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REPORT TO PHYSICIANS

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Pediatric Brain Tumor Studies Focus on Reducing Side Effects, Locating Biological Targets

by Dawn Chalaire

Balancing aggressive therapies that improve survival with efforts to decrease long-term side effects makes the treatment of brain tumors a major challenge in pediatric oncology, say physicians at The University of Texas M. D. Anderson Cancer Center.

Pediatric brain tumors are not a single disease but rather a heterogeneous collection of diseases with five-year survival rates that range anywhere from 10% to 95%. Many types of pediatric brain tumors are so rare that it often takes years to recruit enough patients to fill a clinical trial. Treating such a wide range of mostly dissimilar tumor subtypes requires mul-

(Continued on **next page***)*

Dr. Joann Ater, *chief of the Section of Pediatric Neural Tumors, shares a hug with*

at the Child and Adolescent Center.

Pediatric Brain Tumor Studies

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tiple approaches and cooperation between several different disciplines. While standard care for most types of pediatric brain tumors continues to be surgery, often followed by radiation therapy with or without chemotherapy, there is increasing emphasis on trying to minimize the long-term effects from these treatments.

"There are tumors that have a very poor prognosis that we are treating very aggressively, but in those in which the prognosis has improved, we are a lot more careful to balance the long-term effects," said Joann Ater, M.D., chief of the Section of Pediatric Neural Tumors at M. D. Anderson. "Acutely and long-term, we worry about intellectual and neurological deficits."

Patients younger than three years old are most likely to experience neuropsychological deficits because their tumors tend to be larger and more aggressive and because they are much more sensitive to the long-term effects of radiation therapy and chemotherapy, Dr. Ater said.

"Even those who go through surgery and initial treatment intact, if they are under age three, we know that radiation therapy can cause a significant drop in IQ over years," said Dr. Ater, referring to studies conducted by Donna Copeland, Ph.D., a professor in the Department of Pediatrics who documented the causes of intellectual deficits in young children.

Dr. Copeland's research led Dr. Ater to organize a protocol in which children less than three years old who have malignant brain tumors are treated with surgery and chemotherapy, but no radiation. The approach, Dr. Ater said, has been moderately successful, especially in patients with medulloblastoma, and there are long-term survivors who have never had radiation therapy—and therefore have no intellectual deficits resulting from radiation exposure.

This and similar protocols have stimulated several cooperative group trials through the Children's Cancer Group that are also aimed at trying to reduce the amount of radiation children are exposed to by replacing it with chemotherapy.

While these trials have yielded results comparable to standard treatments with radiation therapy in certain tumors, chemotherapy has not supplanted radiation therapy as standard care in the treatment of childhood brain tumors. Moreover, in recent years, new techniques in radiation therapy have led to the more precise treatment of pediatric brain tumors and better sparing of the developing brain than conventional radiation therapy allows.

The most important of these advances is three-dimensional conformal radiation therapy, which involves highly precise dose delivery to a target volume that is defined with radiographic imaging. It is not

PROTOCOLS

Pediatric Brain Tumor Clinical Trials

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following for pediatric patients with brain tumors.

- A phase II study of high-dose cyclophosphamide, triethylenethiophosphoramide (thiotepa), and melphalan with autologous blood stem cell transplantation for the treatment of high-risk **embryonal brain tumors** (ID98-032). *Physician: Ka Wah Chan, M.D.*

  Patients five to 50 years old with recurrent or high-risk embryonal brain tumors will receive two courses of high-dose chemotherapy, each with stem cell rescue.

- Phase I study of intrathecal mafosfamide (DM98-061). *Physician: Kurt Jaeckle, M.D.*

  Patients more than three years old with **meningeal malignancies** that are progressive or refractory to conventional therapy are eligible.

- A phase II study of methotrexate, folinic acid, mechlorethamine (nitrogen mustard), procarbazine, and prednisone (MMOPP) as primary therapy for **infants with brain tumors** (P88-006). *Physician: Joann Ater, M.D.*

  Infants and children four years old or younger with primitive neuroectodermal tumors and high-grade astrocytomas who have not had previous therapy (other than surgery) are eligible. Infants and children with low-grade astrocytomas or optic tract tumors that are incompletely resected and have a progressive course not amenable to further surgery may also be eligible.

- A group-wide pilot study of concurrent carboplatin, vincristine, and radiotherapy followed by adjuvant chemotherapy in patients with newly diagnosed high-risk **central nervous system embryonal tumors (PNET)** (CCG98-99701). *Physician: John Kuttesch, M.D., Ph.D.*

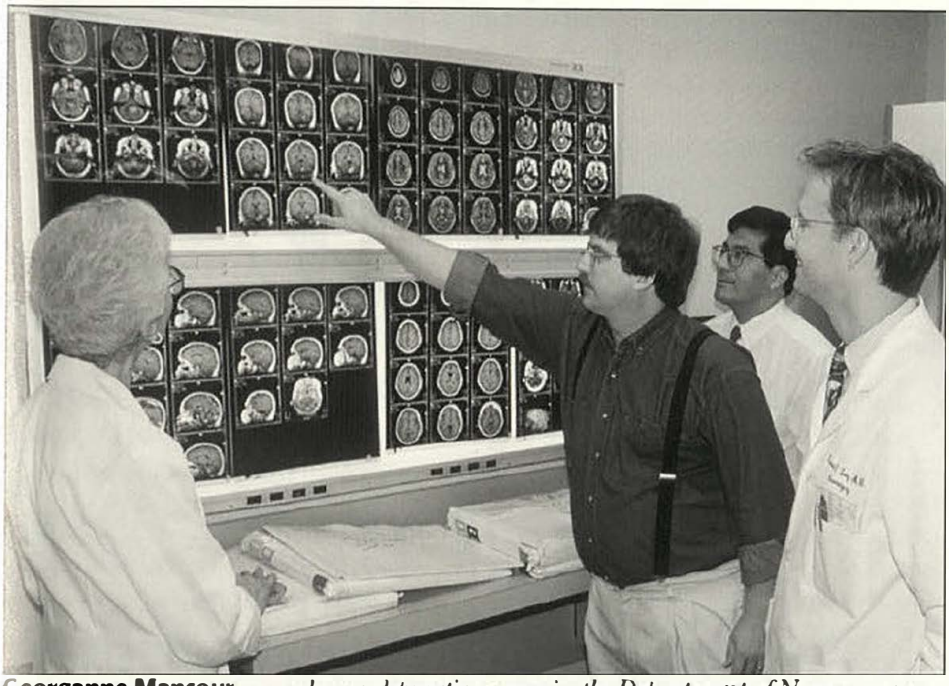
  Patients three to 22 years old with histologic verification of a PNET at diagnosis and no prior radiation therapy or chemotherapy are eligible.

- Phase II study of temodal (SCH 52365; temozolomide, IND #52797) in children and adolescents with **recurrent central nervous system (CNS) tumors** (CCG98A09701). *Physician: John Kuttesch, M.D., Ph.D.*

  Patients younger than 21 years old who have measurable disease or disease that has relapsed or become refractory to conventional therapy are eligible.

- Chemotherapy for progressive low-grade **astrocytoma** in children less than 10 years old (CCG97-9952). *Physician: Joann Ater, M.D.*

  Patients who have clear radiological or clinical evidence of progressive



Georganne Mansour, *an advanced practice nurse in the Department of Neurosurgery,* **Dr. John Kuttesch**, *assistant professor in the Department of Pediatrics, pediatric fellow* **Dr. Cesar Nunez**, *and* **Dr. Frederick Lang**, *assistant professor in the Department of Neurosurgery (left to right), discuss treatment options for a pediatric patient with a brain tumor.*

yet known how such treatments affect outcomes, but it is hoped that they will allow physicians to reduce the long-term toxicities that can be associated with radiation therapy, said Eric L. Chang, M.D., assistant professor in the Department of Radiation Oncology.

One approach to improve outcomes and limit side effects of therapy is the study of cytoprotective agents, in particular amifostine, used in combination with standard therapies. John Kuttesch, Ph.D., M.D., a neuro-oncologist and head of the Pediatric New Agents Program, leads a phase I trial of amifostine in children with recurrent solid tumors. Amifostine has already been shown to protect against renal toxicity of cisplatin in adult studies, and some data suggest that it may also protect against cisplatin-induced hearing loss. Its effectiveness as a bone marrow protectant is also being studied.

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PROTOCOLS

disease following resection or patients who had an incomplete resection are eligible to receive oral administration of carboplatin and vincristine at home through this study.

- A pediatric phase I study of intravenous dolastatin-10 (NSC 376128) in patients with **refractory solid tumors** (CCG98-09718). *Physician: Cynthia Herzog, M.D.*

  Patients 21 years old or younger with histologically verified malignancies that are refractory to conventional therapy and other therapies of higher priority are eligible. Adequate cardiac and pulmonary function are required.

- A phase II study of continuous 21-day infusion of topotecan (NSC 609699) in children with **relapsed solid tumors** (CCG99-09713). *Physician: John Kuttesch, M.D., Ph.D.*

  Patients with brain tumors, sarcomas, or neuroblastomas that have relapsed or become refractory to conventional therapy will receive topotecan on an outpatient basis.

- Phase II study of docetaxel (Taxotere) (NSC#628503) in children with **recurrent solid tumors** (CCG97-0962). *Physician: Cynthia Herzog, M.D.*

  Eligible for this protocol are patients age 21 and younger with clinically or radiographically documented measurable disease that has relapsed or become refractory to conventional therapy.

- A phase III prospective randomized study of craniospinal radiotherapy followed by one of two adjuvant chemotherapy regimens in children with newly diagnosed average-risk **medulloblastoma** (CCG97-A9961). *Physician: Joann Ater, M.D.*

  This protocol includes both inpatient and outpatient treatment of patients three to 21 years old with nondisseminated posterior fossa medulloblastoma.

- Phase II group-wide trial of pre-irradiation vincristine, cyclophosphamide, and etoposide chemotherapy for children aged three to 21 years with newly diagnosed **intracranial ependymoma** and radiologic evidence of postoperative residual tumor (CCG96-9942). *Physician: Joann Ater, M.D.*

  To be eligible for this study, patients must have histologically proven intracranial ependymoma that has not been previously treated with chemotherapy or radiation therapy. ●

FOR MORE INFORMATION *about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611; those in Houston or outside the United States should call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials web site at http://www.clinicaltrials.org for a broader listing of treatment research protocols.*

Pediatric Brain Tumor Studies

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According to the trial's co-investigator, Archie Bleyer, M.D., chairman of the Children's Cancer Group and professor in the Department of Pediatrics, if amifostine proves safe and effective in children, it would allow for multiple courses of intense chemotherapy to be given and result in decreased side effects.

While outcomes vary according to tumor type, most of the evidence suggests that gross total resection of pediatric brain tumors results in an increase in survival, said Frederick Lang, M.D., assistant professor in the Department of Neurosurgery. Because of this, neurosurgeons at M. D. Anderson have developed an aggressive surgical approach to pediatric brain tumors, including deep brain tumors such as focal brain stem gliomas.

Removal of focal brain stem tumors, Dr. Lang said, is made possible by frameless stereotactic surgery, intraoperative stimulation to identify critical structures in the brain stem, and the use of anesthesia techniques that allow the surgeons to identify brain stem structures that control breathing.

While studies and refinements of standard treatments continue, most researchers agree that any real breakthroughs in the treatment of pediatric brain tumors will come from a better understanding of the biology of these tumors.

"Our current treatments were identified empirically," said Dr. Kuttesch. "Major limitations in these therapies are that they are not 100% successful and are associated with side effects. In the past, we lacked the tools to study the biology of these tumors. With current technology, however, we can dissect the molecular biology of these malignancies; with this knowledge, we then may identify molecular factors that are different between patients who respond to therapy and those who don't. Of greater importance, these molecular factors are potential selective and specific therapeutic targets."

Several investigators at M. D. Anderson are currently studying the biology of pediatric brain tumors. Dr. Kuttesch's studies have recently begun to focus on expression of the bcl2 family—proteins involved in the regulation of apoptosis—in medulloblastoma.

"If we confirm our preliminary observations that the expression of these proteins is predictive of treatment outcome, it will give us a biologic target for development of novel treatment approaches," Dr. Kuttesch said.

Sadhan Majumder, Ph.D., assistant professor in the Department of Neuro-Oncology, has been studying the developmental biology of the central nervous system. His studies indicate that medulloblastoma cells arise mainly because of the abnormal arrest of neuroectodermal stem cells in their differentiation pathway, and the neural repressor REST/NRSF is a critical regulator in this process. Preliminary results suggest that blocking REST/NRSF activity in medulloblastoma cells triggers apoptosis and blocks the tumorigenic potential of these cells.

It is still too early to draw any definite conclusions from these laboratory studies, but Dr. Lang is applying earlier genetic research to the first U.S. trial of *p53* gene therapy in adult patients with malignant gliomas. In the phase I trial, adenovirus-mediated *p53* tumor suppressor genes are injected into the walls of the resected cavity within the brain. Depending on the outcome of this phase I trial, Dr. Lang plans to begin a similar study in children with malignant gliomas.

"Within this eclectic group of tumors, we have made progress in improving both survival rates and quality of life for patients," Dr. Kuttesch said. "In the future, we hope to further improve outcomes through identifying specific targets for the development of more selective therapies." •

For more information, *contact Dr. Ater at (713) 792-6665, Dr. Kuttesch at (713) 792-6559, or Dr. Lang at (713) 792-2400.*

Retinoid Chemo to Reverse Gene

by Kerry L. Wright

While quitting smoking at any age will improve overall health, many former smokers have made the unfortunate discovery that some of the molecular damage caused by tobacco use may be permanent, and the risk for developing cancer remains high even after years of not smoking.

A new chemopreventive agent being tested at The University of Texas M. D. Anderson Cancer Center, however, may take advantage of a window of opportunity in former smokers by reversing the damage and stopping the development of lung cancer before the traditional signs of cancer even begin to present themselves.

A team of four physicians led by Waun Ki Hong, M.D., chairman of the Department of Thoracic/Head and Neck Medical Oncology and head of M. D. Anderson's Lung Cancer Chemoprevention Program, is conducting a clinical trial to identify premalignant genetic changes in former smokers and to try to reverse them by short-term treatment with 9-*cis*-retinoic acid (9cRA), a new synthetic retinoid.

"Through this study, there is no question in my mind that we can identify some specific genetic changes in the bronchial epithelium, and we'll have an opportunity also to find out if the new agent can modulate these genetic changes. That is the crucial question," said Dr. Hong.

Dr. Hong thinks that differences in individuals' biologic responses to tobacco carcinogens may determine why lung cancer develops in some smokers and not in others. If these

prevention Trial Aims tic Changes Caused by Smoking

differences can be identified and manipulated, then perhaps thousands of cases of lung cancer can be prevented.

Retinoids, or vitamin A derivatives, act as ligands for retinoic acid receptors (RARs) and retinoid X receptors, which dimerize to form transcription factors responsible for the regulation of many genes. Retinoids are important in the maintenance of normal differentiation and proliferation of nearly all cell types, and their disruption may have severe consequences for a cell.

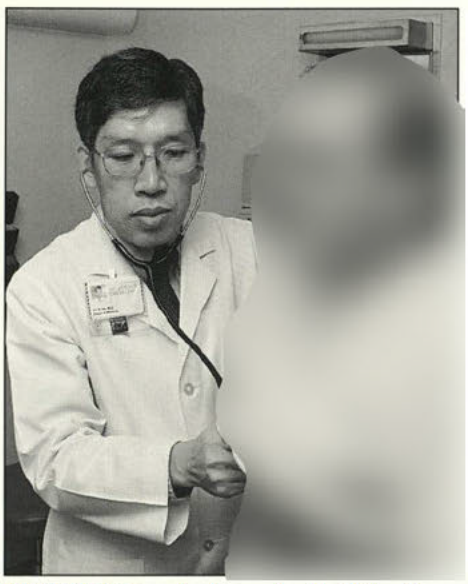
"One theory is that it is the absence of retinoids that can cause lung cancer or contribute to it, and maybe cells in smokers become either depleted or functionally depleted of vitamin A," said Jonathan M. Kurie, M.D., associate professor in the Department of Thoracic/Head and Neck Medical Oncology.

This depletion may cause the abnormal or premalignant cells to function improperly, but if vitamin A can be restored, function may be restored as well, said Dr. Kurie. However, many of the previous retinoid trials have yielded little evidence of this restoration.

"There have been some really big studies involving tens of thousands of patients both here in the United States and in other countries," said Dr. Kurie. "They have all involved active smokers and have included people with a very heavy smoking exposure and people who have had prior cancers. Those studies have been uniformly disappointing," he said.

Dr. Hong and his colleagues theorize that retinoids may not be strong enough to reregulate abnormal cells in the face of ongoing exposure to tobacco carcinogens.

The current trial at M. D. Anderson is a randomized, double-blind study comparing the effects of a placebo to treatment with either high-dose 9cRA or high-dose 13-*cis*-retinoic acid (13cRA) plus α-tocopherol (vitamin E) over a three-month period. It differs from previous studies in that it addresses a population of cancer-free former smokers rather than active smokers, it is the first test of 9cRA as a chemopreventive agent for lung cancer, and it is the first time that 13cRA and α-tocopherol, which may reduce the side effects of 13cRA, are being administered together.



Dr. Jin S. Lee, *a professor in the Department of Thoracic/Head and Neck Medical Oncology, examines in the thoracic clinic. Dr. Lee is one of four collaborators in a retinoid chemoprevention trial to prevent lung cancer in former smokers.*

Serial bronchoscopies are performed on each participant before treatment, at three months, and at six months to evaluate the presence and reversal o and dysplasia. studies sugges metaplasia ma best intermediate biomarkers for evaluating the efficacy of retinoids, according to Jin S. Lee, M.D., professor in the Department of Thoracic/Head and Neck Medical Oncology. Therefore, the current study also aims to identify novel and more useful endpoints.

"We are trying to find biomarkers that are really promising for future chemoprevention trials," said Dr. Lee. This will include identifying accurate, reliable markers of the early stages of cancer development that cannot necessarily be seen under a microscope.

To reach this goal, researchers are focusing molecular studies on expression of RAR-β, a receptor subtype that is downregulated in many lung cancers. Genetic analysis is also evaluating the presence or loss of several tumor suppressor genes and oncogenes and the loss of heterozygosity on regions of chromosomes 3p, 9p, and 17p, which are often affected in former smokers.

The trial has recruited approximately two thirds of the 225 patients needed for completion, and endpoint analysis has already begun.

"About 67% of those individuals who did not have bronchial metaplasia or dysplasia did have loss of heterozygosity at at least one of the three chromosomal sites we examined," said Fadlo Khuri, M.D., assistant professor in the Department of Thoracic/Head and Neck Medical Oncology. In other words, according to Dr. Khuri, tissue that looks histologically normal can still have underlying abnormalities.

Colleagues working on the clinical trial agree that although stopping smoking is important, it sometimes happens too late to prevent lung cancer. Of the more than 170,000 estimated cases of lung cancer that occurred in 1999, over 50% occurred in people who had already quit smoking. The question remains as to whether retinoids will be effective in preventing some of these cases.

As the current trial nears completion, additional retinoids are being developed and tested at M. D. Anderson and other centers across the country. According to Dr. Khuri,

(Continued on **page 6)**

Chemoprevention Studies Feature a Variety of Agents

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following that investigate the effectiveness of chemopreventive agents.

- A randomized, double-blind, chemoprevention trial of 13-*cis*-retinoic acid and α-tocopherol (vitamin E) vs. 9-*cis*-retinoic acid vs. placebo in former smokers (DM94-121). *Physician: Waun Ki Hong, M.D.*

  To be eligible, study participants must have had at least a 20 pack-year history of smoking before quitting at least 12 months before enrollment.

- Randomized chemoprevention trial with fenretinide (4-HPR) in superficial bladder cancer (ID95-236). *Physician: H. Barton Grossman, M.D.*

  Study participants must have either newly diagnosed or secondary solitary or multifocal superficial bladder transitional cell carcinoma.

- Phase III trial of low-dose 13-*cis*-retinoic acid to prevent second primary tumors in head and neck cancer (DM90-094). *Physician: Waun Ki Hong, M.D.*

  This trial is open to patients who have been free of disease for 16 weeks to three years after completion of surgery, radiation therapy, or both for histologically confirmed squamous cell carcinoma of the upper aerodigestive tract.

- A phase II chemoprevention trial of fenretinide (4-HPR) in retinoid-resistant oral premalignant lesions (ID95-088). *Physician: Scott Lippman, M.D.*

  To be eligible, patients must have measurable or evaluable oral premalignant lesions that [illegible]nt.

- Phase II study of eflornithine (DFMO) in patients with Barrett's esophagus with dysplasia (DM98-204). *Physician: Frank A. Sinicrope, M.D.*

  Patients 18 years of age and older with histologically confirmed or suspected Barrett's esophagus with any degree of mucosal dysplasia are eligible for treatment on an outpatient basis in this study.

- A phase II trial of fenretinide (4-HPR) and tamoxifen administered during the period between the diagnostic core biopsy and definitive surgery in patients with breast neoplasia (ID94-029). *Physician: S. Eva Singletary, M.D.*

  Patients who have had a mammogram that is highly suspicious for ductal carcinoma in situ or early invasive carcinoma with no definitive local therapy are eligible for this study.

- Study of tamoxifen and raloxifene (STAR) for the prevention of breast cancer (NSABP99-2). *Physician: Therese B. Bevers, M.D.*

  Postmenopausal women who are 35 years old or older and are at increased risk for developing breast cancer are eligible for this randomized study. Women are considered to be at increased risk if they have a personal history of lobular carcinoma in situ or an estimated five-year risk of developing invasive breast cancer ≥17% as established by the modified Gail model.

- A phase II chemoprevention study of calcium and aspirin in adults with previously resected adenomatous polyps of the colon (DM93-129). *Physician: Frank A. Sinicrope, M.D.*

  To be eligible for this study, participants must be 40 to 80 years old, and they must have had a premalignant, adenomatous colon polyp removed within the past five years.

- A phase II study of adenovirus ONYX-015 administered by mouthwash as a chemopreventive agent and for the treatment of oral dysplastic lesions (HNS99-140). *Physician: Vassiliki Papadimitrakopolou, M.D.*

  Patients 18 years or older with a clinical diagnosis of oral dysplasia, but no evidence of malignancy or open ulceration of the oral mucosa, are eligible for this study. ●

For more information *about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611; those in Houston or outside the United States should call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials web site at http://www.clinicaltrials.org for a broader listing of treatment research protocols.*

Retinoid Chemoprevention Trial

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many of these agents are being synthesized to have specificity for particular receptor subtypes and therefore have more selective effects.

"I think as we become more sophisticated at synthesizing retinoids, we can not only select for the potential effects of a subclass of receptors but also against certain toxicities, or certain side effect profiles," said Dr. Khuri. Some of these retinoids will not only have receptor specificity but will also be able to induce apoptosis in specific types of cancer cells.

No matter what new retinoids are synthesized, how and when they are administered, or who receives them during clinical trials, they are all being used to achieve the same goal. Research scientists and clinicians hope to be able to identify genetic changes that occur in the early stages of cancer and either reverse those changes or remove altered cells before the cancer has time to develop.

"We want to take a genetically altered cell before it is a cancer cell and get rid of it—induce apoptosis and allow the genetically altered cell to die," said Dr. Hong. "That is the exciting part of the work." ●

For more information, *contact Dr. Hong, Dr. Kurie, Dr. Lee, or Dr. Khuri at (713) 792-6363.*

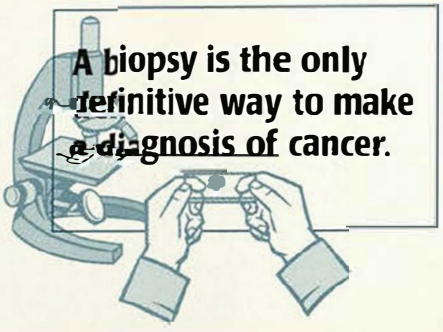
HOUSE·CALL

From Biopsy to Diagnosis: Understanding the Process

It is never easy to hear that you or someone you love may have cancer, and the thought of undergoing a biopsy to confirm a preliminary diagnosis can be frightening. Knowing what to expect from the biopsy process and being familiar with the types of biopsies commonly used for diagnosis, however, can ease some of your worries and make the procedure less stressful.

What is a biopsy?

A biopsy is the removal and examination of a tissue sample from an area of suspected cancer. Physical examinations and laboratory tests can show if abnormalities are present in your body, but a biopsy is the only definitive way to make a diagnosis of cancer. The decision as to what type of biopsy is performed depends on the location of a tumor, as well as its type, size, and growth characteristics.



Types of biopsies

Core needle biopsy uses a large needle that is inserted into the tumor to withdraw cells for examination. A local anesthetic is usually administered at the insertion site. This method is often used for masses located in muscle or just under the skin, such as in the breast.

Fine needle aspiration (FNA) is a more common type of needle biopsy. In FNA, a needle no wider than a normal injection needle is inserted into the tumor, and tumor cells are aspirated (removed from the tumor) into a syringe for examination. No anesthesia is necessary, and diagnosis can be made within hours.

Endoscopic biopsy utilizes a thin flexible tube with a light or camera on one end (endoscope). The endoscope is inserted through an incision or natural opening, and forceps, a brush, or a needle attached to a cable within the endoscope are used to snip off, brush off, or aspirate tissue from a tumor. Depending on the endoscope insertion site, local anesthesia or a sedative is sometimes used.

Incisional biopsy involves surgical incision and removal of a larger segment of a tumor. It is often the biopsy of choice for extremely large masses and is most commonly used to remove sections of soft tissue tumors (in muscle, fat, and connective tissues).

Excisional biopsy involves complete removal of a tumor or organ. Excisional biopsies are best suited for removal of very small tumors (such as skin tumors), or for situations where removal of the entire organ is necessary. Excisional and incisional biopsies are often performed with local or regional anesthesia; however, tumors inside the chest or abdomen require the use of general anesthesia.

Because needle biopsy removes individual cells, and may not effectively demonstrate how cancer cells relate to each other, incisional or excisional biopsy may be required even when needle biopsy is simpler and less painful.

Examination and diagnosis

After a tissue sample is removed, it is taken to a laboratory and examined by a pathologist (a doctor who studies cells and tissues to identify disease). Pathologists place tiny layers of tumor cells onto small glass slides and stain them with chemicals that distinguish different parts of the cells. They cover each slide with a very thin pane of glass to protect the sample, and view the processed tissue under a microscope.

Pathologists then write detailed reports of their observations and conclusions, and a report and diagnosis are given to the patient's oncologist. Information obtained from a biopsy includes whether the tumor is benign (noncancerous) or malignant (cancerous), what type of cancer may be present, and how the tumor may affect the patient's health.

Will a biopsy cause cancer to spread?

In almost all cases, a biopsy will not cause cancer to spread. The majority of cancers are safely sampled with a needle or incisional biopsy. For rare exceptions, experienced doctors troubleshoot beforehand and can perform follow-up operations to remove more of the cancer if necessary. Though patients may feel physically worse after biopsy or surgery, it does not mean their cancer has spread. It is normal to feel this way after any invasive procedure. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

(800) 392-1611 *within the United States, or*

(713) 792-6161 *in Houston and outside the United States.*

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Surviving Cancer and Staying Healthy

Rena Sellin, M.D.
Professor, Department of Internal Medicine Specialties

As we begin a new century, I am heartened by the knowledge that an increasing number of cancer survivors are living beyond their disease and enjoying a full life after cancer treatment. Once the risk of recurrence has become sufficiently low, cancer survivors can usually be treated by their primary care physicians. Treating cancer survivors, however, requires careful evaluation, regular surveillance, and no small measure of discernment. Certain symptoms may reflect health problems that are related to earlier cancer treatments or may be early signs of cancer recurrence, while other symptoms may stem from causes unrelated to cancer.

There are unique and long-lasting side effects associated with cancer treatments. Surgery may cause physical limitations or swelling from blockage of lymphatic drainage. Chemotherapy may damage the testes or ovaries, causing premature menopause in women and delayed or abnormal puberty in children; other drugs may make the heart or the lungs more susceptible to abnormalities. Radiotherapy may create abnormalities in the normal tissues or endocrine glands that are included in the radiation field. When a combination of treatments is used, the side effects may be compounded.

Some side effects occur during or soon after cancer treatment. Other side effects may not become apparent until the cancer survivor becomes older or develops additional medical conditions. The effects of radiotherapy on normal tissues develop slowly, and clinical symptoms may not be appreciated for many years after treatment.

Some cancer survivors will never develop the specific, treatment-related problems outlined above, but their treatment choices for more common health problems may be limited (for example, a breast cancer survivor who needs to avoid estrogen replacement at the time of menopause).

A regular (even if infrequent) cancer-specific evaluation is helpful for at least 10 years after treatment and, preferably, for the rest of the cancer survivor's life. Services such as the Life After Cancer Care medical clinic at M. D. Anderson offer cancer survivors access to experienced specialists who can anticipate and treat their special problems. Effective interventions, including medical management, physical therapy, or even corrective surgery, are available to treat most cancer therapy-related complications; the earlier a problem is uncovered, the more effective the therapy.

The effects of cancer and its treatments can make staying healthy a challenge, but advanced treatments and increased vigilance are helping cancer survivors meet that challenge.

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