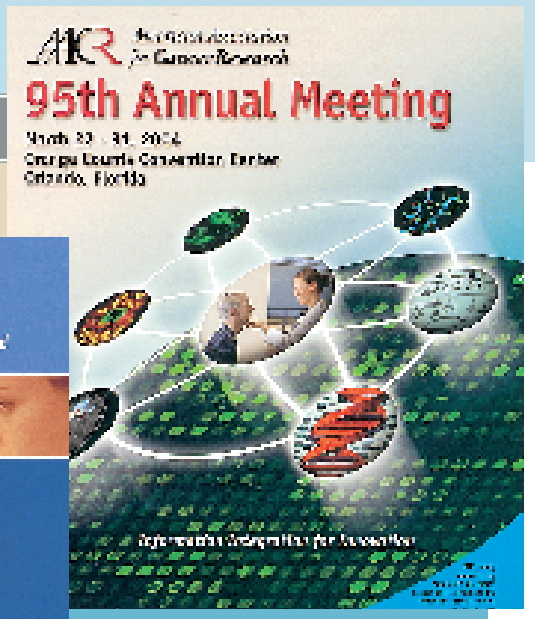
ASCO & AACR:

A Preview of What's to Come Next Month at ASCO's 40th Annual Meeting

First Highlights of AACR's 95th Annual Meeting



Page 31



Page 3

NCCN

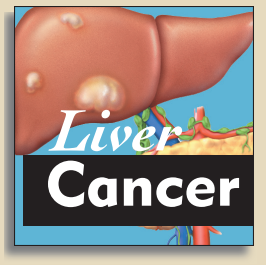
(1) Anti-Emesis Guidelines Add Aprepitant & Palonosetron; and (2) Confirmation that Pain Remains Unrelieved in Many Cancer Patients *Pages 64, 67*

Miami Breast Cancer Conference:

(1) New Devices, Techniques Improve Clean-Margin Rates; (2) Innovative Imaging Refines Surgical Staging; (3) MRI for Routine Evaluation of Axilla; (4) Correlating FDG-PET with Sentinel Node Biopsy *Pages 27, 57, 58*

Liver Cancer: NIH Conference Finds HCC Incidence & Mortality on the Upswing

Page 22

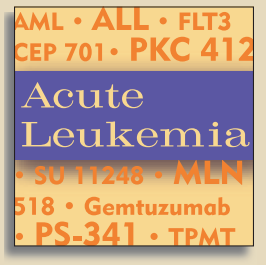


Improving Cervical Cancer Screening in Developing Countries

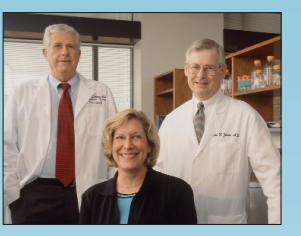
HPV vaccines and alternatives to cytology *Page 41*

Progress in Acute Leukemia: The Latest in Genetic Profiling

Page 49



DEPARTMENTS



HEMATOLOGY ONCOLOGY NEWS CENTER PHARMACY IN

HEMATOLOGY ONCOLOGY NEWS CENTER PHARMACY

Improving Cervical Cancer Screening in Developing Countries (Part 2)

Alternatives to Cytology, HPV Vaccines

By Heather Lindsey

Because of the limitations that many researchers associate with the Pap smear to screen cervical cancer patients in developing countries, various alternatives are being explored, including visual inspection techniques and human papillomavirus (HPV) screening.

Micol Salvetto, MSc: "If the money currently spent on piloting techniques of unproved efficiency were invested in the improvement of existing, traditional programs, the health of women of developing countries would stand to gain much more."

Both have clinical benefits and drawbacks, and researchers and patients must also contend with economic and public education challenges.

Visual Screening with Acetic Acid

The efficacy and practicality of visual-inspection screening are being evaluated using a 3% to 5% acetic acid solution on the cervix. The solution causes abnormal cervical cells to turn white, making it possible to obtain an immediate test result.

"You can say to a woman, 'You're fine—go home and don't worry,'" said Jacqueline Sherris, PhD, Strategic Program Leader of Reproductive Health at the Program for Appropriate Technology in Health (PATH) in Seattle. Or the health care provider can tell the patient she needs further evaluation. Telling her right away increases the likelihood of her returning in a week for therapy.

Even better, said Dr. Sherris, some programs treat women immediately with cryotherapy. While not perfect, visual inspection differentiates most of the individuals who have disease from those who don't, said Paul Blumenthal,

(continued on page 42)

2nd of 2 Parts

The first part of this two-part article, published in *OT*'s May 10 issue, examined the debate about the use of the Pap smear for developing countries.

HPV Vaccine: Early Data Promising

By Heather Lindsey

Preliminary study results for HPV vaccination are very promising, noted Jacqueline Sherris, PhD, a reproductive health specialist at PATH, the Program for Appropriate Technology in Health.

However, preventing cervical cancer in the developing world with an HPV vaccine will not replace screening and treatment, she cautioned. "It will be very difficult to get 100% coverage [with an HPV vaccine]."

Modeling studies indicate that HPV vaccines can provide about 30% to 40% reduction of incidence of cervical cancer, said Sylvia C. Robles, MD, MSc, Unit Chief of Noncommunicable Diseases for the Pan American Health Organization, who predicted that preventing cervical cancer will involve HPV vaccination in addition to screening programs.

And as Micol Salvetto, MSc, a Nicaragua-based health consultant for the Central American Health Institute, noted, because a number of HPV types exist, vaccines are likely to be type specific, which would limit their impact and make some form of screening still necessary.

At Least 10-20 Years

Paul Blumenthal, MD, Director of the Cervical Cancer Prevention Program at JHPIEGO, a not-for-profit international public health organization, said he doesn't anticipate the vaccine being widely distributed in developing countries for at least 10 to 20 years. And even if it was available tomorrow, health care providers still have a generation or more of women who have been exposed to the virus and need more traditional screening and care.

Vaccination also involves contending with logistical problems, Dr. Blumenthal noted: "Who are you going to vaccinate? Maybe you offer it in schools. Maybe you offer it when kids get polio shots—if they get polio shots."

Another problem, noted Eduardo L. Franco, MPH, DrPH, a cancer epidemiologist at McGill University, involves ministers of health, who may decide to put money into vaccines once they become available and decrease spending on screening.

Cost will definitely be a challenge for some developing countries, noted Rengaswamy Sankaranarayanan, MD, a staff scientist at the International Agency for Research on Cancer. For example, although a hepatitis B vaccine is available, many countries in Africa cannot afford to offer it to its population.

These countries will most likely not be able to afford an HPV vaccine. Despite these obstacles, researchers are encouraged by current HPV vaccines research.

Vaccines Furthest Along in Development

Some of the vaccines further along in development include the US NCI's monovalent HPV-16 virus-like particle (VLP) vaccine produced in insect cells using the recombinant baculovirus technology.

MedImmune and GlaxoSmithKline, have completed three Phase II trials using HPV-VLPs and a large 3,000 patient epidemiology study. Based on promising preliminary data, GlaxoSmithKline plans to initiate Phase III trials.

That company is also pursuing Phase II clinical trials focusing on the bivalent HPV-16/18 VLPs vaccine candidate, also based on baculovirus technology.

Merck is developing a quadrivalent vaccine using yeast-recombinant technology and based on VLPs from HPV-6, 11, 16, and 18, which is currently well into Phase III trials in the US, Europe, Southeast Asia, and South America.

Previous data demonstrate that the incidence of persistent HPV-16 infection and HPV-16-related cervical intraepithelial neoplasia was reduced in vaccinated women with a 100% efficacy rate over a 1.7-year follow-up period.

"Efforts and investments in research aimed at speeding up the development of a vaccine against HPV are paramount," Ms. Salvetto said. "The sooner we have this available, the better."

Cervical Ca Screening

continued from page 41

MD, Associate Professor of Gynecology and Obstetrics at Johns Hopkins University School of Medicine and Director of the Cervical Cancer Prevention Program at JHPIEGO, a not-for-profit international public health organization.

Additionally, the immediate treatment gets around the problem of the majority of women not undergoing further follow-up, said Sylvia Robles, MD, MSc, Unit Chief of Non-Communicable Diseases at the Pan American Health Organization (PAHO), part of the World Health Organization.

Some women may want to go home and talk to their families before receiving therapy, but they are more likely to come back knowing their diagnosis, Dr. Robles continued.

She related a recent experience she had in El Salvador where a 34-year-old woman with six children was screened with the acetic acid test and a lesion was found and was treated immediately with cryotherapy.

In photos provided by Rengaswamy Sankaranarayanan, MD, (top) he is shown training nurses in cervical cancer screening methods in Jaipur, Rajasthan State, India; and (bottom) health workers interview and invite women for screening in Barshi, Osmanabad District, Maharashtra State, India.

"She would have developed cancer," Dr. Robles said. "We haven't seen serious complications in the thousands and thousands of women we've treated so far."

In truly poor countries, people need some form of low-tech screening, said Eduardo L. Franco, MPH, DrPH, Professor of Epidemiology and Oncology Director in the Division of Cancer Epidemiology at McGill University.

Visual inspection seems to work in Peru, South Africa, and India, he said, adding that it's very efficacious when compared with the Pap test. The sensitivity of detecting high-grade lesions is at least equal to that of cytology, although the specificity may be lower.

In some of Thailand's provinces, JHPIEGO is beginning to implement the alternative approach of visual inspection plus the offer of treatment.

The program is in its initial stages and the start-up costs are high, noted Dr. Blumenthal, adding that $400 million can generally get a program up and running. Programs have to include the cost of human resources, transportation, and technology.

Visual Inspection Using Lugol's Iodine

Another visual test being evaluated involves the use of Lugol's iodine, which stains normal cervical cells brown, leaving abnormal areas a yellowish color. Studies indicate that sensitivity is at least as good as Pap screening, Dr. Sherris said, and as with the acetic acid test, the results can be seen immediately, enabling the patient to be treated with cryotherapy.

Visual inspection with iodine is now under investigation in India and Africa and appears to be working well, Dr. Robles noted.

Training for Visual Inspection

Overall, visual screening training does not take a long time, said Rengaswamy Sankaranarayanan, MD, a staff scientist for the Unit of Descriptive Epidemiology at the International Agency for Research on Cancer in Lyon, France. Dr. Sankaranarayanan has worked on cervical cancer screening research in India and Africa.

Nurses, health care workers, and midwives can generally be trained in one to two weeks. "But quality of training is very important," he noted. On a long-term basis, the performance of the workers has to be carefully monitored, and they need retraining for quality assurance.

Drawbacks of Visual Inspection

Others have problems with visual inspection, however. "Personally, I do

(continued on page 44)

On the Cover:

Illustration from **4Woman.gov**, the National Women's Health Information Center of the Department of Health and Human Services.

Cervical Ca Screening

continued from page 42

not have much faith in alternative methods such as visual inspection of the cervix," said Micol Salvetto, MSc, a consultant in Managua, Nicaragua, for the Central American Health Institute, a non-governmental organization with branches in Central America.

"Wherever I have seen countries experimenting with this technique—Peru was one of them—it has invariably translated to a huge amount of work and money invested in pilot programs, which have not yielded the desired results."

Ms. Salvetto acknowledges the advantage of having an immediate test result, which cytology does not provide, but said she is particularly concerned about nurses making diagnostic decisions: "They would have to make a diagnostic decision, for which I do not think they are qualified," she said.

Visual inspection also has a low specificity. If treated immediately without a biopsy, many women will receive cryotherapy unnecessarily.

"If these women are not part of a structured system and there is no chance of following them up, the effectiveness of the treatment may never be known," she said.

While the acetic acid test is an extremely inexpensive and attractive alternative that produces immediate results, it tends to overdiagnose quite significantly and therefore it is not a practical alternative, agreed Hennie Cronjé, MD, Professor in the Department of Obstetrics and Gynecology at the University of the Free State in Bloemfontein, South Africa.

If the specificity of the acetic acid test can be improved, it might be invaluable, he said.

Despite these drawbacks, local governments generally welcome these pilot programs for visual inspection but are unwilling to consider changing the existing system based on a Pap smear, Ms. Salvetto said.

However, neither the pilots nor the international literature have proven a definite advantage of visual inspection, she noted.

"If the money currently spent on piloting techniques of unproved efficiency were invested in the improvement of existing, traditional programs, the health of women in developing countries would greatly improve."

HPV Testing

HPV DNA testing is another area of screening that researchers are investigating for developing countries. Shunro Sonoda, MD, DMedSci., Professor Emeritus of Virology at Kagoshima University in Kagoshima, Japan, and his colleagues are introducing HPV molecular diagnosis with the Pap smear test in developing countries.

Fifty to 70 percent of cases with Grade II-III lesions on the Pap test are positive for HPV DNA, he said, and 80 to 90 percent of cervical cancers are associated with HPV infection.

Paul Blumenthal, MD: "While not perfect, visual inspection differentiates most of the individuals who have disease from those who don't."

HPV testing as a primary screening may be effective in women who are in their 30s, 40s, and 50s who have persistent infection, Dr. Sherri said.

A positive result strongly correlates with a precancerous lesion in this population, but younger women would not benefit from such screening, because about 90% have a transient HPV infection of mild dysplasia that will resolve spontaneously.

HPV is a relatively objective test with yes-or-no results that are accurate, while visual tests leave a lot of room for interpretation, Dr. Sherri explained.

The HPV test is sensitive, Dr. Franco said, and "if you don't have the virus, you are free of lesions."

The self-collection of vaginal samples is another area of interest, Dr. Sherris said. Women need to take a swab and insert it into their vagina, rotate it around several times, remove it, and put it in a collection bottle.

The strategy is easier to implement in some settings than in others. "It's not difficult, but women who are not used to tampons or other intravaginal

(continued on page 45)

POETRY BY CANCER CAREGIVERS

Poetry is a means of expression and source of comfort for many people who care for cancer patients. We welcome poems from oncologists, oncology nurses, oncology pharmacists, and other cancer caregivers. E-mail only, please, to OT@LWW.com

***Judy Garfield, RN, OCN**, a radiation oncology nurse at St. Joseph Hospital in Marshfield, Wisconsin, notes: "I wrote this one morning when I was very angry and disturbed at an MD's impatience with a new consult who was extremely hard of hearing. He was uncharacteristically acting like a child in front of the whole department and I thought we all needed a reminder of exactly what we were here for."*

A Life

By Judy Garfield, RN, OCN

His fragrance was that of
the Old Country.
His clothes stained from years
of honest toil,
but clean nonetheless.
His skin dry,
precancerous,
from countless, sun-baked days,
thickened
from this abuse and the
age-old habit of once-a-week baths.

His hearing,
impaired,
from whatever clamorous,
a-b-r-a-s-i-v-e
life-tasks that took their stealthy toll.

His speech that of innocence and simplicity;
His smile, that of a life lived in honesty,
before God.
His life,
worth the efforts of us all.

***Patricia Najamy, RN**, is an oncology staff nurse at Danbury Hospital in Danbury, Connecticut.*

You: The Survivor

By Patricia Najamy, RN

You are newly diagnosed
You have hardly time to think;
You are worried about your family
Is your life on the brink?
You need to hear the positive
The negatives have been told.
You have a lot of life to live,
You decide to be brave and bold.
You muster a good outlook
You receive all the treatment you need;
You feel you've survived
You're an inspiration to all and a Hero, Indeed!

Cervical Ca Screening

continued from page 44

devices are often uncomfortable with the self-test," she explained.

HPV Limitations

HPV testing's impact will be very limited in the short term, said Ms. Salvetto. "Even if it was possible to test for all the known high-risk HPV types, or the most prevalent ones in a country, there is no guarantee that this will result in an invasive lesion in that particular woman," she noted. This is also not a once in a lifetime test, unless it is used to dismiss older women from a screening program. Having a negative result does not mean that the patient can't acquire the virus in the future, she explained.

HPV testing is expensive and relies on highly specialized laboratory equipment and specific antibodies, which are rarely available in developing countries, she added. "Our own experience with PCR testing for HPV in Nicaragua was not encouraging," she said.

"I do not see how it could be of any benefit in screening programs, which are still struggling to cope with covering the cost of performing a Pap on all high-risk women."

Because of its cost, using the test in middle resource countries makes more sense than trying to use it in developing countries, said Dr. Franco.

Dr. Cronjé also acknowledges that the test is expensive. He believes that the development of a cheap on-site HPV test would be beneficial to women.

Continuing and Future Challenges

Regardless of what screening test researchers find works best for a specific population, still to be considered are the economic and public education issues.

Economics

For many governments cervical cancer is not a very high priority, Dr. Cronjé noted. Nutrition, AIDS, and tuberculosis are considered to be much more urgent, with the result that there is little money available for control of cervical cancer.

Making a direct cost comparison among the different cervical cancer screening tests is difficult because of the variations in different countries' infrastructures, health care systems, and human and technical resources.

Dr. Sankaranarayanan and his colleagues are evaluating conventional cytology, HPV, and acetic visual testing in a large randomized trial in India. Although results are not yet available, he noted that all the three methods are promising but have different economic implications.

Generally, visual screening methods require less of a financial investment than Pap screening, he said. However, countries that have already invested in cytology screening, such as Chile and Brazil, should make further investments to further improving their programs with internal and external quality controls, and the quality of Pap smear, evaluation, and reporting.

In other countries, such as those in Sub-Saharan Africa, implementing a cytology-based program is not practical because of costs, Dr. Sankaranarayanan noted. These countries may instead benefit from visual inspection. In India, for example, some states may be able to introduce cytology, while in others introducing visual tests may be more economically feasible.

Public Education

In addition to finding economic support for screening programs, both developing and industrialized countries need to have an understanding of the impact of cervical cancer on the global level.

"We in the United States and developed countries are used to not worrying about this disease," Dr. Sherris said. "We seldom know someone who has been impacted by it."

In contrast, more than 60,000 women in India die from cervical cancer each year, she said—women in their 30s and 40s, who have children and who have a role in their community.

In developing countries, health care programs need to encourage women to continue with their care if they have a positive test or don't feel well, Dr. Robles said.

Women must be told exactly why they need to go through the bother of doing an unpleasant test when they believe they are and possibly feel healthy, agreed Ms. Salvetto.

Cultural beliefs and preferences change between countries and among different communities in the same country, she added. An effective screening program should target its campaign accordingly.

Additionally, public education programs need to focus on any needed follow-up visits to health care providers and treatment options.

Partnership Crucial to Success

To help address the challenges inherent in cervical cancer screening, industrialized countries need to partner with scientists in developing countries to increase research capacity and to complement each others' strengths and weaknesses, said Sylvia C. Robles, MD, MSc, Unit Chief of Noncommunicable Diseases for the Pan American Health Organization.

"Scientists around the world can continue to work on looking for ways to test and treat women at lower costs and under difficult circumstances," concluded Micol Salvetto, MSc, a Nicaragua-based health consultant for the Central American Health Institute.