

DIRECTOR'S MESSAGE

JOHN S. KOVACH, MD



FOR ADVANCING CARE, CLINICAL TRIALS REMAIN IMPORTANT

Investigators at the Dana-Farber Cancer Institute in Boston recently reported in a prestigious medical journal, *The Lancet*, that, contrary to expectations, patients who enroll in clinical trials do not do any better than those who do not enroll. The lead author is quoted in *The New York Times* (1/23/04) as saying that he and his co-investigators undertook the study after "hearing prominent folks in the field...saying that being in a trial contributes to better outcomes."

Although the authors scoured the literature and found 24 usable reports involving a few thousand patients over several years, it is good to keep in mind that in the United States alone there are about 1,200,000 new cancer cases (excluding the most common and curable type of skin cancer) each year and only 5% or fewer enter clinical trials. The results of most clinical trials are published, but the results of the treatment of the 95+% of those who did not go on clinical trials are not reported and therefore not analyzable. Thus, the possibility that overall patients in clinical trials do "better" than those who are not in clinical trials is open to question.

Why belabor the point? Based on the findings, the authors recommend that patients should not be misled into participation in a clinical trial with the expectation of a better outcome for themselves. Fair enough. But when such a report hits the mainstream press with a headline in *The New York Times* of "Study Devalues a Popular Idea on Evaluating Medical Trials" a caution flag about clinical trials in general is raised in the eyes of the public – a result that is unwarranted and unnecessary and could well discourage patients from considering participation in studies.

Phase III Trials

The largest cancer trials are Phase III studies in which the best available therapy for a specific type of cancer at a specific stage is compared to another "investigational" treatment that has the

potential of greater benefit based on preliminary data from earlier non-comparative trials. Most Phase III studies are carried out by large collaborative groups consisting of the leading cancer centers in the United States and multidisciplinary cancer practices in which physicians take the extra time to explain the current standard treatments and expected benefits and alternative approaches to the standard that may be superior.

Because of the discipline intrinsic to the clinical trials process, including agreement by the most experienced physicians in the field on the treatments offered, there is good reason to believe that patients treated in clinical trials do better or at least have a good possibility of doing better overall by participating in these studies. And there is no question that a comparative clinical trial is the only method for establishing that a new treatment is more effective than the "community" standard.

There have been some clear successes with patient outcomes in clinical trials during the past 30 years, most notably vastly improved outcomes and cure rates for virtually all childhood cancers. There have also been positive results with comparative trials on particular cancers for adults. One example is the approach to treatment of rectal cancer by numerous institutions worldwide. Two large Phase III studies, one from Sweden and another from the Netherlands, revealed a significant reduction in the rate of local recurrence of rectal cancer after radiating rectal cancer before surgical resection (compared to radiation afterward). One of the studies indicated improvement in overall survival as well. Another major benefit of this treatment approach was that some patients did not have to have their entire rectum removed, thus sparing them colostomy for life.

The Long Island Cancer Center has made this improved approach the institutional standard. A summary of the LICC's approach to treating rectal cancer and the importance of clinical trials for this form of cancer is highlighted in this issue (page 3).

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HAPPENINGS

April 7 Breast Cancer Education & Support Group
Topic: "Blood Tests and Early Detection"
Holiday Inn Express, Stony Brook
7 PM to 9 PM
Speaker: John S. Kovach, MD,
LICC Director
Contact: Pat Cellini at 631-444-4605

Sponsored by the Carol M. Baldwin Breast Care Center, these lectures feature information on the diagnosis, treatment, and recovery from breast cancer, as well as other issues pertaining to the disease. The support group is for women and men who have already been diagnosed with breast cancer.

April 15 Oral Cancer Screenings
Stony Brook University
Dental Care Center
West Campus
9 AM to 6 PM
Contact: Dental Care Center
at 631-632-8989

The one-day event offers free and confidential screening for oral cancer, which has a high death rate if not detected early. Participants receive a comprehensive oral cancer examination that takes approximately 15 to 30 minutes. Information about how to identify oral cancer risk factors and symptoms will also be available.

April 30 – American Cancer Society's Relay for Life
May 1 Stony Brook University
Indoor Sports Complex
West Campus
6 PM to 7 AM
Contact: 1-800-ACS-2345 or
www.cancer.org/relayonline

Stony Brook University is hosting its 3rd annual Relay for Life, which raises money for the American Cancer Society. The overnight event is a walk-a-thon that involves teams of 8 to 10 people who walk the university track. Team members secure sponsor donations for their participation. The atmosphere is a festive one for participants, survivors, and other supporters of the Relay for Life.

May 1 The Witness Walk
Town of Babylon Annex
281 Phelps Lane, North Babylon
Starting Time: 9 AM
Contact: Peg Davis at Stony Brook
University (631-444-7789) or
Town of Babylon at (631-422-7642)

This is a fundraising event to foster awareness about breast cancer for women of color in Long Island communities. All women are invited to walk. The event is sponsored by the Witness Project® of Long Island and the Long Island Cancer Center at Stony Brook University, in collaboration with the Town of Babylon and many Long Island community organizations. The walk will honor those battling breast cancer and others who have died from the disease. Entertainment and refreshments will follow the walk.

May 5 Breast Cancer Education & Support Group
Topic: " 'Look Good, Feel Better' and Reconstruction"
Holiday Inn Express, Stony Brook
7 PM to 9 PM
Speaker: Balvantray P. Arora, MD

Lecture sponsored by the Carol M. Baldwin Breast Care Center. See a description of the public educational series under the entry for April 7 lecture.

NUTRITIONISTS ADDED TO CANCER SUPPORT STAFF

Two recently hired nutritionists, Linda Gilliard, RD, and Gretchen Garlow, RD, are counseling patients who have difficulty maintaining their weight during treatment or have other nutritional or eating problems. Their availability adds to the ancillary services provided by Long Island Cancer Center multi-disciplinary clinical programs.

Appointed by Stony Brook University Hospital's Nutrition Services, the registered dietitians discuss diet and nutritional issues with patients and direct them according to their health status and nutritional needs. Counseling includes information about symptom management (such as nausea and taste changes), tube feedings, diet education for specific surgeries, and diet and cancer prevention. Patients who wish to meet with one of the nutritionists are required to have a written referral from an attending physician. In the future, the nutritionists expect to run theme-oriented educational classes for patients, particularly about diet and cancer prevention.

News & Views

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\$300,000 FEDERAL GRANT EXPANDS LICC RESEARCH FUNDS SLATED FOR CREATION OF FROZEN TISSUE BANK

Congressman Tim Bishop, Dem., of the First Congressional District, helped secure a \$300,000 federal grant that will jumpstart a program to develop a pathology network among Stony Brook University Hospital (SBUH) and area community hospitals. He presented the grant to the Long Island Cancer Center (LICC) at SBUH in February. The funds will be used to begin creating a frozen tissue bank, an essential resource for the study of genetic alterations that lead to cancer.

A Long Island native, Congressman Bishop pushed the legislation that allots the funds for the LICC. He was pleased to present the grant to the LICC and mentioned that his mother was treated at SBUH for breast cancer more than 15 years ago and is in good health. The funds will specifically be used to purchase equipment such as special freezers, refrigerated microtomes.

The need for frozen tissue from surgery is important for current and future research. Normal and cancerous tissue removed during surgery is routinely placed in a solution that preserves the sample for microscopic study but not for long-term molecular study. Frozen tissue would allow for molecular analyses of gene and protein differences between normal and abnormal cells.

"An understanding of these differences will help sort out the role of environmental cancer causation, provide new means for early diagnosis, and reveal genetically based targets for develop-



Democratic Congressman Tim Bishop secured federal funds for the LICC to begin developing a frozen tissue bank that would allow researchers to analyze genetic damage that leads to cancer. Also present at the announcement was Shirley Strum Kenny, President, Stony Brook University.

ment of more effective treatments," says John S. Kovach, LICC Director. He says that the tissue bank is an essential component to creating a pathology network that would provide a regional sharing of information.

PATIENT OUTCOMES IN RECTAL CANCER CLINICAL TRIALS HOPEFUL LICC GASTROINTESTINAL TEAM CENTERS ON COMBINATION TREATMENT

More than 40,000 cases of rectal cancer occur in the United States each year, and if you combine that with cases of colon cancer, the total is nearly 150,000, making colorectal cancer the third most common form of cancer in the country. Therefore, advancing treatment for these forms of cancer would improve the lives of many Americans. Newer methods for treating rectal cancer have resulted from excellent results from clinical trials worldwide during the past five plus years. These results have shown reduced recurrence rates and better survival.

The Long Island Cancer Center's (LICC) multidisciplinary gastrointestinal cancer clinical team at Stony Brook University Hospital (SBUH) has analyzed these results and has incorporated treatments from these trials that appear to significantly improve outcomes in patients with rectal cancer.

"The number of rectal cancer patients being diagnosed and treated at SBUH is increasing and our gastrointestinal cancer team is routinely offering these treatment methods to patients," says Martin Karpeh, MD, Chief of Surgical Oncology. Patients are also being asked to enroll in various clinical trials for rectal cancer. These trials are aimed at improving the effect of radiation, chemotherapy and surgery in the management of this devastating disease. Dr. Karpeh says that by applying newer treatment strategies based on the results of well designed clinical trials, rectal cancer patients treated at the LICC will benefit from the worldwide treatment advancements to date.

Rectal cancers involving the lower third of the rectum are traditionally treated by surgical removal of the rectum and

anus, leaving the patient with a permanent ostomy "bag" or colostomy. The first new treatment approach used in the trials and incorporated at SBUH involves the use of combined radiation and chemotherapy before the patient has surgery. This appears to reduce the risk of disease recurrence. The second advance has to do with the way the operation is performed. Using sharp dissection, tumors are removed outside the investing layer of tissue of the rectum (mesorectum) without breaking it, thus lowering the risk of leaving cancer cells behind in the pelvis.

The 2003 recruitment of David Rivadeneira, MD, a specialist in colorectal surgery, from the Lahey Clinic Medical Center in Burlington, Mass, brings additional expertise needed for these operations. "He has the skills to perform rectal cancer surgery in this manner, and the use of less invasive laparoscopic techniques minimizes postoperative recovery without compromising the cancer operation," says Dr. Karpeh. An added advantage of this preoperative combination of radiation and chemotherapy is that the anal sphincter muscle can be spared, greatly reducing the chances of the patient having a permanent colostomy.

Dr. Karpeh says that SBUH's gastrointestinal cancer clinical team expects to continue participating in clinical trials that focus on the preoperative use of combination radiation and chemotherapy treatment to increase the amount of sphincter-sparing surgery for rectal cancers. Such trials may help to further reduce disease recurrence and improve survival rates for Long Islanders with these forms of cancer.

GENETIC COUNSELING PROGRAM ASSESSES INDIVIDUAL CANCER RISK

By Greg Filiano

Many people think that medical care based on genetics lies in the future when it is already here. Stony Brook University Hospital (SBUH) is attempting to change this perception with its Cancer Genetic Counseling Program. The SBUH program educates people on their potential genetic risks of developing cancer, provides individualized guidelines for cancer screening and risk-reduction, and facilitates genetic testing. Because medicine is now more firmly based on a molecular understanding of disease, genetic counseling has become more valuable.

Although anyone may request a consultation, individuals who are at a higher risk for a specific cancer based on a family history of disease should benefit most from the program. Genetic counseling has been available through SBUH for more than a decade. The current program is a joint venture by the Division of Medical Genetics, Department of Internal Medicine, and the Long Island Cancer Center.

The program expanded in 2003 by designating two additional cancer genetic counselors under the direction of David Tegay, DO, a clinical geneticist and recently appointed assistant professor in Internal Medicine and Pediatrics.

Genetic research has advanced medicine to the point where specific genetic defects are known to be associated with an increased risk of developing certain types of cancer. Genetic testing can identify some high-risk patients before cancer occurs.

Dr Tegay emphasizes that if a person is identified as being at high risk, it does not mean that a diagnosis of cancer is inevitable. In fact, many individuals in families at high risk will not develop cancer. Nonetheless, if an individual at SBUH's program is identified as having a genetic predisposition to cancer, that person is advised on what screening, risk reduction, or treatment options are available – information that can possibly reduce cancer risk or detect disease early.

Reasons for Referral

According to Dr Tegay, patient referrals from area physicians and oncologists are increasing. On average, three-to-five individuals per week come to SBUH to inquire about genetic predispositions that they may have for certain types of cancer. The

information gathered is used as the basis for informed decision making.

One of most common reasons for referral is for individuals with a personal or family history of breast or ovarian cancer. These individuals can be tested for variants in two genes, BRCA1 and BRCA2, which are implicated in inherited risks for both breast and ovarian cancer. In patients without a family history of breast or ovarian cancer, BRCA mutations are found in approximately 5% of individuals with breast cancer and 10%

of those with ovarian cancer. However, if a person has had other family members with either breast or ovarian cancer, then BRCA gene mutations are found more frequently.

Another common reason for referral is family history of one of the colorectal cancer syndromes, familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). Hundreds to thousands of

precancerous polyps develop in those who have FAP, and if untreated, those individuals will develop colon cancer. The diagnosis of FAP relies primarily on clinical findings, but the gene that causes FAP can be detected by molecular genetic testing.

"Many of the patients who come to see us on their own are suspicious that they may be at increased risk for cancers because of their family history, but they tend to either under- or overestimate their risk," says Dr Tegay.

Those who underestimate their risk include people who are aware that a certain mutation places them at risk for developing one form of cancer but are not aware it may place them at high risk for another. For example, an individual with a BRCA mutation is at risk for both breast and ovarian cancer, even if there is only a family history of breast cancer. Those who overestimate risk may not understand these mutations are usually inherited in an autosomal dominant manner, meaning that a person who has one affected parent has a 50/50 chance of also inheriting that genetic predisposition. If that individual does not inherit the predisposition, his/her risk for developing the form of cancer linked to that mutation may be no higher than someone in the general population, despite having a family history of the disease.

“Our hope is that people become more proactive in taking care of their health to improve outcomes, whether they develop cancer or not.”

*—David Tegay, DO, Director,
Cancer Genetic Counseling Program*

Procedure and Intervention

Cancer genetic counseling first entails constructing a detailed medical and family history. Then, there is a discussion about why it may be important to test for an inherited mutation that predisposes a person to the disease in question. After gaining sufficient knowledge about that mutation, individuals may choose to be tested for it or not. The analysis is done from a blood sample given at SBUH and sent to a certified molecular genetics laboratory for testing. When the results are known, the individual returns for a risk assessment profile. In developing the profile, a counselor takes into account the genetic results and previously documented information, such as the person's medical and surgical history, medication, and environmental exposures.

"Our hope is that people become more proactive in taking care of their health to improve outcomes, whether they develop cancer or not," says Dr Tegay. For those whose assessment places them at high risk, deciding on a course of action always involves a careful assessment of potential risks and benefits. "On one hand, an individual may not feel compelled to increase the frequency of his/her screening habits, or add risk reducing medications, or have surgery on the basis of risk. On the other hand, if there is a proven strategy that greatly reduces risk and is beneficial to a patient, the information is useful and potentially life-saving," he explains.

Risk-reducing therapy may involve certain medications. An example is the use of Tamoxifen® in women at an increased risk for breast cancer. Use of this medicine has decreased breast cancer rates, including for BRCA positive individuals. Some people with genetic abnormalities linked to a specific cancer are offered "prophylactic" surgery as a risk-reducing measure, such as removal of the ovaries or breasts of individuals with BRCA mutations. "These seemingly radical procedures can dramatically reduce rates of cancer for individuals at high risk for these cancers," says Dr Tegay. "But the hope remains that through continued research, improved risk-reducing medications and screening techniques, prophylactic surgery will become obsolete."

Cancer genetic counselors Jody Weiss, MS, left, and Gwen Goldstein, MS, display one of the Cancer Genetic Counseling Program's aid booklets about cancer genetics. Also pictured are David Tegay, DO, Program Director, and Lisa Debir, Secretary. Other cancer genetic counselors, not pictured, are Linda Buttice, MS; Jennifer Neil Partlow, MS; Kathleen O'Brian, MS, and Kinjal Shah, MS.



Research: An Important Component to Future Therapy

Investigations worldwide continue the search for mutations associated with cancers, but it is a long and painstaking process to translate findings from these into advances in patient care. Molecular genetic researchers at SBU are involved in numerous projects that attempt to connect genes and their products to specific cancers. Many of these involve animal models. The results of these investigations could help further knowledge of the genetic basis of cancer.

Scientists may never be able to predict the exact genetic risk for all cancers, and unraveling the interactions between the 30,000 human genes to solve this puzzle may never be complete. But medicine based on genetics is already proven to be valuable, and many researchers and clinicians agree that genetically based treatments will someday be the cornerstone of cancer therapy.

ADDITIONAL INFORMATION:

Cancer Genetic Counseling Program
Jody Weiss
Stony Brook University Hospital

Phone: 631-444-2790
Hours: M-F; 9:00 AM to 5:00 PM

CANCER GENETIC COUNSELING PROGRAM

FAST FACTS:

- Most common reasons for referral to program: family history of breast or ovarian cancer, or a colorectal cancer syndrome
- Counselors construct a detailed medical and family history for each case
- Counselors explain inherited predispositions for cancer
- Individuals choose to be tested or not
- Genetic testing requires a blood sample
- Counselors develop a risk-assessment profile based on test results
- Risk-reducing intervention may include use of surgery or medication

HUNDREDS ATTEND TOWN OF BABYLON'S "BREAST HEALTH AWARENESS" EVENT

"Breast Health Awareness," a public education event sponsored by the Witness Project® of Long Island, in collaboration with the Long Island Cancer Center (LICC) and the Town of Babylon, launched a day-long celebration at Babylon's Town Hall Annex commemorating Women's History Month. More than 300 attended the March 13 affair, titled "Celebrating Women – Celebrating Life." Approximately 200 attended the morning education program on breast health alone.

Because of the Witness Project's success as a community educational and inspirational program in which African American women discuss their triumphs against breast cancer, the event drew many women from the township and neighboring areas. Stony Brook University faculty Martin Karpeh, MD, John Kovach,

MD, Jedan Phillips, MD, Brian O'Hea, MD, and Elinor Schoenfeld, PhD, discussed causes of breast cancer, diagnosis and treatment, and disparities in health care. The attendees gained knowledge about the importance of breast health and how to be vigilant about breast cancer screening or treatment for the disease.

During the afternoon, the town recognized 14 local women for their community service achievements and presented Senator Hillary Rodham Clinton (D-NY) with the first Maxine S. Postal Humanitarian Award. The award is named after the late Long Island legislator who was committed to helping underserved communities regarding health, human rights and women's issues. A town spokesperson said that Senator Clinton's record made her a natural fit for the award.



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