

1991

## Oncolog, Volume 36, Issue 02, April-June 1991

Gilbert H. Fletcher M.D.

*The University of Texas MD Anderson Cancer Center*

James M. Bowen

*The University of Texas MD Anderson Cancer Center*

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### Recommended Citation

Fletcher, Gilbert H. M.D. and Bowen, James M., "Oncolog, Volume 36, Issue 02, April-June 1991" (1991).  
*OncoLog MD Anderson's Report to Physicians*. 36.  
<https://openworks.mdanderson.org/oncolog/36>

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# MD Anderson Oncolog

*A new study reassesses the belief that pregnant women with breast cancer cannot receive chemotherapy.*

## **Redefining the risks of chemotherapy during pregnancy**

When breast cancer is discovered during a pregnancy, the moment can be truly poignant for both physician and patient. The fearful mother has many questions: Will the baby suffer from chemotherapy? If the treatment is delayed, will her cancer recur? Will she live long enough to see her baby grow up? Should she terminate her pregnancy? Or is her husband prepared to be a single father?

Twenty-five years ago, obstetricians and oncologists were likely to recommend that a woman terminate her pregnancy so that the standard treatment involving mastectomy, radiation, or chemotherapy could begin. Even today, many physicians are still reluctant to give the necessary treatment to pregnant women, said Richard Theriault, D.O., an assistant professor of medicine in the Department of Medical Oncology at The University of Texas M. D. Anderson Cancer Center. Much of this reluctance is due to the lack of data on the effects that some regimens have on fetal development. As part of the M. D. Anderson Cancer Center's breast medical oncology team, Theriault and other physicians are often called upon to advise physicians around the country on treatment of these patients. "I can describe the regimen that we would follow, but there are no real data to back it up," said Theriault.

Recognizing this need, he and Frankie Holmes, M.D., who is also an assistant professor of medicine and another member of the breast medical oncology team, launched a study two years ago to assess the long-term effects of chemotherapy on both the mother and the baby. Thus far, 12 pregnant patients with breast cancer have been entered. All received standard doses of 5-fluorouracil, doxorubicin, and cyclophosphamide every three to four weeks. Of the eight mothers who have given birth, all have had normal deliveries, and all babies have reached normal developmental milestones. "We're excited that we've been able to give patients effective treatment

that didn't apparently affect the babies' health and, with proper timing and scheduling of treatment, did not increase the risks associated with delivery," said Theriault.

### **Numerous diagnostic, treatment options available for pregnant women**

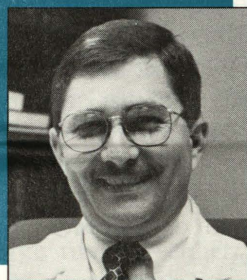
For pregnant women who have breast cancer, there are certain accepted diagnostic and treatment options available at every stage of pregnancy, Holmes and Theriault concurred.

As with nonpregnant patients, the majority will first discover a lump in the breast. Diagnosis, however, is often delayed; mammograms are difficult to interpret in pregnant women because of the increased density of breast tissue. Therefore, pregnant patients often have more advanced disease than other women might.

Theriault and Holmes advise that, once diagnosis has been made, a complete history and detailed physical examination be done, with attention to the presence of bone pain, neurologic defects, and hepatic size to determine pathologic staging. Laboratory tests to detect liver or renal dysfunction or hematologic abnormalities can be performed with no risk to the mother or fetus. A standard chest radiograph poses little risk in early pregnancy if proper shielding is used.

Ultrasound of the liver and kidneys can define anatomic structure and organ position in relation to the uterus and will detect the position of the uterus in relation to any metastases. If indicated, radiographs for bone pain and computed tomographic brain scans for neurologic dysfunction may be conducted safely, said Theriault. Most x-ray procedures result in fetal radiation doses of less than 5 cGy. There has been little or no reported increase in incidence of congenital malformations, growth retardation, or fetal death caused

### **Treatment Update**



Richard Theriault is an assistant professor of medicine in the Department of Medical Oncology

## “The mother walked in for her appointment, wearing her wig and carrying her little fuzzy-headed baby”

by use of nuclear medicine, he said, but advised that such procedures should be used only when their outcome will influence treatment-related decisions. “The need to know must be sufficient to justify the risk of radiation exposure and, of course, the fetus should be shielded whenever possible.”

Therapy for the primary tumor should be considered in light of clinical staging and anticipated outcome. The options include surgery, chemotherapy, and, in extremely advanced cases, termination of pregnancy.

With modern anesthetic techniques, surgery is quite safe, said Theriault. If tumors are known to be surgically resectable and there are no known metastases, a modified radical mastectomy with axillary node sampling can be recommended. Only 1% of mastectomies result in spontaneous abortion; when compared with the benefits of disease control and information to be gained from histologic analysis, the surgery is well advised. However, lumpectomy with local radiation “remains an investigational therapy in pregnant patients,” he added. It is generally not recommended because of lack of data on radiation’s effects on the fetus. Radiation therapy is widely considered to be harmful to the fetus during any stage of pregnancy.

### Pregnancy does not alter disease progression

Termination of pregnancy as an option is recommended in cases of advanced disease, when very aggressive treatment is needed to save the mother. At that juncture, the patient and husband must decide whose life they wish to save. “We generally choose to treat the mother, unless that is not the parents’ desire,” said Theriault. Some physicians recommend termination because the elevated hormone levels associated with pregnancy might stimulate tumor growth. Theriault has found extensive documentation to the contrary. “The pregnancy itself does not alter the course of breast disease, and termination of pregnancy will not improve a patient’s chances of survival or cure,” he said.

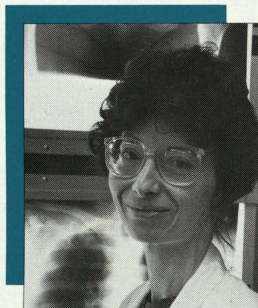
Because the effects of chemotherapy on the fetus and mother remain undocumented, fetal development during each stage of pregnancy has become a

critical factor in determining whether chemotherapy is advised.

Treatment options are few during the early months of pregnancy. Mastectomy is very appropriate and very safe, but chemotherapy is not advised. “The first trimester is very tender. We try to avoid chemotherapy during this time because fetal organs are developing,” said Theriault. “Major fetal damage can occur; the risks are just too high.” For women with stage I or II disease, chemotherapy can be delayed up to 12 weeks without affecting the mother’s prognosis, research has shown. However, their advice is different for patients with advanced-stage disease or inflammatory breast cancer, a rapidly progressive disease. The aggressive chemotherapy necessary to save the mother may threaten the fetus’ life or development. Even that effort may be futile, since the advanced stages of disease offer slim chances that the mother will survive. A choice often must be made between keeping the mother alive long enough to give birth or aggressively trying to save the mother only.

When early-stage breast cancer is discovered during the second trimester, the patient should have a mastectomy with adjuvant chemotherapy, as appropriate. By that time, the major fetal organs have been formed and the risk of major fetal malformation is significantly reduced. “It appears that chemotherapy is very safe in the second and third trimesters; babies may have low birth weight but all have been normal and healthy,” said Theriault. Chemotherapy might cause miscarriage because it reduces white cell counts, but that risk is small and can be avoided by properly timing the last dose so that white cell counts are high enough at birth. Patients with advanced disease may need to consider termination of pregnancy to allow for more aggressive treatments.

By the third trimester, the risks of chemotherapy to both mother and fetus have decreased significantly. The fetus is nearly fully developed, and standard chemotherapy regimens can be safely administered either before or after mastectomy. Patients with advanced disease may be advised to have labor induced so that aggressive treatments can begin.



Frankie Holmes is an assistant professor of medicine in the Department of Medical Oncology

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The overall cure rate for human cancer now approaches 50%. Surgery and radiotherapy, alone or in combination, still account for the majority of cures. Radiotherapy, the first nonsurgical cancer treatment, remains one of the most fertile areas for research and application in cancer treatment.

Dr. Gilbert H. Fletcher is uniquely qualified to write on the evolution of modern radiotherapy. Leader of the team that designed, built, and used the first American cobalt-60 radiation therapy delivery unit, he pioneered research in radiotherapy and radiobiology. He has trained a generation of radiation therapists, physicists, and radiobiologists. Dr. Fletcher led the radiotherapy program at The University of Texas M. D. Anderson Cancer Center from its

creation in 1947 until his partial retirement in 1981, when he gave up administrative duties to return once again to teaching, writing, research, and patient care.

Dr. Fletcher is a highly respected and much honored international leader in radiation oncology and a great observer of both science and philosophy. He is a significant player in both the history and future of modern radiotherapy. In this article, he traces the growth of radiotherapeutic theory and application, highlighting some of the important events in the development of our current approaches to successful cancer treatment.

—James M. Bowen, Ph.D., Professor of Virology, Vice President for Academic Affairs

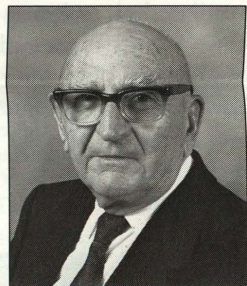
## Significance of cancer volume in radiotherapy

By Gilbert H. Fletcher, M.D.

During the first half of the century, irradiation was tried in all tumors. Small squamous cell carcinomas of the oral cavity and of the uterine cervix were successfully treated by brachytherapy. Cancers of the skin could be cured by external irradiation, and lymphomas could also to some extent be controlled by irradiation. These tumors were considered "radiosensitive." On the other hand, large tumors—either squamous cell carcinoma, adenocarcinoma of the breast, the malignant tumors of the salivary glands, or soft tissue sarcoma—when irradiated, showed very limited, if any, response.

At mid-century, the practice of radiotherapy and its place in the management of the cancer patient was based on three rigid concepts: First, there was an "all or none cancerocidal dose," irrespective of the cancer volume. In world-famous institutions like the Christie Hospital in Manchester, United Kingdom, the same dose was given to all lesions. Second, a homogeneous radiation dose had to be given to the whole target volume. And third, the surgical procedure had to be radical and was called a "cancerwise procedure."

Because of the lack of skin sparing of kilovoltage radiation, skin sequelae were severe. Neither the combination of irradiation and surgery nor the use of large-volume irradiation, such as elective irradiation of clinically uninvolved lymphatic areas, could be done freely.



Gilbert H. Fletcher, clinical professor of radiotherapy, Department of Clinical Radiotherapy

In the 1950s, cobalt-60 units, million-volt generators, linear accelerators, and betatrons were made available for clinical use. A cobalt-60 unit was developed at The University of Texas M. D. Anderson Cancer Center (then called the The

University of Texas M. D. Anderson Hospital and Tumor Institute) in cooperation with the Oak Ridge Institute of Nuclear Studies, one of the Atomic Energy Commission institutes devoted to the peaceful use of atomic energy. Because of the skin sparing of these megavoltage beams, it was possible to give higher doses to deep-seated tumors and to use irradiation freely for elective treatment of clinically uninvolved lymphatic areas and postoperatively after removal of gross cancer to treat residual disease.

In the ensuing years, several analyses were made of the results obtained with megavoltage irradiation used either as primary treatment for the tumors, as elective irradiation of potentially involved lymphatic areas, or in association with surgical procedures.

### Relationship between cancer volume and tumor-controlling dose

The analyses showed that, if there is no gross disease in areas accessible to inspection and palpation, lesser doses of irradiation (e.g., 50 Gy) were adequate to eradicate occult disease, i.e., subclinical disease. As the tumor size increases, higher doses were necessary to obtain significant control rates. Irradiation is most effective in controlling microscopic disease. Conversely, surgery is effective,

### Special Series



**“At mid-century, the practice of radiotherapy and its place in the management of the cancer patient was based on three rigid concepts”**

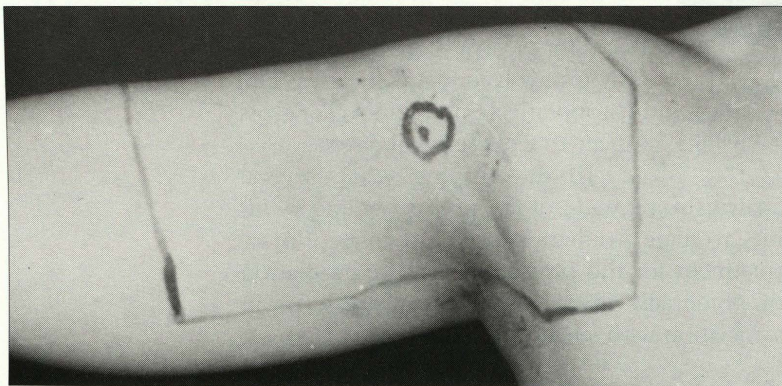
provided the tumor is resectable, in removing gross cancer but too often fails to remove, irrespective of how radical the procedure is, the diffuse microscopic disease around the gross mass. Therefore, the two modalities can often be used in a complementary mode: surgery to remove gross cancer and pre- or postoperative irradiation to eradicate microscopic disease around the gross mass. As an important corollary, the classical radical surgical procedures, such as radical neck dissection or radical mastectomy, need not be performed. The surgical goal should be to remove only gross disease. It was also found that the combined treatment could be more effective than the radical surgical procedure. Conservative surgical procedures combined with modest doses of irradiation may leave the organs less mutilated, thereby affording a better quality of life.

These concepts have revolutionized the practice of surgery and radiotherapy in many clinical situations, even in tumors previously thought to be radioresistant. For example, the sacrifice of the facial nerve had been part of the surgical procedure

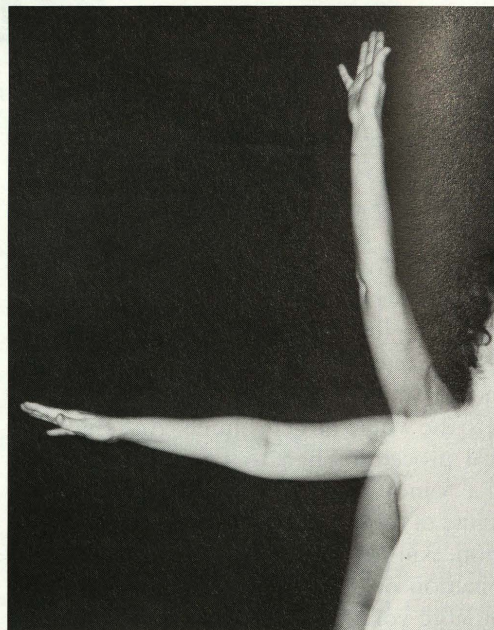
to resect highly malignant tumors of the parotid, since the facial nerve runs through the superficial lobe of the parotid gland. With postoperative irradiation, however, one can preserve the facial nerve. Similarly, with small-volume breast cancers, which are detected more and more by mammography, tumor excision followed by irradiation yields control rates comparable to those of radical mastectomy. The cosmetic results are usually excellent.

The treatment of soft-tissue sarcomas at the M. D. Anderson Cancer Center has been, since the 1960s, excision of gross disease, whenever possible, followed by postoperative irradiation. Preoperative irradiation has been used in unresectable tumors. Results have shown control rates superior to the ones obtained by the most radical operations. Furthermore, it is a limb-saving procedure. ■

Physicians who desire additional information may write Gilbert H. Fletcher, M.D., Department of Clinical Radiotherapy, Box 97, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 792-3445.



The beneficial effects of the complementary use of conservative surgery with radiation. A 40-year-old woman presented with pain in the right arm on motion. A 2x4-cm subcutaneous mass just anterior to the head of the humerus (above) was excised on November 17, 1972. The mass was diagnosed as high-grade fibrosarcoma. She received postoperative irradiation. In 1976, the patient had excellent arm function (right). In 1986, the patient was disease free and still had excellent arm function. Reprinted with permission from Fletcher GH, *Textbook of Radiotherapy*, 3rd ed., Philadelphia: Lea & Febiger, 1980, p. 925.



## Pancreatic Cancer

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been devascularized, and (3) implantation and dissemination of tumor cells during laparotomy may be prevented by preoperative chemoradiation, thus reducing the risk of disease recurrence in the peritoneum.

"Preoperative chemoradiation is also an important stress test," Evans said. "If the patient cannot withstand chemoradiation, it is certain he would not withstand major surgery."

Preliminary data from 10 patients who underwent surgery after chemoradiation suggest that the concern over tissue integrity is not a significant contraindication to preoperative radiation. A small pancreatic leak occurred in one patient, and the leak resolved spontaneously. Based on these data, Evans and his colleagues (Tyvin Rich, M.D., Department of Clinical Radiotherapy, Jaffer Ajani, M.D., Department of Medical Oncology, and John Hoffman, M.D., from the Fox Chase Cancer Center) hope to initiate a multi-institutional Radiotherapy Oncology Group (RTOG) study, which will also evaluate a second component of the protocol, intraoperative radiotherapy.

The rationale behind intraoperative radiotherapy is to improve local tumor control by irradiating the tumor bed or residual tumor while sparing surrounding tissue. Studies at the Mayo Clinic and the Massachusetts General Hospital suggest that such treatments can reduce the rate of recurrence at the primary tumor site. The therapy is well tolerated and improves pain control. Under the direction of Rich, the M. D. Anderson Cancer Center was the first institution in the United States to develop a dedicated intraoperative radiotherapy suite in a central operating room. Linear accelerators have also been installed in operating rooms at the Mayo Clinic and in several hospitals in Germany. This set-up reduces treatment time for two reasons: (1) the linear accelerator, as opposed to conventional orthovoltage irradiation devices, can deliver a higher dose in a shorter time, and (2) the patient does not have to be moved from surgery to the radiation therapy department. Total treatment time, including instrument set-up and delivery of intraoperative radiation, averages 30-45 minutes.

"Another advantage is our laser-guided 'docking' system, which was developed by Dr. Rich, Mr. Tim Ochrans, and Siemens Medical Laboratories," Evans said. Using lasers, the treatment cone can be aligned with the radiation field without

touching the patient, thus providing the safest treatment possible.

In light of surgery's ineffectiveness, changing treatment protocols seems a logical step, but doing so addresses only the purely medical issue of cure. It does not, in itself, address what Evans feels is a stifling sense of hopelessness that surrounds pancreatic cancer, a hopelessness that perhaps has been engendered by the medical community's tacit acceptance of the disease's fatality and by the low volume of patients.

For Evans, these two factors are mutually reinforcing and tend to deteriorate, though subtly, the momentum of research. Health-care providers like to help as many patients as possible, but because of the lack of effective treatment for pancreatic cancer, many patients are sent to their local hospital for palliative care. As a result, no center has a consistent patient volume. The sporadic patient becomes, then, an anomaly. "If you see only one case every two or three months, it is very difficult to energize people to work toward a goal," Evans said.

His solution was to develop an organized approach to pancreatic cancer treatment, one based on a new protocol, driven by consistent patient volume, and supported by every member of the treatment team.

Two key departments in this approach are Diagnostic Imaging and Pathology. "We work very closely with Dr. Chuslip Charnsangavej in Diagnostic Imaging. Since he understands our treatment approach and objectives, he can complete a diagnostic workup rapidly and efficiently."

Another key member is Ruth Katz, M.D., a cytologist in the Department of Pathology. Using high-resolution thin-cut computed tomography (CT), Katz, working with Charnsangavej, will perform a transabdominal fine-needle aspiration, if indicated. "The result of this close teamwork is a much faster diagnosis. The patient can come in on Wednesday, have a diagnosis by Friday, and begin treatment on Monday," Evans said.

Such collaboration is not limited to the clinic. Evans works closely with two pathologists, Karen Cleary, M.D., and John Connelly, M.D., who rigorously classify all tumor specimens. "To assess treatment, it is essential to have a complete pathology report," Evans said. "Cleary and Connelly ensure that all pertinent criteria are evaluated and recorded. All pancreatic cancer is not the same. Tumor size, degree of differentiation, the presence of vascular, lymphatic, or perineural invasion, and careful assessment of all margins are

Intraoperative radiotherapy unit, operating table, and treatment cone. After chemoradiation, pancreatic cancer patients undergoing the new M. D. Anderson protocol receive intraoperative radiotherapy at this facility, the first of its kind in the United States.



analyzed for every tumor specimen.” Evans is also collaborating with basic scientists Marsha Frazier, Ph.D., and David Byrd, M.D.

“This is perhaps the most exciting area,” Evans said. Frazier and Byrd are looking at fundamental basic science issues. For example, one crucial hindrance to past studies of pancreatic cancer has been a lack of experimental models. Frazier is attempting to develop a transgenic mouse model for pancreatic duct cell cancer, since most human tumors are ductal in origin. The transgenic animals will be genetically programmed to develop pancreatic duct cell tumors at a fairly precise time point in the animal’s life. Because of the reproducibility of the model, it will be useful in studying the early events in tumor development and should therefore provide important information regarding the prevention and early detection of the disease. Frazier is also trying to identify gene markers of pancreatic cancer that would allow earlier detection. Considering that many patients present with advanced disease, such a marker would be an important step toward improving survival.

Byrd has begun a comprehensive tumor bank of primary and metastatic pancreatic tumor specimens. Some fresh specimens are frozen for future DNA, RNA, and immunohistochemical analysis. Other specimens are cultured and used to inoculate athymic mice, the intent being to develop an in vivo model of liver metastasis and peritoneal carcinomatosis. In in vitro studies, Byrd is also testing immunotherapeutic approaches and studying stromal/pancreatic tumor cell interaction.

Such basic research efforts are essential, but there is also another side that Evans believes is just as important. It is very easy to reduce patients to statistics, to gauge a treatment solely based on numbers, to think of progress only in terms of long-term survival. That temptation is especially powerful when caring for pancreatic cancer patients, who have so few treatment options. But such advances can be pyrrhic unless weighed against the treatment’s effect on quality of life. (Evans intends to gauge each patient’s emotional response during the experimental chemoradiation/intraoperative radiotherapy protocol using a quality-of-life study.)

For Evans, every member of the health-care team should be concerned about quality of life, but especially important to him are such ancillary services staff as social workers and dietitians. “Two people who are crucial to this effort are social worker Judy Weil, M.S.W., and dietitian Dana Martin, R.D., C.N.S.D. Both Weil and Martin have a specific interest in pancreatic cancer; they know what these patients are facing and are familiar with their needs. It is very important for patients to know that their caregivers understand their disease,” Evans said.

Such patients certainly need hope, and that is one thing Evans hopes the new protocol will instill, but some patients facing a terminal disease also need to know that something is being done, that they are not going to die without a fight, and that there are health-care providers who are genuinely and actively trying to cure their disease.

We should not underestimate the psychological benefit of such a treatment environment, one based on an active pursuit of cure rather than a tacit acceptance of death. “Patients come here upset; they’re pessimistic; they’ve been told that nothing can be done for them,” Evans said. “But they find that we’re interested in their disease, that we have an organization designed to treat them. They know they may die, but they also know that they are being seen by people who come to work each day to treat pancreatic cancer, and that the knowledge gained from the experimental treatment they receive now may ultimately benefit someone else later.”

In the 1950s and 1960s, any pediatrician treating leukemia was faced with the same challenge: Before attempting to find a cure, one first had to overcome the pervasive pessimism against such an attempt. But with action, hope, and small successes, the promise of cure was finally achieved for a large percentage of patients. Whether Evans’ and his colleagues’ commitment to action will

have the same result is still in question, but without it, pancreatic cancer will certainly remain an incurable disease. ■

Physicians who desire additional information may write Douglas B. Evans, M.D., Department of General Surgery, Box 106, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 794-4324.

## Chemotherapy during pregnancy

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### Normal deliveries, normal babies after treatment

Holmes has seen four patients in the last year give birth to normal babies. Of these, two cases represent typical decisions that these women must make.

One mother in her late 30s was in the middle of her second trimester when breast cancer was diagnosed. Her chemotherapy extended from the end of that trimester until three weeks before her estimated due date. Holmes had developed this schedule so that she would give birth when her white cell count was normal. The baby was born on schedule, and "it was a perfectly normal delivery," said Holmes. Both mother and baby are fine.

Not all mothers are so lucky. A 28-year-old woman came to Holmes when she was 18 weeks pregnant, and she had to learn the hard truth that the breast cancer she thought she had overcome two years earlier had recurred. "Other doctors had advised abortion because she was a high-risk case. She wanted my opinion," said Holmes. "It was obvious that she would not live a normal life expectancy, and she had to decide whether she wanted to fight the cancer with aggressive treatment or whether she wanted the baby. She decided she wanted this baby." The patient was given chemotherapy and the tumor disappeared, so the treatment ended about six weeks before her delivery. "She did well until after the delivery," said Holmes. At that time the patient was given the anti-hormone drug tamoxifen, a treatment that cannot be given during pregnancy because it interrupts the sequence of hormones necessary to maintain the placenta and uterus. She later developed a recurrence in the liver. The patient almost died in October and "is living from day to day," said Holmes. Her baby, however, is healthy.

While chemotherapy can be safe for both mother and fetus during the second and third trimesters, it does have certain short-term side effects beyond the normal nausea and hair loss. Some mothers are distressed to find that they are unable to nurse their babies. Chemotherapy prevents normal breast development that allows milk production after delivery.

The long-term side effects remain to be determined; although chemotherapy has been available in aggressive combinations since 1974, it has not been used as widely as it is now, said Holmes. "We don't have 25 years of experience in monitoring its effects on the growing fetus. At least in the short-term, there don't seem to be any differences in fetus growth and development."

### Chromosome status and physical/cognitive milestones to be tracked

Questions remain. Are the chromosomes of these babies more susceptible to damage by environmental carcinogens? "There's a question of fragility, because they've already been exposed to one type of injury," said Holmes. Do the children reach their normal milestones within the appropriate ages? Would their prognosis be different if the mother had been nearing the end of her child-bearing years, when chromosomal damage is a higher risk?

Holmes and Theriault said that the babies they have seen were born normally and are developing normally. "It's a good sign," said Holmes. They plan to follow all the babies through their childhood and adolescence, conducting chromosome studies and monitoring achievement of physical and cognitive goals. *New patients and their babies will be added to the study when they are seen by the breast medical oncology group.*

For Holmes, the hope increases with every patient who gives birth to a baby with hair. "All our patients are bald because of the doxorubicin, but the babies are born with lots of hair," she said. "So obviously the doxorubicin doesn't cross the placenta in sufficient amounts to cause the baby to be bald." She recalls her first experience with this phenomenon. "The mother walked in for her appointment, wearing her wig and carrying her little fuzzy-headed baby. Obviously pleased that her baby had suffered no ill effects from the drugs, she just kept rubbing that baby's head," Holmes concluded, with a satisfied smile. ■

Physicians who desire additional information may write Frankie Holmes, M.D., or Richard Theriault, D.O., Department of Medical Oncology, Box 95, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 792-2817.



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The University of Texas  
M. D. Anderson Cancer Center

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Published quarterly by the  
Department of Scientific  
Publications, Division of Academic  
Affairs, The University of Texas  
M. D. Anderson Cancer Center,  
1515 Holcombe Boulevard,  
Houston, Texas 77030.

Made possible by a gift from  
the late Mrs. Harry C. Wiess  
and by grants from The University  
Cancer Foundation.



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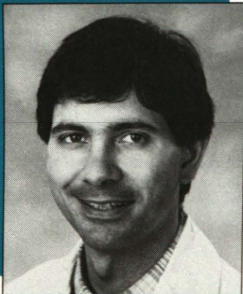
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## ***Renewing the assault on pancreatic cancer***

### **Treatment Update**



Douglas B. Evans is chief of the Pancreatic Tumor Section in the Department of General Surgery

All cancer patients must come to grips with fear, but those with pancreatic cancer also face frustration. Treatment options are few and ineffective. Surgery confers a slight long-term survival advantage, but only 10–20% of patients are eligible, and the operation is extensive, requiring 8–10 weeks of recuperation. The presumption that “nothing can be done,” that they must await death rather than attempt cure, is something that pancreatic cancer patients are often asked to accept.

Douglas B. Evans, M.D., a surgeon in the Department of General Surgery at The University of Texas M. D. Anderson Cancer Center, is familiar with the pessimism, but his response is not resignation, but action. As chief of the Pancreatic Tumor Section, he is developing a team of radiologists, cytologists, surgeons, medical oncologists, radiotherapists, pathologists, basic scientists, nurses, social workers, and dietitians for a renewed assault on pancreatic cancer.

“A few years ago, no questions were being asked, no ongoing protocols being studied.” In an effort to counter the hopelessness that had per-

vaded the medical community, “we made a commitment to develop an organized approach to pancreatic cancer,” Evans said.

A key component of this strategy is a new protocol: preoperative chemotherapy and external-beam radiotherapy (chemoradiation) followed by resection and intraoperative radiotherapy. “Surgery alone is inadequate,” Evans said. “We’re convinced that potentially curative treatment will be multimodal.”

But first, several questions surrounding the timing and efficacy of adjuvant chemotherapy and radiation must be resolved. For many patients, the stress of surgery precludes postoperative therapy. An obvious alternative is to give the treatment first. “But some clinicians feel that if you give radiotherapy first, the tissues would fall apart during surgery,” Evans said.

If this concern proves misplaced, however, then there are compelling reasons for preoperative chemoradiation: (1) an unresectable tumor may be downstaged to a resectable size, (2) radiation therapy is more effective in tissues that have not