A REPORT TO THE PHYSICIANS OF TEXAS

newsletter

THE UNIVERSITY OF TEXAS SYSTEM CANCER CENTER

May-June 1982 M. D. Anderson Hospital and Tumor Institute at Houston Volume 27, Number 3

UT MDAH Maintains High Cure Rate, Low Recurrence Rate for Rare Uterine Cancer

UT MDAH is one of a handful of institutions in the United States that yearly treats a number of women with trophoblastic disease, a rare type of cancer. In its benign form, trophoblastic disease is often mistaken for pregnancy and may be left undiagnosed for some time.

The term trophoblastic disease can apply to the hydatidiform mole, or benign tissue mass, that, as a result of conception, develops from the trophoblastic tissue; in a normal pregnancy, this tissue becomes the placenta. This term also includes the malignant tumor that may form after the hydatidiform mole has been removed, or after normal pregnancies, spontaneous abortions, or tubal pregnancies have occurred. In fact, any abnormal growth of trophoblastic tissue is considered to be trophoblastic disease, according to David M. Gershenson, MD, Department of Gynecology, who often treats patients with this type of cancer.

Trophoblastic disease in its benign form occurs in one of every 2000 pregnancies. The patient initially suffers the same symptoms as in pregnancy: missed menstrual period, nausea and vomiting, and breast tenderness. Later, however, usually in the first 12 weeks of the disease, the patient may develop vaginal bleeding, pelvic pain, a higher human chorionic gonadotropin (HCG) titer than is normal in pregnancy, a discrepancy between uterine size and the elapsed time from conception, hyperthyroidism, and toxemia. In addition, a sonogram of the patient's uterus may show a speckled, amorphous pattern rather than the form of a fetus. Eighty percent of patients with trophoblastic disease suffer no malignant complications after the mass is removed, usually by a suction evacuation apparatus. The remaining 20% develop malignant transformation after treatment.

The main indicator of such complications is a rise in the HCG level. In most successfully treated patients, the HCG level falls to normal within the first few weeks after treatment. An abnormally high HCG titer, in addition to vaginal bleeding, often prompts the physician to refer the patient to UT MDAH, where 10 to 20 patients with trophoblastic disease are treated yearly. Often these symptoms signify that a malignancy is developing. According to Dr Gershenson, "If the HCG titer begins to rise, that is an indication of proliferation and that the patient probably needs to have chemotherapy."

Dr Gershenson explained that of the 20% of patients who develop this cancer, approximately 15% have an invasive mole, which locally invades the uterine wall and may metastasize to the lungs and vagina; five percent have choriocarcinoma, which may or may not metastasize but, potentially, can spread to any part of the body. Patients with both kinds of malignancies sometimes experience uterine enlargement in addition to vaginal bleeding and a rising HCG titer.

Patients with choriocarcinoma commonly suffer metastasis in the lungs, vagina, liver, and brain. Those with lung involvement, 80% of choriocarcinoma patients, may develop chest pain, hemoptysis, dyspnea, cough, or asymptomatic lesions in the lungs, detectable with a chest x-ray. Purulent discharge and irregular bleeding are symptoms of vaginal metastasis, found in 30% of choriocarcinoma patients. Patients who experience liver involvement (10%) may suffer epigastric or right upper quadrant pain. Those with cerebral involvement (10%) may have focal neurologic deficits and elevated HCG levels in the cerebrospinal fluid.

Upon entering UT MDAH, the patient receives a series of diagnostic tests and tests designed to determine if and where the disease has metastasized. She is given chest x-rays, a liver scan, and a computed tomographic brain scan in addition to blood tests, an intravenous pyelogram, and a lumbar puncture. The results of these tests help determine the type of malignancy, the patient's risk status, and the treatment chosen.

As Dr Gershenson explained, "Based on the duration of her disease, where the disease has spread, and how high her HCG

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The speckled, amorphous pattern *shown in the uterine sonogram on the left confirms the existence of a hydatidiform mole 12 weeks after conception. In 20% of the women who undergo removal of the mole, a uterine malignancy develops. In the sonogram of a normal pregnancy (right), a 14-week-old fetus is clearly delineated.*

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UT MDAH Offers Oncology Lecture Series

UT MDAH is offering a two-part series of lectures, "Fundamentals of Oncology," to clinical residents, fellows, and staff members and others in the medical and academic communities during the 1982-83 academic year. Part I, approximately 25 weekly lectures, will provide an overview of the basic science principles underlying cancer treatment. Part II, which will be approximately the same length, will provide an introduction to the application of those principles to clinical research.

The series, which is being offered for the fourth consecutive year, was established to keep clinicians abreast of the mushrooming amount of new oncology-related information in the basic sciences, to refresh the knowledge of health professionals who have not been involved recently with basic science research, and to present recent innovations in oncology. According to Yaal Silberberg, DrPH, Office of Academic Affairs, who organized the lecture series with the aid of members of the basic science and clinical staffs, "The lecture series is a tool that provides a transaction of knowlecge among people in the field."

The lectures will be given primarily by members of the UT MDAH staff and will examine topics similar to those covered during the 1981-82 lecture series. During the first part of last year's series, the basic science topics covered included molecular biology and biochemical anatomy, viruses and cancer in animals and man, cellular genetics and phenotypic expression, intermediary metabolism, whole-organism cancer consequences, and immunology. The second part of the series consisted of lectures on physics, pharmacology and chemotherapy, clinical trial design and statistics, pathology, principles of surgical physiology in cancer therapy, supportive care of the cancer patient, and immunological and biological therapy. According to Dr Silberberg, this year's syllabus will include essentially the same topics but is being modified to include areas in which recent developments have occurred and to exclude subjects that have diminished in importance.

The subjects covered in the lectures will be interrelated, and knowledge of previously presented material may be assumed by the lecturers. During the lectures, questions and comments addressed to the speakers will be encouraged, and a list of additional readings will be provided for those who desire more information on a subject.

Fundamentals of Oncology—Part I is scheduled to begin in July 1982, with part II beginning in the latter part of January 1983. No fee will be charged for the lectures, which will be given in the UT MDAH main auditorium from 5:00 p.m. to 6:00 p.m. each Wednesday. Continuing education credits are being offered by the Physician's Recognition Award of the American Medical Association.

For additional information, write or call Yaal Silberberg, DrPH, Office of Academic Affairs, Room C10.004, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030, (713) 792-7238/9.

newsletter

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26th Annual Clinical Conference

Current Controversies in Breast Cancer

November 3-5, 1982
Shamrock Hilton Hotel
Houston, Texas

Presented by
The University of Texas
M. D. Anderson Hospital and Tumor Institute
at Houston

Cochairpersons: George R. Blumenschein, MD, Department of Internal Medicine; Eleanor D. Montague, MD, Department of Radiotherapy; and Frederick C. Ames, MD, Department of General Surgery.

The conference will examine the current therapeutic and diagnostic controversies surrounding breast cancer. The program will focus on the topics of limited mastectomy and irradiation, pathologic prognostic factors, breast cancer screening, long-term results of adjuvant chemotherapy, the value of biological markers, strategies for complete remission of metastatic disease, and second- and third-line therapies for advanced disease.

For registration information, write or call Ms Frances Goff, Office of Conference Services, MDAH Box 18, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030, (713) 792-2222.

Biomathematicians Develop Software for Clinical Trial Design and Analysis

Members of the Computer Science Section of the Department of Biomathematics have developed new statistical methods and several new computer programs in response to two problems inherent in the conduct of clinical trials—one relating to ethical considerations and the other to the need for efficiency in the design of trials and the analysis of results.

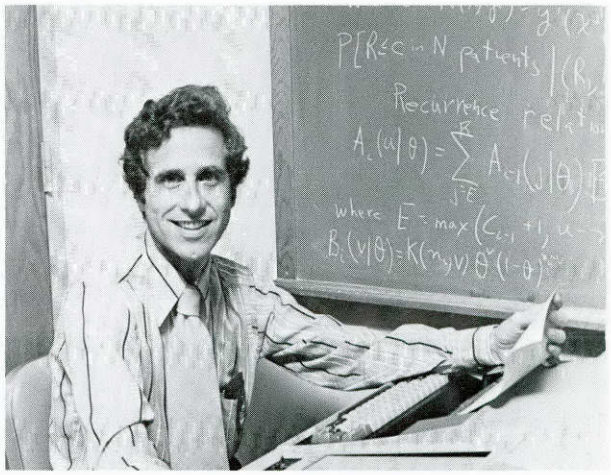
Jay Herson, PhD, Department of Biomathematics, has spent the last five years studying the conduct of phase II clinical trials—those designed to test the efficacy of a new agent. At the outset, he recognized an ethical dilemma caused by an apparent conflict between statistical requirements, determined from the statistician's pretrial specification of the minimal number of patients to be entered in a trial, and clinical considerations related to a lack of response to therapy among the first few patients entered in a trial.

The minimal number of patients in a trial, or the "sample size," is computed to control the probability that two types of inferential errors will occur in the conclusions of a phase II trial: Investigators can make a false-positive error, concluding that an ineffective drug is effective; or a false-negative error, concluding that an effective drug is ineffective. These errors can occur because conclusions about drug efficacy in a clinical trial are based on only limited numbers of patients.

Dr Herson explained that statisticians generally specify that 20 to 30 patients be treated in a trial in order to keep the probability of false-positive and false-negative errors at acceptable levels. The dilemma emerges, he believes, if, for example, after the first 10 patients have been treated, none have responded to the therapy. At this point, physicians might be reluctant to enroll still more patients in the trial and might feel an obligation to publish their results to date to alert other physicians to the apparent ineffectiveness of the drug. However, higher-than-desired error probabilities might then result because of the disregard for the necessary minimal sample size.

In an attempt to solve this dilemma, Dr Herson developed "predictive-probability" phase II trial designs, which overcome the problems inherent in fixed sample-size designs. A predictive-probability design, he explained, might specify that, although 30 patients are needed, the trial be conducted in "stages" of 10 patients each. The trial would proceed to each successive stage only if favorable results were observed among the patients already treated. (Statistical methods determine the definition of favorable results at each stage.) Otherwise, the trial would terminate at the end of a stage, and the treatment's inefficacy would be reported.

According to Dr Herson, this multistage design still controls false-positive and false-negative error probabilities, thus meeting all specified statistical requirements. Predictive-probability methods even allow investigators to incorporate information gathered from previous research on the effectiveness of a new chemotherapeutic agent into the design of the trial. Dr Herson has also designed special data management procedures to record patient progress; these procedures are necessary because of the sequential nature of predictive-probability clinical trials.



***Jay Herson, PhD,** has developed computer software to overcome the problems inherent in fixed sample-size phase II clinical trial designs.*

Dr Herson collaborated with Barry W. Brown, PhD, and E. Neely Atkinson, PhD, both of the Department of Biomathematics, in writing a computer program known as KSTAGE, a program that creates predictive-probability designs that meet investigator-specified statistical requirements to control estimated trial duration and false-positive and false-negative error probabilities.

In addition to KSTAGE, the Department of Biomathematics has developed two additional computer programs useful in cancer research. STPLAN—study planning package—enables statisticians to determine minimal sample-size requirements for phase I, II, and III clinical trials and laboratory studies. According to Dr Herson, the availability of STPLAN will contribute to better-planned and more scientifically meaningful studies. RANDLIST generates a list of treatments in random order in accordance with investigator specifications. The treatment list is printed on computer output paper, one regimen to a line, with room on each line for a patient's name and other identifying information. This list is used for enrolling patients in phase III clinical trials and assigning each new patient to a treatment regimen.

Dr Brown, Elizabeth Rozell, ME, and Eula Webster, BSAS, also of the Department of Biomathematics, are in the final stages of developing a survival analysis program, which will enable efficient and highly sophisticated analysis of phase III clinical trial data.

The KSTAGE, STPLAN, and RANDLIST programs replace the cumbersome and less accurate printed tables that historically have been used for clinical trial design and patient randomization. According to Dr Herson, all the programs are interactive, in that the reseacher using the program directs the computer to solve his problem through a "friendly" question-and-answer "conversation" with the computer using a computer terminal. The programs are written so that they can be run on any computer, regardless of manufacturer. In addition to their use at UT MDAH, the programs are currently being used by statisticians and other scientists at research centers in North America, Europe, and Australia.

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Uterine Cancer . . .

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titer is at the time we see her, we can make some prediction about how well she'll do and administer treatment accordingly."

Treatment for the patient with metastatic choriocarcinoma depends largely upon what category she falls into, low risk or high risk. Patients with nonmetastatic choriocarcinoma and those with invasive mole are usually given the same treatment as those with low-risk metastatic choriocarcinoma.

The low-risk category most commonly includes patients with metastasis in only the lungs and vagina. These patients are treated with a single agent, either methotrexate or actinomycin D, daily for five days, with a period of seven to nine days between repetitive chemotherapy courses. The number of treatment courses depends upon the patient's response to therapy, measured again by weekly HCG titers.

"We start the treatment, and we follow the serum HCG titer until it falls to normal. That may take two courses or five courses," Dr Gershenson explained. Treatment is continued for one course past a normal HCG titer. If the patient does not respond to this treatment, multiagent therapy is administered.

Patients in the high-risk category usually have metastasis to the brain or liver (with or without metastasis to the vagina or lungs), have had the disease longer than four months, or continue to have an HCG titer of above 40,000 mIU/ml, often in spite of previous chemotherapy. These patients are given a combination of methotrexate, actinomycin D, and cyclophosphamide (Cytoxan) (MAC) every day for five days, again with a period of seven to nine days between courses. The number of courses administered, as in the low-risk category, depends upon response. Patients not responsive to MAC are treated with a combination of vinblastine, bleomycin, and cis-platin. Those whose HCG titers remain elevated afterward receive individualized treatment. Patients past the childbearing age are likely to consider the option of hysterectomy, which may shorten the duration of the chemotherapy. In patients with long-term malignancies, hysterectomy often may be used as an adjunct to chemotherapy.

After therapy is completed, HCG titers are monitored every week for three weeks and then every month for a year, every three months for the following year, and periodically for life. Patients should not become pregnant for six to twelve months after treatment because, as Dr Gershenson explained, during pregnancy the HCG titer rises and can no longer be used as an indicator of relapse.

The risk of spontaneous abortion and recurrent episodes of either molar pregnancy or trophoblastic malignancies in patients who become pregnant after treatment is slight. An ultrasound examination during the first trimester of pregnancy should be conducted, however, to ensure normal gestation. After the pregnancy is completed, HCG titers should be obtained to signal any recurrent trophoblastic growth.

According to Dr Gershenson, the high cure rate for patients with malignant trophoblastic disease in comparison to that of other types of cancer can largely be attributed to the disease's innate sensitivity to some chemotherapeutic drugs. Approximately 95% of patients treated on the regimen for the low-risk group are cured, as are 50% to 70% of high-risk patients. Before the advent of chemotherapy in the late 1950s, the overall cure rate was only 40%. Another major factor contributing to such successful treatment is the built-in HCG marker, an immediate indicator of response to therapy, something not found in most other cancers. A normal HCG titer in a patient with metastases is a good sign that all sites of metastasis are responding to chemotherapy, Dr Gershenson said. Yet, he was quick to qualify his optimism, stating that the clinical course of most patients is very straightforward; the patient undergoes chemotherapy and is cured. Other cases, however, are extremely complicated, and some patients die of the disease.

UT MDAH has been fortunate to have a high success rate with trophoblastic disease, primarily because of its experience in treating this rare disorder, Dr Gershenson explained. UT MDAH was one of the three centers set up to treat trophoblastic disease in the 1960s after the initiation of chemotherapy, the other two being The New England Trophoblastic Disease Center in Boston and the center established at Duke University in Durham, North Carolina. Since that time, a number of other centers have been established to treat the disease.

(Physicians requiring additional information should write or call David M. Gershenson, MD, Department of Gynecology, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030, (713) 792-2770.—ED)

Lectureship Honors Taylor

The Second Annual Grant Taylor Lecture, one in the series of lectures established to recognize the ideals and work of H. Grant Taylor, MD, emeritus professor of pediatrics, was delivered on April 14, 1982, by Edmund D. Pellegrino, MD, president of The Catholic University of America and professor of clinical medicine and community medicine at Georgetown University School of Medicine in Washington, D.C. Dr Pellegrino addressed the issue of medical ethics in a lecture entitled, "What is Medicine: The Crisis of Definition," presented at The University of Texas Medical School at Houston, which, along with Baylor College of Medicine and UT MDAH, hosts the lectureship.

The Grant Taylor Lectureship, devoted to science and human values in medicine, was founded in 1981 by John P. McGovern, MD, director of the McGovern Allergy Clinic in Houston. Dr McGovern studied under Dr Taylor in the late 1940s, when Dr Taylor was associate dean and associate professor of pediatrics at Duke University School of Medicine. After World War II, Dr Taylor went to Japan to serve as deputy medical director in charge of research and later as director of the Atomic Bomb Casualty Commission in Hiroshima. In 1954, he was appointed head of the Department of Pediatrics at UT MDAH, a position he held for 14 years.

Murray M. Copeland Dies

Murray M. Copeland

Murray M. Copeland, MD, DSc, an internationally known expert on bone and colorectal cancer, died April 2, 1982, at the age of 79. Dr Copeland, who, at the time of his death, was director emeritus of the National Large Bowel Cancer Project, had been a member of the UT MDAH staff since 1960.

Charles A. LeMaistre, MD, president, said of Dr Copeland, "He was internationally acclaimed for his work in the fight against large bowel cancer and his superior surgical knowledge, particularly in the field of bone cancer. He was also known and loved by physicians around the world for his willingness and ability to support organizations designed to facilitate the spread of knowledge about cancer."

Dr Copeland earned his medical degree from Johns Hopkins University School of Medicine in Baltimore, Maryland, in 1927 after receiving his bachelor's degree from Oglethorpe University in Atlanta, Georgia, the institution that later awarded him an honorary doctor of science degree. After completing his postgraduate training in 1937, he was appointed clinical instructor in surgery at Johns Hopkins University School of Medicine. In 1941, Dr Copeland entered the U. S. Army as a major and was honorably discharged as a colonel five years later. During his military service, he commanded the 142nd General Hospital, one of the largest army hospitals in the South Pacific theater.

After World War II, Dr Copeland joined the staff of Georgetown University School of Medicine in Washington, D.C., as professor of oncology and chairman of the Department of Oncology. In 1960, he joined the UT MDAH staff as assistant director for education and was later appointed associate director for education and professor of surgery. In 1967, he became vice president for international affairs of The University Cancer Foundation.

In 1972, Dr Copeland was appointed the first director of the National Large Bowel Cancer Project, supported by the National Cancer Institute and headquartered at UT MDAH. He held this position until 1981, at which time he was appointed director emeritus.

The author of more than 170 articles and books, Dr Copeland coauthored the authoritative textbook *Tumors of Bone*. He served as national president of the American Cancer Society and as chairman of the Commission on Cancer of the American College of Surgeons. He also served as secretary general of the Tenth Congress of the International Union Against Cancer, attended by 6000 scientists from 60 countries, and as chairman of the American Joint Committee for Cancer Staging and End Result Reporting. During his lifetime, Dr Copeland received 12 national and international awards, including the American Cancer Society's President's Medal in 1965 and their Distinguished Service Award in 1972.

At memorial services for Dr Copeland, R. Lee Clark, MD, president emeritus, said, "There are few people who have filled their lives to the fullest with total involvement in whatever task presented itself and with undeviating insistence on quality—in documentation of facts, in choice of words for the expression of ideas and accomplishments, in thoughtful decisions that would affect many activities and many lives into the distant as well as the near future. Such a person was Dr Murray M. Copeland."

Dr Copeland is survived by his wife, Jean, and his nephew, Edward M. Copeland, III, MD, Department of General Surgery and director of the National Large Bowel Cancer Project. A memorial fund has been established in Dr Copeland's honor.

The University of Texas
M. D. Anderson Hospital and Tumor Institute
at Houston

Department of Nursing

Presents

Oncology Nursing Conference IV

August 30–September 1, 1982
Shamrock Hilton Hotel
Houston, Texas

This program will review current trends in cancer nursing and will provide practical information that can be incorporated in nursing practice. Emphasis will be placed on the needs of the individual with cancer and on innovative nursing care directed toward meeting those needs.

For registration information, write or call Ms Frances Goff, Office of Conference Services, MDAH Box 18, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030, (713) 792-2222.

A REPORT TO THE PHYSICIANS OF TEXAS
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Genetic Markers May Identify Chromosomal Deletion Associated with Retinoblastoma

Louise C. Strong, MD*

Retinoblastoma is unique among the childhood cancers in that frequent familial occurrences can be traced back to the 1800s and that individuals with the disease have a relatively favorable prognosis, permitting them to survive and reproduce. The frequent reports of familial retinoblastoma, some consistent with autosomal dominant inheritance, suggested to Falls and Neel in 1951 that all retinoblastoma might be attributable to a mutation—germinal in familial cases and somatic in nonfamilial cases. The germinal mutation could be transmitted by affected individuals to their offspring in an autosomal dominant manner. Therefore, chromosomal and biochemical genetic markers may play an important role in determining the genetic basis of retinoblastoma.

Systematic follow-up of progeny of all bilateral retinoblastoma survivors, both familial and sporadic, indicates that nearly 50% of their offspring develop retinoblastoma, most often bilateral. Progeny of unilateral sporadic retinoblastoma patients only occasionally develop retinoblastoma, although when it is present, it is most often bilateral. These findings support the existence of both a hereditary and nonhereditary form of retinoblastoma and indicate that all bilateral cases, but only a small fraction of unilateral cases, are hereditary.

Falls and Neel's mutation model was expanded by Knudson in 1971. He noted that gene carriers develop a mean of only three to four independent tumors, implying that only rare retinal cells develop into tumors, even in the presence of the retinoblastoma gene. He therefore suggested that all retinoblastoma might be attributable to a series of two cellular events: In the hereditary form, a mutation, or hit, would occur in a germinal cell and would thus be present in all cells of the resultant embryo, in which case a single second event, or second hit, in any target tissue cell might trigger the development of a tumor. Such tumors might occur at earlier-than-average ages; gene carriers might develop no tumors, one tumor, or multiple tumors, according to the number of second hits, which Knudson suggested occur according to a Poisson distribution. In the nonhereditary form, a mutation and a second hit would occur, but they would have to take place within the same somatic cell line, an occurrence so rare that such tumors would never occur multiply. All bilateral cases of retinoblastoma are attributable to a hereditary origin, whereas most unilateral cases are ascribed to nonhereditary factors.

Penetrance, the probability of tumor in a gene carrier, may be variable in families. Prospective studies of the offspring of patients with retinoblastoma indicate a highly penetrant (95%) retinoblastoma gene. However, retrospective studies of the occurrence of retinoblastoma in relatives of a proband have often revealed many families with more than one affected sibling or cousin in the absence of affected parents, indicating low (20%) gene penetrance. This latter pattern of inheritance has been observed in animals and is attributed to partial gonadal mosaicism, premutation (a delayed mutation that requires more than one generation to be expressed), or host resistance genes.

Data supporting the genetic etiology of retinoblastoma have accumulated through chromosomal analysis of retinoblastoma patients. In 1963, Lele and co-workers reported a patient with retinoblastoma who had a deletion of a D-group chromosome. Further studies and refinement of chromosomal analysis have determined that a detectable chromosome deletion occurs in 1-2% of retinoblastoma patients and consistently involves the q14 region of chromosome 13. To date, all reported patients with 13q14 deletions have developed retinoblastoma. Clinical findings in these patients have been somewhat variable but frequently include failure to thrive in infancy and some degree of psychomotor retardation. Retinoblastoma has also been observed in patients with a translocation between the X chromosome and chromosome 13 (X;13 translocation), apparently resulting in an inactive region of chromosome 13, and in patients with chromosome 13-deletion mosaicism.

Esterase D is an enzyme found in many human tissues whose gene is located on chromosome 13. All patients with retinoblastoma and 13q14 deletions have exhibited hemizygous expression of the enzyme. These findings suggest that the esterase-D gene was also deleted and, hence, may be located on the 13q14 region, which, when deleted, predisposes an individual to retinoblastoma.

Chromosomal and biochemical genetic analyses have recently provided new insight into the occurrence of familial retinoblastoma. We recently studied four generations of a family in which 10 individuals in seven different sibships developed retinoblastoma. The family was unusual in that retinoblastoma seemed to be transmitted by unaffected individuals, as no parent of an affected individual had developed retinoblastoma. Chromosomal analysis of the surviving individuals with retinoblastoma revealed that each had a specific chromosome-13 deletion, resulting in a net loss of a small amount of genetic material. In each instance, the chromosome deletion had been inherited from a parent who had a chromosomal rearrangement, such that although the parent carried the chromosome deletion, the missing segment of genetic material had been inserted into another chromosome, resulting in a normal net amount of genetic material. The chromosomal analysis further revealed the chromosome deletion in a two-month-old infant hospitalized because of its failure to thrive. Subsequent ophthalmologic examination revealed a small focus of retinoblastoma in one eye.

The infant's family members who were balanced translocation carriers were informed that they had approximately a 25% probability, with each pregnancy, of having a child with the unbalanced deletion and associated retinoblastoma. At least in this family, chromosomal analysis could identify unaffected individuals at risk of having a child with the unbalanced chromosome deletion and the resulting disease. The techniques used to determine this, including esterase-D determinations, could also be used in prenatal diagnosis.

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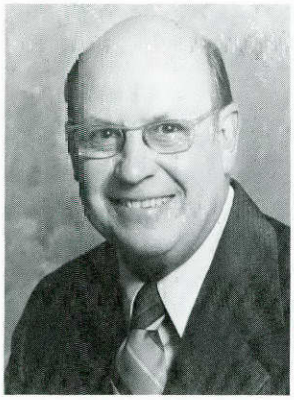
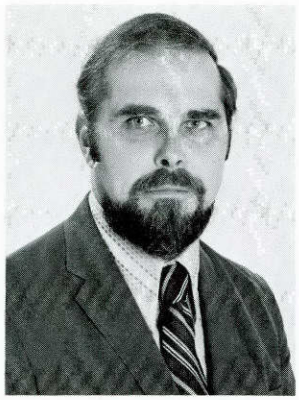
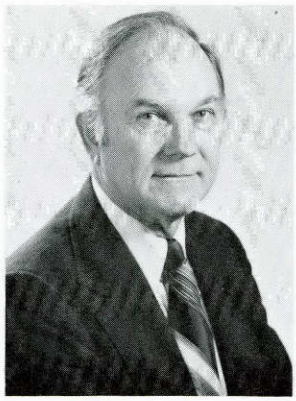


Robert D. Moreton



Stuart O. Zimmerman



Joseph T. Ainsworth

Andrea L. Morgan

The University of Texas
M. D. Anderson Hospital and Tumor Institute
at Houston

Department of Urology

Presents

The Seventh Annual Urologic Oncology Seminar

August 26–28, 1982
Shamrock Hilton Hotel
Houston, Texas

Chairperson: Douglas E. Johnson, MD, head of the Department of Urology

This program is designed to provide an in-depth review of the common urologic malignancies (bladder, testicular, renal, and prostatic). Emphasis will be placed on multidisciplinary treatment as is practiced at UT MDAH, and open discussions regarding its rationale will be strongly encouraged. Presentations by prominent guest faculty will highlight current differences among therapies and provide stimuli for panel discussions and questions from the registrants.

For registration information, write or call Ms Frances Goff, Office of Conference Services, MDAH Box 18, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030, (713) 792-2222.

Noteworthy

Robert D. Moreton, MD, vice president for patient affairs, has been appointed executive director of The University Cancer Foundation. The foundation, established in 1955 by The University of Texas Board of Regents, manages funds raised by the UT MDAH Development Office and The University Cancer Foundation Board of Visitors. Dr Moreton came to UT MDAH in 1965 from private practice in Fort Worth. Active in many civic and professional organizations, he served as chairman of the Texas Board of Health from 1975 to 1980.

Stuart O. Zimmerman, PhD, has been named head of the newly formed Division of Biomedical Information Resources. Composed of the Department of Biomathematics, headed by Dr Zimmerman, and the Department of Patient Studies, headed by Vincent F. Guinee, MD, the division combines the departments' information-processing resources used to support both basic and clinical research at UT MDAH. Dr Zimmerman has served as head of the Department of Biomathematics since 1968.

Joseph T. Ainsworth, MD, associate vice president for patient care, has been appointed to the American Academy of Family Physicians' Committee on Cancer. The committee investigates and gathers data on the incidence and treatment of all forms of cancer, disseminates pertinent information about new developments in cancer therapy to academy members, encourages constituent chapters to establish committees on cancer, maintains a liaison with the National Cancer Institute and the American Cancer Society, and establishes liaisons with other medical groups and agencies involved in programs dealing with cancer. Dr Ainsworth, who has served as the director of Personnel Health Services at UT MDAH since 1977, is currently a member of the American Medical Association's Council on Legislation and the State of Texas Hospital Advisory Council.

Andrea L. Morgan has been named director of development for The University of Texas System Cancer Center. She will work with The University Cancer Foundation Board of Visitors to secure the resources needed to promote high-quality cancer patient care, research, education, and cancer prevention programs. Ms Morgan, a member of the National Association for Hospital Development and the National Society of Fund-Raising Executives, has served as assistant director and then associate director for development since joining the UT System Cancer Center staff in 1979.

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Retinoblastoma . . .

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The finding of a consistent heritable chromosome deletion in the 10 retinoblastoma patients in this large family in which no individual was found to have retinoblastoma without the specific deletion, plus the fact that no net loss of this specific region was detected in the absence of retinoblastoma, strengthens the association between retinoblastoma and the specific chromosome deletion. The absence of retinoblastoma in the balanced translocation carriers indicates that rearrangement of genes alone is not sufficient to predispose an individual to retinoblastoma, but rather that the loss of genetic material is associated with the occurrence of the disease. The finding of a chromosome rearrangement in unaffected individuals who transmit the predisposition to their offspring demonstrates that a chromosomal mechanism may account for the otherwise unpredictable familial pattern and could also account for the predictable transmission of retinoblastoma to offspring of affected individuals.

The relationship between retinoblastoma development and the chromosome-13 deletion has been further strengthened by chromosomal analysis of the tumor cells. In patients with retinoblastoma and normal constitutional (hereditary) chromosomes, the tumor karyotypes show a chromosome-13 deletion. The chromosome-13 deletion, therefore, may be heritable and may predispose an individual to retinoblastoma, or it may be acquired in the development of retinoblastoma and, hence, may represent a critical and perhaps essential event in tumor development.

Most individuals with retinoblastoma, including those with familial retinoblastoma, however, have normal-appearing karyotypes and esterase-D activity. It is not clear whether the gene or genes predisposing an individual to retinoblastoma are located on chromosome 13 in the same region as the deletion or elsewhere in the genome. Based on the differences in bilateral and unilateral tumor development between individuals with the chromosome-13 deletion and individuals with familial retinoblastoma and normal chromosomes, Matsunaga suggested in 1980 that the familial retinoblastoma gene probably is located in some other portion of the genome. Other investigators have studied the cosegregation of heritable variants, or polymorphisms, of esterase D (alleles for esterase D1 or D2) and retinoblastoma in families. Although data are limited—study of additional families is needed—the information available is consistent with the concept that the heritable retinoblastoma gene is closely linked to esterase D and segregates with a single esterase-D allele in any given family. These limited data imply that the 13q14 region may be the site of the gene that predisposes individuals to retinoblastoma in the presence of normal chromosomes, suggesting that other types of mutation or submicroscopic deletions in this region may be involved.

If the data involving the relationship between esterase D and retinoblastoma are confirmed, then esterase-D determinations may provide a mechanism for genetic counseling, including prenatal diagnosis. However, as esterase D has only limited polymorphisms in most populations, other genetic markers should be sought for this purpose. Given the advances in technology for the study of human DNA, new types of polymorphic markers, including DNA restriction-enzyme fragment-length polymorphisms, could be developed for the 13q14 region of the genome. Therefore, in the future, it may be possible to determine, using genetic markers, whether all retinoblastoma is related to changes in the same portion of the genome and whether the same genetic changes occur in individuals with the heritable and nonheritable forms of the disease.

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