Conference Report: Gynecologic Cancer Outcome Improves Because of New Treatment Applications

by Ralph S. Freedman, M.D., Ph.D.
Associate Professor and Director of Research, Department of Gynecology

The 29th Annual Clinical Conference of the U.T. M. D. Anderson Hospital and Tumor Institute last November was devoted to reviewing progress in the treatment and diagnosis of gynecologic cancers.

Speakers from the Houston cancer center were joined by clinicians and researchers from universities and hospitals in the United States and Canada. Many noted significant improvements in the administration of conventional therapies, accompanied by an increase in survival rates generally and a decrease in treatment-related deaths from several types of cancer. The papers given at the conference are scheduled to be published later this year by the University of Texas Press; here I will concentrate on some of the discussions led by MDAH colleagues.

Heath Lecture on Exenteration Experience

Felix N. Rutledge, M.D., professor and head, Department of Gynecology, gave the Heath Memorial Lecture in which he reviewed the UT MDAH experience with pelvic exenteration in gynecologic cancer treatment. This operation, in which either bladder or rectum or both are removed together with the vagina and portions of the vulva, is the most radical surgical procedure employed by gynecologic oncologists. It is used only when less severe therapies have failed or are predicted to fail. The operation is used mainly but not exclusively for treating recurrent uterine cervical cancer, and it is rarely recommended until after irradiation has been tried. The recent literature indicates a decline in the number of exenterations performed, yet the incidence at UT MDAH has remained constant, for reasons that are not clear, Rutledge said.

He reported on 448 patients who underwent this procedure here between 1955 and 1984, noting significant reductions in postoperative mortality, more long-term survivors, and improved restoration of patients' sexual function. Postoperative mortality declined from 13.5% among the 296 earlier (1955-1976) patients to 3.9% of the 152 later (1977-1984) patients, and 53% of the patients survived five years or longer. New techniques for preoperative identification of metastases and more precise criteria for choosing patients who will benefit from exenteration have reduced the incidence of incomplete resections.

The current method of vaginal reconstruction seems to be successful. Myocutaneous grafts taken from a segment of gracilis muscle, an island of skin, and subcutaneous tissue from the medial thigh serve several purposes: vaginal restoration, perineal support, cosmetic normalcy, and faster healing of the perineal defect.

Rutledge's conclusion was that pelvic exenteration is successful as a salvage treatment, especially when the five-year survival rate is compared with that of patients undergoing primary surgical treatment for cancer at other body sites.

Radical Compared with Conservative Surgery

Radical surgery for gynecologic cancer was discussed also by Creighton L. Edwards, M.D., professor and holder of the Ann Rife Cox Chair in Gynecology. Radical vulvectomy and bilateral groin lymphadenectomy, with or without pelvic lymphadenectomy, is the traditional treatment for carcinoma of the vulva, he said. Radical surgical intervention early in the disease does not, however, protect against local recurrence and may produce high postoperative morbidity.

In contrast, Edwards said, conservative surgical techniques such as wide local excision or hemivulvectomy and ipsilateral groin dissection do not increase the recurrence risk, and they are associated with shorter hospital stays, fewer wound breakdowns and infections, less chronic leg edema, and fewer psychosocial consequences. Moreover, the corrected survival figures for patients with stages I and II squamous carcinoma of the vulva treated with standard radical methods, compared with survival rates of patients treated by conservative surgical methods, are not statistically different.

Edwards suggested that if the vulva is otherwise normal, wide local excision is appropriate treatment for the primary lesion continued on page 2
regardless of depth of invasion. If there is stromal invasion of more than 1 mm and the lesion is unilateral, only an ipsilateral groin lymphadenectomy is necessary. If test results of the ipsilateral nodes are positive, dissection or irradiation of the contralateral nodes may be appropriate.

**Epithelial Ovarian Cancer**

In a minisymposium on treatment for epithelial ovarian cancer, J. Taylor Wharton, M.D., deputy head, Department of Gynecology, reported that long-term remissions are most likely in patients who have only minimal residual disease in the abdomen after initial surgery. An analysis of patients with stage III disease showed that the most favorable results occurred in patients whose lesions were 2 cm or smaller when therapy began. If these patients' tumors can be reduced further with chemotherapy, additional therapy such as irradiation of the entire abdomen or intraperitoneal injections of biological response modifiers—for example, viral oncolysates—may be considered.

David M. Gershenson, M.D., associate professor, Department of Gynecology, whose primary interest is the chemotherapy of epithelial tumors, germ cell tumors, and stromal tumors of ovarian origin, reviewed the status of chemotherapy for advanced epithelial ovarian cancer.

Combination chemotherapy seems to be superior to single-agent therapy, cisplatin-containing regimens being the ones most widely used. Preliminary information suggests that two-drug combinations may be as effective as three- and four-drug regimens. Second-line therapy for patients with refractory ovarian cancer continues to have poor results, he said.

**Second-Look Laparotomy**

Larry J. Copeland, M.D., associate professor, Department of Gynecology, reviewed the UT MDAH experience with second-look laparotomy, a procedure that is usually performed between six and 12 months after the initial surgery for ovarian cancer. Current treatment programs leave 50% to 60% of patients who had advanced disease clinically free of cancer. Second-look laparotomy has shown about 30% of these patients to have no evidence of disease, about 20% to have persistent tumor that is identified only microscopically, and about 50% to have macroscopically identifiable tumor. The five-year survival rate of patients whose second-look laparotomy produces negative or microscopic positive findings is about 70%, compared with 10% to 15% of patients who have macroscopic positive findings.

When well-differentiated lesions are excluded from analysis, however, the recurrence rate is about 50% for patients with either negative or microscopic positive second-look findings. Copeland expressed the hope that innovations in therapy would sustain or complete the tumor response in this patient group. For patients with macroscopic tumor at second-look laparotomy the prognosis is dismal, and the value of debulking persistent tumors has not been proved.

**Gynecologic Cancer Research**

Ovarian cancer, today the major cause of gynecologic cancer-related deaths, is the focus of intensive clinical and laboratory research. I described my group's trials with intraperitoneal injection of new immunotherapeutic agents in patients with advanced ovarian cancer. In collaboration with James M. Bowen, Ph.D., professor of virology and vice president for academic affairs, we developed an immunogenic "vaccine" of viral oncolysates, which are extracts of cultured ovarian carcinoma cells whose antigenicity is altered by the incorporation of a harmless virus before the cells are disrupted.

When we tested these extracts in 40 patients whose advanced ovarian cancer had not responded to conventional therapy, nine patients responded, including seven in whom malignant ascites disappeared and two in whom the tumor masses decreased.
Counseling, Practical Advice Help Women with Cervical Cancer Resume Sexual Activity

Patients can be as sexually active after treatment for cervical cancer as they were before the illness was diagnosed, but many are unable to do so without counseling and practical advice, according to Leslie R. Schover, Ph.D., assistant professor of urology (psychology) and assistant clinical psychologist at UT MDAH.

Sexual counseling for these patients "needs to be a routine part of patient care. All women should be screened for sexual problems because perhaps one woman in 10 is willing to ask a physician for help," she said.

Preliminary results of a study done here by Schover and colleagues Michael Fife, M.S.W., and David M. Gershenson, M.D., show that women who receive counseling along with cancer therapy have the same rate of sexual activity and sexual satisfaction they had before the disease was diagnosed. These results are in contrast to those from studies of patients elsewhere who had no counseling and whose rates of sexual dysfunction and marital dissolution increased dramatically after cancer treatment. So far, the MDAH study has included 51 women.

As Schover explained, "I like to see the patients when they are just beginning their cancer treatment. That's the best time, at least for preventive counseling, because I can alleviate their anxieties before their relationships become affected and make sure that they have the information they need to stay sexually active during treatment and afterward."

Since Schover is the sole sex therapist on the hospital staff, however, she can counsel only a small percentage of the women treated here annually for gynecologic cancer.

"I get to know the woman and her background and history, how she feels about the cancer, how much the illness affects her daily life, how much family support she has, and how her children are being cared for during the cancer treatment," Schover said.

She asks about "all those different things that affect the woman's ability to cope, as well as her sexual history—whether she has had difficulties in the past with low sexual desire, for example, or painful intercourse, or not being able to reach orgasm."

Schover spends at least a couple of hours in one or two sessions with the patient, and when possible she likes to meet with both members of a couple. Her semistructured interviews include the use of formal questionnaires—for example, the Brief Symptom Inventory, a measure of psychological distress, and a multiple-choice questionnaire on sexuality.

Don't assume that if the patient doesn't ask, she doesn't have a problem.

Education and Advice

"To allay common fears," she said, "I counsel the woman on the causes of cervical cancer and the fact that the disease is not contagious. Resuming her sex life won't cause cancer to recur. We give the patient some ideas on how to resume sex comfortably. We let her know that she should still be able to reach orgasm, and that the cancer treatment should not impair her ability to feel pleasure." Women undergoing radiotherapy are told about lubricants to use for vaginal dryness and about comfortable use of the vaginal dilators they may need.

"Couples may have to try new types of caressing or positions for intercourse," Schover said. She sometimes recommends general self-help books, for example, For Yourself and For Each Other by Lonnie Barbach (Anchor Press, 1974 and 1982) or Becoming Orgasmic by Julia R. Heiman, Leslie LoPiccolo, and Joseph LoPiccolo (Prentice-Hall, 1976).

Using three-dimensional models, she shows patients the parts of the body involved in sexual activity and their function both before and after cancer treatment.

Resume Normal Sex Life? Yes.

When patients ask if they can have a normal sex life after their treatment for gynecologic cancer, Schover says emphatically, "Yes, you can." She explains that the patient may experience some mild discomfort and some symptoms from the cancer treatment. If the patient has had a hysterectomy, for example, her vagina may feel shorter at first, and if she has had radiotherapy, she may, in rare instances, have problems with radiation ulcers. The majority of patients who have undergone radiotherapy will experience less lubrication during intercourse. The vagina will not be able to expand as much as previously, so it may feel dry or tight.

"That's why vaginal dilation and frequent intercourse are important during the healing period after radiation therapy, along with using adequate lubricants for intercourse. Even women who have had a total pelvic exenteration and a neovagina created with myocutaneous gracilis flaps can resume intercourse if they want to," she explained.

An important topic often overlooked in counseling cancer continued on page 5
These results are comparable to those of intraperitoneal administration of Corynebacterium parvum and interferon reported by others, and the toxicity of viral oncolysates seems to be less than expected.

In a related report, Eva Lotzová, Ph.D., professor of immunology and chief of the Section of Immunogenetics, Department of General Surgery, described her research with natural killer (NK) cells, which are large granular lymphocytes considered important in the defense against various types of cancer. She demonstrated that ovarian cancer patients have low NK cell antitumor potential in peripheral blood and virtually no cytoxicity in peritoneal fluid. Her investigations have opened new avenues to correcting NK cell defects in these patients.

Intraperitoneal injections of viral oncolysates into ovarian cancer patients resulted in 60% to 80% tumor cell lysis and caused sustained potentiation, for seven to 21 days, of NK cell antitumor activity in the patients' peritoneal fluids. Viral oncolysate-induced NK cell activity reflected both the increase in the number of NK cells and augmentation of these cells' lytic activity. Along with regional augmentation of NK cells came regression of malignant ascites. Viral oncolysates administered intraperitoneally were not always effective in augmenting peripheral blood NK activity; Lotzová reported, however, that peripheral blood NK activity could be stimulated in culture with interleukin-2 (IL-2) within three to seven days.

Regional augmentation of NK cells was accompanied by regression of ascites.

Because of these promising results, patients who have persistent but relatively small-volume disease at second-look laparotomy will now be eligible to receive intraperitoneal immunotherapy with viral oncolysates. In addition, Lotzová and I have begun working on a new clinical protocol that involves treatment with intraperitoneal oncolysates in combination with adoptive transfer of IL-2-activated autologous NK cells.

Endometrial Cancer

In his report on treatment of endometrial cancer, Luis Delclos, M.D., professor of radiotherapy, said that, beginning in 1969, 58 patients with minimal disease and well-differentiated tumors (stage IA, grade 1) were treated with one intracavitary radium insertion followed by an extrafascial hysterectomy at the same admission. The results at three years were encouraging, and in 1978 it was decided to simplify treatment for all patients with stage IA, grade 2, and stage IB, grade 1, disease.

Delclos showed data on 53 patients with stage IA, grade 2, and stage IB, grade 1, endometrial cancer who had responded favorably to treatment with either one radium insertion and hysterectomy at the same admission or with two radium insertions three weeks apart and hysterectomy six weeks later. The results were comparable—100% and 90% five-year and longer survivals for grade 1 and grade 2 patients, respectively—and therefore the single-radium technique has become the technique of choice. Only one patient in the group experienced a vaginal cancer recurrence.

The second group of 37 patients, who had grade 3 (stage IA plus IB) and grade 2 (stage IB) tumors, were treated with two radium insertions three weeks apart and hysterectomy six weeks later or with external irradiation (4,000 rad/4 weeks) plus one radium insertion followed by hysterectomy. Results were the same for both groups; 50% of the patients died because of progressive disease.

Combined Therapies for Pelvic Tumors

Joseph S. Kong, M.D., assistant professor of radiotherapy, reported on a new study to examine the role of combined hyperthermia and irradiation in patients with advanced pelvic cancer. Four of six patients with metastatic gynecologic cancers achieved a complete tumor response for 10 to 52 weeks after treatment with radiation and ultrasound or magnetic induction heating. A pilot study of the effectiveness of interstitial hyperthermia and irradiation for deep pelvic tumors began this year.

Of the four patients with recurrent cervical carcinoma treated so far for palliation, two achieved complete pain relief, one for two and the other for six months.

Tumor Markers

Herbert A. Fritsche, Ph.D., professor of clinical chemistry, Department of Laboratory Medicine, discussed an array of new tumor markers being evaluated for diagnosing ovarian and uterine cancer. New immunoassay test procedures employing monoclonal antibodies are being developed for alpha-fetoprotein and human chorionic gonadotrophin (HCG) to improve the tests' specificity. The tests are needed to establish the clinical
The Thirty-ninth Annual Symposium on Fundamental Cancer Research, Critical Molecular Determinants in Carcinogenesis, will be chaired by Frederick F. Becker, M.D., vice president for research, and Thomas J. Slaga, Ph.D., director of the Science Park-Research Division of the UT System Cancer Center. Following is Becker's prospective view of the conference:

The enormous advances recently attained in the areas of molecular and cellular biology make it possible to analyze the complex process of carcinogenesis for critical molecular determinants. Carcinogenesis is the sequential induction of a series of cellular alterations by chemical, physical, or viral agents, which results in the appearance of the abnormal and damaging cell known as a cancer cell.

This symposium is aimed at bringing together experts in these crucial and relatively new areas of scientific investigation in an attempt to synthesize a picture of the carcinogenic process at the molecular level.

Among the topics to be emphasized will be the crucial role played by the genetic makeup of the target cell in terms of its susceptibility to carcinogenic agents, the expression of oncogenes, and the role played by exogenous agents in promoting this process.

New technological advances such as the use of transgenic mice—mice that arise from a normal embryo into which a foreign gene has been injected—will be prominently discussed at the meeting. Instead of the usual broad approach to the role of oncogenes, the conference organizers chose to use ras as the model for function of this class of abnormal genes.

The final session will concentrate on the intracellular signals that control normal function of a cell and that may become aberrant under the influence of oncogenes or other factors. Abnormalities in these normal intracellular signals may result in the phenotype known as cancer.

Free discussion and interchange will take place throughout the meeting. In addition to the program components now listed, an attempt will be made during the last three months before the meeting to add brief presentations of the most advanced findings available.

The University of Texas System Cancer Center
Gastrointestinal cancer causes more deaths and more pain than any other cancer, Bernard Levin, M.D., chief of the Section of Gastrointestinal Oncology and Digestive Diseases, said about the disease that is the topic of the clinical conference he will chair Nov. 11-15, *Current Approaches to the Diagnosis and Treatment of Gastrointestinal Cancer*.

In its eight sessions with about 45 lectures and panel discussions, the conference will provide information on the best in diagnosis and treatment of this type of disease. It will be a forum for sharing new ideas and learning about advances.

"We hope to appeal to a broad range of internists, family physicians, gastroenterologists, medical and radiation oncologists, and surgeons," Levin said.

A Saturday session follows the regular conference, this one organized by pathologists and addressed by the winner of the Joanne Vandenberge Hill Award and William O. Russell Lectureship in Anatomical Pathology.

Similarly, the preceding sessions will have special lectures by recipients of the Heath Memorial and the Jeffrey A. Gottlieb Memorial Lecture awards. "We are awaiting the nominations for these awards with great interest," Levin said.

Holding the meeting at the Hotel Inter-Continental in the Galleria area is a change of scene from the Shamrock Hilton, which will close this summer. The new site, about eight miles from the Texas Medical Center, might be attractive, Levin said, to physicians and family members who like to visit this outstanding commercial center.

Mayor Kathy Whitmire or Councilman George Greenias will address the conference and, as Levin said, "give recognition to the importance of this conference and to M. D. Anderson Hospital's contribution to graduate education, and acknowledge the importance of Houston as a center of higher education and medical research."

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significance of various forms of circulating HCG (alpha and beta chains, hyper- and hypoglycosylated HCG) in the serum of patients with germ cell tumors. Carcinoembryonic antigen, Fritsche said, has had minimal application to gynecologic cancer. It seems to be a useful tumor marker only for patients with undifferentiated mucinous adenocarcinoma of the ovary, but it may have prognostic value in adenocarcinoma of the uterine cervix.

Carcinoembryonic antigen has had minimal application to gynecologic cancer.

Several new tumor markers have become available for gynecologic cancer, one of which is tumor antigen 4 (TA-4), a glycoprotein isolated from cervical squamous cell carcinoma. Early studies suggest that 50% of patients with this type of cancer may have elevated serum TA-4 levels. Another marker is cancer antigen 125 (CA-125), a high-molecular-weight glycoprotein that is present in the circulation of 60% to 80% of patients with epithelial ovarian cancers. CA-125 has received considerable study, and it seems to be useful for assessing a patient’s response to therapy and for detecting disease recurrence early. The cancer antigen 19-9 (CA-19-9), a high-molecular-weight mucin expressed by ovarian carcinomas, may in turn be a useful tumor marker for patients whose tumors do not produce CA-125.

Fritsche reported on a variety of putative tumor markers, among them NB/70K, which is a 70,000 molecular weight glycoprotein produced by all histologic cell types of ovarian epithelial tumors and may be a useful adjunct to the CA-125 test.

Quality of Life

Some of the quality of life questions for cancer patients were discussed by Leslie R. Schover, Ph.D., who said that women treated for gynecologic cancer are at risk of sexual dysfunction. Most of these problems can be prevented or at least alleviated by brief sexual counseling and appropriate medical intervention. Her report is the topic of an article in this issue.

Counseling, Practical Advice . . .

continued from page 3

patients is contraception, and this should be discussed before the cancer treatment, Schover said, recalling that tragic pregnancies have occurred during treatment because patients thought they were infertile. This is not usually a problem for women with cervical cancer, but it is relevant to young women who undergo chemotherapy, she said.

Training Counselors

When no counselors trained in sex therapy are available, Schover recommends that physicians advise patients themselves or train a social worker or oncology nurse to do it. “Physicians should not assume that if the patient doesn’t ask, she doesn’t have a problem and doesn’t need education,” Schover said.

Those who have little training in sexuality might want to go to a workshop on sex therapy, she advised. She recommends such basic textbooks as The New Sex Therapy by Helen S. Kaplan (Brunner/Mazel, 1974). “Whoever does the counseling,” Schover said, “needs practice to feel comfortable discussing sexuality with patients and to avoid being judgmental. The point is that patients do what feels right for them.”

Counseling Should Be Offered All Patients

Schover noted that in the current study at MDAH participation was offered to all stage I through stage IIA cervical cancer patients. The typical patient in the study is in her late twenties or early thirties, comes from a lower-middle-class background, and has had a “life of turmoil” that may have included physical and sexual abuse. Several of the women have been raped and some of their children have been sexually abused by the women’s husbands. Few of the women are heavy drinkers or drug users, but at least a third of them have lived with men who are, she said.

She stressed the importance of making sexual counseling available to all patients undergoing treatment for gynecologic cancer. “Ask a question about the patient’s sex life and give her the opportunity to tell you if she’s having problems,” she recommended. “Many physicians don’t do this,” Schover said, “because, unfortunately, most physicians really don’t have much training in asking about these things. All physicians who treat these patients should be familiar with what happens to patients’ sex lives afterwards. It’s a matter of taking the time and energy to ask them.”

(Physicians who desire additional information may write Ralph S. Freedman, M.D., Department of Gynecology, Box 67, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030.)

(Physicians who desire additional information may write Leslie R. Schover, Ph.D., Department of Urology, Box 110, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030.)
A Geneticist's View of Cancer: New Insight from Developmental Mechanisms

by Elton Stubblefield, Ph.D.
Professor of Genetics

We have been struggling to understand the basic difference between a normal cell and a cancer cell. Without that knowledge, our attempts at cancer therapy have been developed empirically, as we search for agents that can selectively destroy cancer cells. If we knew the defect in a cancer cell, it might be possible to bypass or correct it and to cure cancer by transforming malignant cells into normal cells. Whether this goal is achievable remains to be seen, but the importance of a fully developed theoretical framework is clear.

The defect in cancer is hidden in the mechanism that controls the behavior of normal cells. Before we can understand this defect, we must comprehend the control mechanisms that govern embryonic development and differentiation. Until recently, I believed embryonic development to be so complex that it would probably not be understood at the molecular level until well into the next century. Yet recent discoveries in the genetics of development gave us evidence for a theoretical framework that might be applied to malignant disease, at least in principle.

Role of Control Genes

The important discoveries in developmental biology all point to a direct role of control genes in embryonic processes. Mutation of control genes in Drosophila melanogaster, a fruit fly, and in Caenorhabditis elegans, a nematode, produces altered developmental patterns that result in abnormal embryos or adults. In a very striking case in Drosophila, mutation of the gene called Antennapedia results in an adult fly with thoracic legs protruding from the head where antennae normally belong. Drosophila is known to have several gene clusters of this kind.

In 1978 E. B. Lewis described a specific control gene cluster as a series of eight large genes in a row, and since then molecular geneticists have confirmed that mutation of any gene in such a cluster alters the developmental pattern of Drosophila. The evidence from many experiments in embryology led me to propose a genetic mechanism by which these control genes are activated sequentially as the developmental program unfolds in embryogenesis. I wrote about this in greater depth than is possible here in the Journal of Theoretical Biology (118: 129-143, 1986).

Theoretically, the developmental control mechanism works this way: The first gene in one part of the program has potential control over optional gene expression in a cell. If that cell is not properly positioned in an embryo to respond to the differentiation signals examined by that particular program gene, the cell duplicates its genome—its set of chromosomes—and divides. In the resulting two daughter cells, the next gene in the program is the active control gene. In this way, successive cell divisions move control along the program from gene to gene, the way the clock in a computer paces a program from one instruction to the next.

Only genetic functions unique to specialized cells are controlled by the developmental program. Most genes encode proteins that are essential to life in all cells, and these are regulated by feedback mechanisms similar to those found in bacteria. But the quite different appearance and behavior of, for example, a neuron compared with a leukocyte rest in an array of specialized gene products unique to each cell type. These are the genes regulated by the developmental control program.

Another principle in the theory is conditional control. In every cell, the newly activated control gene must first ascertain the suitability of the cellular environment for expression or repression of the genes under its control. It does so by making cell surface proteins, which are specific receptor molecules for embryonic inducers, hormones, and growth factors. When these appropriate molecules are present in the environment, specific enhancers or repressors are made by the cell to control the array of genes needed at that point in development.

In relation to cancer, the proposed control mechanism's critical feature is that with each genome replication and mitosis, control is transferred from one gene to the next in the developmental program. But in leukemia, for example, the cells behave as if they were arrested in development in a partly differentiated state, each daughter cell repeating parental behavior and failing to progress to the next part of the program. The molecular defect is that the same program instruction is repeated generation after cell generation.

Two Genetic Errors

My theory is that the decision-making apparatus makes two kinds of errors. One type of error occurs when the control gene decides to pass control to the next cell generation and, without appropriate testing of cellular status or environment, sends the cell through DNA replication and mitosis. In the second error,
the defective control gene fails to pass control to the next gene in the sequence and retains control itself. The simultaneous presence of both errors is necessary for a full-blown malignant disease, because if the cell does not divide repeatedly, it is no threat, and if gene control is passed on, the cell will ultimately differentiate.

In the last decade we have seen the discovery of oncogenes, which are derived from normal cellular genes but clearly able to cause malignant disease when inserted into cells by retroviruses. Some of the oncogenes contain the genetic code for proteins that resemble either growth factors or receptors for growth factors. Others are protein kinases that add phosphate to cellular proteins.

I believe that oncogenes interfere with normal control gene function. Those in the growth factor or receptor category probably promote the first error, sending the cell repeatedly through DNA replication and mitosis without allowing informative testing of cellular status or environment by the control program. As the control gene queries the environment, it probably receives an answer mediated by DNA-binding proteins, either enhancers or repressors. If these are inappropriately altered by protein kinases, the other class of oncogenes, they may promote either kind of error. As a result, the cell will be stuck at an intermediate state, repeatedly dividing and unable to find the next instruction in the developmental program.

We have known for decades that carcinogenesis involves two biochemical events, initiation and promotion. Now that the development of normal cells is becoming clearer, we are also beginning to understand how the two carcinogenic events might be related to molecular processes in the cell. Further research should soon give us a precise description of the specific defects in individual human tumors. With that kind of knowledge, rational therapeutic strategies to correct or bypass defective mechanisms in the cancer cell genome may be within reach.

**Spring Publication: Immunology and Cancer**

Margaret L. Kripke, Ph.D., Kathryn O'Connor Research Professor of Immunology, and Philip Frost, M.D., Ph.D., professor of medicine and cell biology, are the editors of *Immunology and Cancer* to be published in May by the University of Texas Press (297 pages, $47.50).

The collected papers of last year's 38th Annual Symposium on Fundamental Cancer Research by The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, the book contains 18 chapters by leading research groups on investigations of immune recognition by T and B cells, cellular communication and interaction, immune responses to cancer, immunologic effector mechanisms, and immunologic approaches to cancer therapy.

The nature and regulation of the immune system is "one of the most rapidly advancing areas of biomedical research," Kripke and Frost state in their preface. "Recent findings on the genetic and biochemical bases for immunologic recognition have revolutionized our understanding of the principles governing the immune system and have made us aware of the intricacies involved in its regulation," they write.

Understanding of the effects of immune responses on carcinogenesis and tumor growth has lagged behind progress in basic immunology, the editors point out. At this meeting, participants shared information and reviewed recent advances in several areas of immunology, particularly as they apply to immune response against cancer.

The book highlights "the gap between basic immunology and tumor immunology and points to areas where bridging of these two disciplines can occur," Kripke and Frost write. "We hope that this information will stimulate analyses of how our better understanding of the nature and regulation of the immune system might be applied to cancer prevention, detection, and treatment," they conclude.

The book may be ordered by writing the University of Texas Press, P.O. Box 7819, Austin, TX 78713 or by calling the publisher's toll-free number for Texas, (800)252-3206, or (512)472-4032.

**Book on Colorectal Cancer Metastasis**

*Biology and Treatment of Colorectal Cancer Metastasis*, edited by Anthony J. Mastromarino, Ph.D., assistant vice president for research, was recently published by Martinus Nijhoff (328 pages, $47.50).

Proceedings of the National Large Bowel Cancer Project's 1984 Houston conference, the book deals with issues ranging from the biology of colorectal cancer metastasis to controversies in treatment and prevention, criteria of response, and analyses of failure.

The book contains 25 papers by research groups throughout the United States, all examining, as Mastromarino writes, "relevant questions related to the clinical management of patients with hepatic metastases from colorectal cancer and the important, but less well-defined issue, their quality of life; the better design and evaluation of clinical trials; and the biologic phenomena associated with metastasis."
Mental Health Conference: The Doctor as a Person

The Eleventh Annual Mental Health Conference, The Doctor as a Person: Caring, Curing, Selling, Searching, is sponsored by the UT MDAH Department of Pediatrics and will be held May 22 and 23 at the Holiday Inn Medical Center. It will be chaired by Jan van Eys, Ph.D., M.D., Mosbacher Professor of Pediatrics and head of the pediatrics division, who originated the series in 1976 with a conference on The Truly Cured Child.

This was followed by yearly conferences spanning a broad range of topics—from the 1977 conference, Research on Children: Medical Imperatives, Ethical Quandaries, and Legal Constraints, to Survival Beyond Cure last year.

This year’s conference, van Eys said, “will examine how physicians, as human beings, see themselves as providers of medical care. Our presentations will focus on the inherent conflict in roles and tasks that physicians must assume at various times. In our discussions, we will use childhood cancer as the paradigm of care for the helpless, medical management of life-threatening illness, and guidance from medical scientific thought.”

John P. McGovern, M.D., director of the McGovern Allergy Clinic and president of the McGovern Foundation, will give the keynote address, “Giving Care and Being a Physician” during the opening session Thursday morning, May 22.

Faculty
Lawrence S. Frankel, M.D., UT MDAH
James G. Haughton, M.D., City of Houston Health Department
James A. Knight, M.D., Louisiana State University, New Orleans
Harry Lipscomb, M.D., Bryan, Texas
John P. McGovern, M.D., McGovern Foundation
Robert F. Murray, M.D., Howard University, Washington
Donald Pinkel, M.D., UT MDAH
John Spinetta, Ph.D., San Diego State University, San Diego
David N. Sundwall, United States Senate
Jan van Eys, Ph.D., M.D., UT MDAH
Kenneth Vaux, D.theol., University of Illinois, Chicago
Andrew C. von Eschenbach, M.D., UT MDAH

Thursday, May 22

The Physician as Scientist
Morning—sessions on the need for medical knowledge and “the dilemma of care by trial.”

The Physician as Bearer of Special Knowledge
Afternoon—sessions on the physician as guardian of public welfare, the physician and public health, and the physician as bearer of good and bad news for the patient.

Friday, May 23

The Physician as Care Giver
Morning—topics include the physician as servant, the practice of medicine, the care giver as a patient.

The Physician as Healer
Afternoon—discussions of the physician as priest, and the goal of medicine. The epilogue, given by van Eys, will sum up the conference and its lessons.

For more information, call or write
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