A Report to Physicians
OncoLog

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Hereditary Colon Cancer: Molecular Research and Family Studies Aim for Early Detection

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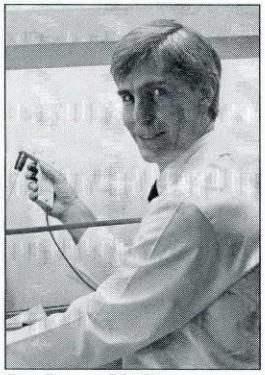

Dr. Bruce M. Boman

Colon cancer, the single most common form of internal malignant disease in the United States, ranks second as a cause of cancer death. Clinical studies attempting to identify factors that contribute to the development of colon cancer have shown that 10% to 15% of patients with colorectal carcinoma have a family history of the disease. Well-defined hereditary forms, which have an autosomal dominant mode of inheritance, include the familial polyposis and nonpolyposis colon cancer syndromes. In the general population, first-degree relatives of colorectal cancer patients have a two- to threefold increased risk of developing colon cancer, but the inheritance patterns are not well understood.

Research and Clinical Collaboration

Several clinical investigators and basic researchers at M. D. Anderson Hospital are collaborating in a study of the hereditary aspects of colon cancer. The major goals of the program are (1) prevention or early detection of colon cancer by screening persons who are at high risk of developing the disease, (2) performing clinical genetic analyses of colorectal cancer patients' families to identify families who may have a genetic predisposition to the disease, and (3) performing molecular and cytogenetic studies that may yield information on the mechanisms of colon carcinogenesis or provide molecular markers for identifying individuals at high risk of developing the disease.

Familial Polyposis

In familial polyposis, patients develop multiple adenomatous polyps of the colon and rectum at an early age. The incidence of the disease is one in 7,000 to 10,000 live births. In affected patients the risk of developing colon cancer approaches 100% by age 45. Several extracolonic lesions may occur in association with familial polyposis. Best known are those of the Gardner syndrome, which consists of osteomas, epidermoid cysts, fibromas, desmoid tumors, and abnormal dentition. The Oldfield syndrome is the association of familial polyposis with sebaceous cysts. Other lesions that may occur in association with familial polyposis include gastric and duodenal polyps and congenital hypertrophy of the retinal pigment epithelium.

In examining patients in MDAH's Special Risk Clinic, physicians evaluate familial polyposis patients for these possible extracolonic manifestations. In addition, the patients are referred to the Department of Dental Oncology for a dental examination, including a panoramic X ray of the mandible and teeth, and to Baylor College of Medicine's Cullen Eye Institute for opthalmologic evaluation with particular attention to possible congenital hypertrophy of the retinal pigment epithelium.

Since these extracolonic manifestations are associated with familial polyposis, their presence may help identify family members with the cancer-prone genotype before premalignant colonic polyps appear.

Nonpolyposis Syndromes

Nonpolyposis colon cancer syndromes, including hereditary site-specific colon cancer syndrome and cancer family syndrome, also are marked by the development of colon cancer at an early age. Although these syndromes are subclassified as nonpolyposis variants, an inherited tendency to develop discrete adenomatous polyps is present in some families. The cancer family syndrome carries an increased risk of cancers of many types, but colon and endometrial malignancies predominate.

Special Risk Clinic

The MDAH Special Risk Clinic was established by Rodger Winn, M.D., director of the Community Oncology Program, to monitor patients whose risk of developing this disease is substantially higher than that of the rest of the population. Clinical criteria of increased risk include histories of

1. two or more relatives in the immediate family (parents, siblings, or children) who have colon cancer,
2. familial polyposis or the Gardner syndrome occurring in the family,
3. heterogeneous tumors in one-fourth or more immediate family members,
4. multiple primary colon cancers or a primary colon cancer that developed in the person before age 40.

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Houston-Galveston Hybridoma Researchers Review Laboratory and Clinical Progress

by Frances M. Davis, Ph.D.
Department of Chemotherapy Research


Dr. Frances M. Davis

Hybridoma technology is one of the most rapidly developing areas in biological research, with new methods to improve hybridoma yield and new uses for the cell products appearing almost daily in the scientific literature. These advances made the Second Texas Medical Center Hybridoma Symposium, held last April at UT MDAH, an optimistic forum for Houston-Galveston researchers.

Hybridoma Cell Types

The most common type of hybridoma cell is formed by the fusion of normal antibody-producing cells with immortal tumor cells. These hybridoma cells reproduce continuously in a laboratory dish and secrete antibodies. When individual antibody-producing cells are segregated, each produces a clone of cells. The antibodies secreted by these cell clones are the monoclonal antibodies. The method of producing these was first described by Cambridge scientists Georges Kohler and Cesar Milstein in 1975; nine years later they won a Nobel Prize for their work.

Another type of hybridoma cell is produced by the fusion of T lymphocytes with tumor cells. Like normal cells, these T-T hybridomas secrete signal molecules—lymphokines—that regulate the activity of the immune system.

Clinical Usefulness Becoming Evident

The monoclonal antibodies and lymphokines secreted by the hybridoma cells have enormous potential usefulness in the diagnosis and treatment of cancer. One method of using hybridoma technology in diagnosis is to attach radioactive chemicals to the antibodies and infuse them into patients. Because the antibodies seek out and bind to cells that have corresponding molecules on their surface, radioactive areas in the patient's body can then be spotted by scintigraphic scanning and the sites of tumor nodules identified. For treatment, radiation may be delivered to the tumor by radioactive molecules attached to antibodies, and chemotherapeutic agents may be delivered the same way.

Monoclonal antibodies . . . have enormous potential usefulness.

Hopeful Reports

Of the 14 papers presented at the one-day conference, 11 described work being done at UT MDAH. Susan M. North, Ph.D., who reported work on metastatic mammary carcinoma in the rat, said that her group in the Department of Tumor Biology has used monoclonal antibodies to inhibit metastasis, a long step up from identifying and characterizing metastasis-related surface antigens. North has found also that the monoclonal antibodies bind to similar antigens in some human breast cancers.

Discussions of clinical investigations dealt with using monoclonal antibodies in immunoscintigraphy to locate metastatic cancers. James L. Murray III, M.D., and Richard J. Babaian, M.D., led a discussion of the potential value and problems of this new diagnostic modality. In collaborations that involved staff members of the MDAH Departments of Clinical Immunology and Biological Therapy, Urology, Medical Onco-

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logy, and Nuclear Medicine, these investigators used a monoclonal antibody to a carcinoembryonic antigen to localize colorectal tumors and a monoclonal antibody to a prostate antigen to scan for metastatic prostate cancer.

A description of several new antibodies specific for human colon cancer cells came from Benjamin Drewinko, M.D., Ph.D., and coworkers Li-Ying K. Yang and Jae Y. Ro, M.D., Ph.D., of the Division of Laboratory Medicine. Because of the antigenic heterogeneity of cancers, mixtures of several monoclonal antibodies that bind to the same tumor cells may be more effective for diagnosis and therapy than one monoclonal antibody alone, which places a high value on finding new tumor-associated markers.

Need Human Antibodies

Most of the monoclonal antibodies produced so far originate in rodents, and the need for repeated infusions of antibodies for scanning and therapy is a compelling reason for developing human monoclonal antibodies. Human antibodies to tumor-associated antigens are needed also to study the immune response to cancer. Ruth Carsetti, M.D., described work in the gynecology department laboratory, in collaboration with Ralph S. Freedman, M.D., with lymphocytes from patients who have ovarian cancer and are immunized with oncolysates of their own tumors to produce monoclonal antibodies specific to these tumors.

Basic Scientific Advances

James C. Chan, Ph.D., who chaired the symposium, described collaborative studies in which epitopes, also known as antigenic determinants, are mapped using a panel of monoclonal antibodies to carcinoembryonic antigen. His group also compared the activity of antibodies from commercial sources with that of antibodies generated at UT MDAH.

Chintaman G. Sahasrabuddhe, Ph.D., reported preparation of monoclonal antibodies to B-cell growth factor, a lymphokine that stimulates proliferation of antibody-producing cells. These antibodies may be used to purify the lymphokine and to study its regulation and mechanism of action.

I reported on my study with Potu N. Rao, Ph.D., in which we use monoclonal antibodies to investigate the process of mitosis. We have identified and defined several mitosis-specific antigens with this method. We are using these antibodies to investigate how a cell accomplishes its reorganization at each mitosis, when the nuclear membrane breaks down, the chromatin condenses into chromosomes, and the cytoskeleton is mobilized to segregate the chromosomes to the two daughter cells. In addition, the proportion of mitotic cells in biopsied tumor tissue is often used for tumor staging, and these antibodies can be used to identify mitotic cells.

That our discussions moved from laboratory findings to clinical uses is one indication of how far hybridoma research has come. We hope to organize the third hybridoma symposium for this area early next year.

Physicians who desire additional information may write Frances M. Davis, Ph.D., Department of Chemotherapy Research, Box 52, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030.

Bright stars Bright futures

Celebrate the Season with Pediatric Christmas Cards

The annual sale of Christmas cards designed by UT MDAH pediatric patients is under way and offers an expanded selection this year, including two new deluxe designs (one featuring a sesquicentennial motif), a gift tag design, and the Collector's Edition—an assortment of cards from past years. Note cards for use year-round are also available.

Volunteer Services, which sponsors the yearly sale, sold a record 2.5 million cards last year. Funds earned from the sale support special activities for the pediatric patients —summer camp and a Colorado ski trip, for example—and they bolster other pediatric programs by providing supervisors, a Spanish-speaking interpreter, school supplies for classes taught at the hospital, and a homelike cottage that provides a place for families to stay together while the children undergo treatment. Fifteen college scholarships and five vocational scholarships are also made possible by the card sales. Sets of cards range in cost from $7 to $10. For an order form and a brochure showing the cards, write M. D. Anderson Volunteer Services, Box 114, 6723 Bertner Avenue, Houston, Texas 77030.

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Surveillance of these patients requires the collaboration of several clinical services. The preventive oncologists and their staff members, under Winn's direction, take the medical and family histories and perform a physical examination that includes a digital rectal examination, fecal occult blood test, blood analysis, and a chest roentgenogram.

The medical history includes information relating to gastrointestinal symptoms, extracolonic manifestations associated with familial polyposis, and any individual history of polyps or cancer. This information is being collected as the Special Risk Clinic data base. We intend to integrate this data base with others at Anderson Hospital including the health survey data base of the Department of Cancer Prevention, the colorectal surgical data base of the Section of Gastrointestinal Surgery, and the endoscopy data base established by the Section of Gastrointestinal Oncology and Digestive Diseases in collaboration with the American Society for Gastrointestinal Endoscopy.

A detailed family history is elicited from each patient referred to the Special Risk Clinic, and the information is reviewed and interpreted by Louise Strong, M.D., Sue and Radcliffe Killam Professor of Genetics. The family history includes information on all of the patient's first-degree relatives—their medical history and current age or age at death.

In collecting the family history, it is as important to include individuals who have no history of colon cancer as it is to include those who have or had this illness. With information on all individuals at risk in a family, it is possible to determine the probability of cancer, colon cancer in particular, occurring by chance or according to some specific genetic or environmental model.

For families in which close relatives have or had colon cancer,

History of a Patient

A 44-year-old woman with a history of familial polyposis was seen at M. D. Anderson Hospital for evaluation of an acute episode of rectal bleeding. Eighteen years ago, when she experienced abdominal discomfort and rectal bleeding, she had been diagnosed as having familial polyposis. At that time, proctoscopic examination and a barium enema had revealed numerous colorectal polyps. She had been treated with a total abdominal colectomy with an ileoproctostomy. Pathologic examination of the resected colon had shown many adenomatous polyps (Fig. 1), one polyp containing carcinoma in situ. Since then her annual screening had included a proctosigmoidoscopic examination; any polyps found in the retained rectal segment were removed. She had been in good health except for the recent episode of rectal bleeding.

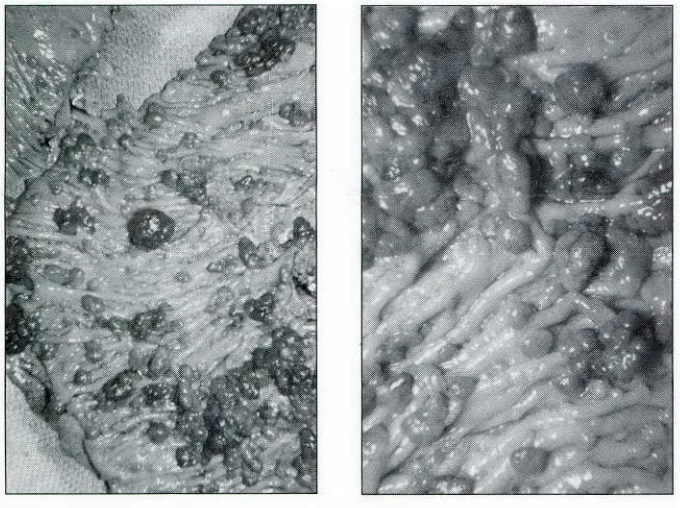

Fig. 1. Adenomatous polyps in resected colon of patient who sought treatment because of abdominal pain and rectal bleeding. Familial polyposis was diagnosed on the basis of medical and family history, proctoscopic examination, and barium enema. A total abdominal colectomy with ileorectostomy was performed because of the patient's 100% risk of colon cancer. One polyp proved to have carcinoma in situ. (From Boman and Levin, Familial polyposis, Hospital Practice, *May 15, 1986, copyright 1986 by HP Publishing Company. Reprinted with permission.)*

Illness Affected Mother, Sister, Daughter

The patient's family history (Fig. 2) was remarkable in that her mother had died at age 36 of generalized sepsis secondary to a perirectal abscess, which, considered in retrospect, may have been an undiagnosed rectal cancer. One of the patient's sisters had also been found to have polyposis of the colon at age 28; a total colectomy with ileorectal anastomosis had been performed, and two synchronous colon carcinomas had been found in the resected colon. She had died at age 37 of metastatic colon cancer.

When the patient's three children were screened, the oldest daughter, 15, was diagnosed as having familial polyposis. A total colectomy with ileorectal anastomosis was performed the following year, and no evidence of malignancy was found. She continues to have semiannual medical evaluations.

A nephew is reported to have multiple polyposis of the colon.

Patient's Examination and Treatment

A detailed ophthalmoscopic examination showed the patient to have bilateral hypertrophic lesions of the retinal pigment epithelium (Fig. 3). A radiographic bone survey showed an

we obtain a more extended family history to determine the most likely genetic or environmental model that can account for the familial aggregation. We construct pedigrees from the family history and counsel patients who are at high risk of colon cancer about their risk and the need for screening.

Surveillance

The screening program for patients involves an endoscopic procedure that is performed by Bernard Levin, M.D., Robert R. Herring Professor and chief of the Section of Gastrointestinal Oncology and Digestive Diseases, and other physicians in that section. The specific recommendations for endoscopy depend on the patient's cancer risk. In families that have one of the well-defined hereditary syndromes, members who inherit that trait have a nearly 100% risk of developing cancer. In persons with familial polyposis syndromes, the polyps usually occur in the second decade of life, which is why annual flexible sigmoidoscopy examinations are usually begun at age 14. In persons who have the nonpolyposis syndromes, the risk of cancer begins in the third decade, so that annual flexible sigmoidoscopy exams are recommended from age 20 on.

In the general population, in contrast, the risk of colon cancer begins at age 40. Not considered at high risk, this group is not screened by the MDAH Special Risk Clinic. Nevertheless, all standard-risk asymptomatic persons should follow the recommendations for screening established by the American Cancer Society and distributed by the Texas Division of the American Cancer Society Colorectal Task Force: an annual digital rectal exam, beginning at age 40; an annual stool blood test, beginning at age 50; and a proctosigmoidoscopic exam every three to five years after two initial negative annual exams are done at age 50 and 51.

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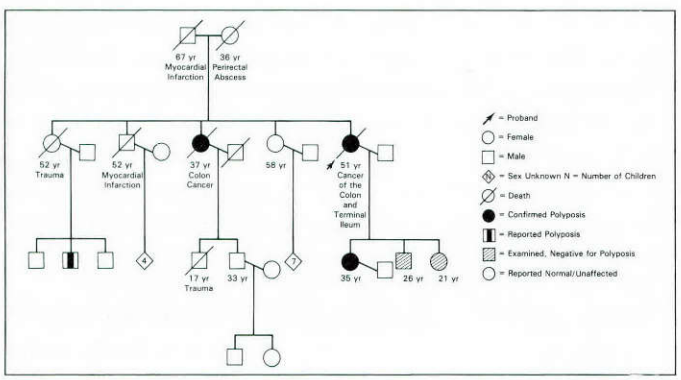

Fig. 2. Family pedigree of the patient (proband) details findings of more than three generations. (Prepared with the assistance of Louise C. Strong, M.D.)

osteoma in the proximal fibula. Proctoscopic examination revealed a 4-cm villous adenomatous polyp in the retained rectal segment.

She was treated surgically with a proctectomy and ileostomy; the pathologic examination showed an adenocarcinoma arising in the villous adenoma with invasion of the inner half of the muscularis propria. Lymph node involvement was not evident.

The patient continued to be screened after the operation. Two years later, she was found to have a villous adenoma of the periampullary region. A subtotal gastrectomy was performed and no evidence of malignancy found. But the patient developed recurrent bleeding from the ileostomy, and ileoscopic examination revealed an adenocarcinoma of the ileum arising in a large ileal polyp.

The patient's ileum was resected and another ileostomy was established; pathologic examination showed cancerous invasion through the bowel wall and metastatic disease in one of 14 regional lymph nodes. A year later, the patient developed locally recurrent metastatic carcinoma of the pelvis. She was treated with systemic chemotherapy but died of recurrent cancer at age 51.

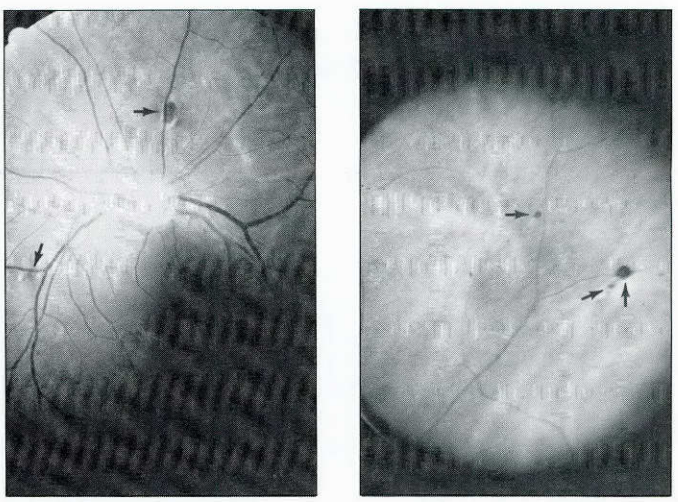

Fig. 3. Congenital hypertrophy of the retinal pigment epithelium is closely linked to the familial polyposis trait in some kindreds. Retinal lesions are asymptomatic and tend to occur in patches in one or both eyes. The patient discussed in the family history had lesions in the central portion of the retina in one eye and on the periphery in the other (arrows). (From Boman and Levin, Familial polyposis, Hospital Practice, *May 15, 1986, copyright 1986 by HP Publishing Company. Reprinted with permission.)*

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Bone Marrow Transplantation Success Brings Patients and Physicians to Reunion

Last June 40 patients who had undergone bone marrow transplantations at UT MDAH came to a hospital reunion to celebrate their improving health after having had leukemia, lymphoma, myeloma, or a solid-tumor type of lung cancer.

To be able to see so many well-functioning transplantation patients all at once made the reunion a grand affair for Karel A. Dicke, M.D., professor of medicine and chief of the Bone Marrow Transplantation Center since 1975.

Since Dicke came from the Netherlands to head the program, transplantations have multiplied from one a year to 145 last year. In the last 10 years, 700 patients ranging in age from 4 to 69 years received bone marrow transplants at UT MDAH. Currently, about 200 patients are alive six months or longer after the procedure, seven years being the longest survival.

Bone marrow transplantation—done to restore a patient's hematopoietic system after it is deliberately disturbed by high-dose cytoreductive therapy—has become a subspecialty with complexities and problems that must be solved by research, Dicke said, and one that is well served by interinstitutional and international collaborations. In 1984, the Anderson people organized the first international symposium on autologous bone marrow transplantation (ABMT), and they will host the third one in Houston December 4-5 (the second was in Parma, Italy), and perhaps the fourth in 1988.

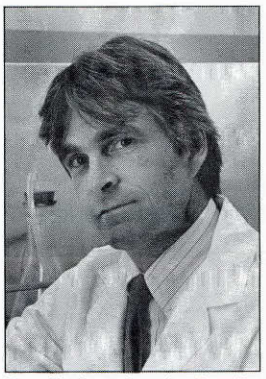
Autologous transplantation has surpassed allogeneic transplantation, Dicke explained. This is so because only 10% to 15% of the patient population is eligible for sibling-to-sibling transplants, and because methods of purging bone marrow of neoplastic cells by high-dose chemotherapy and of testing bone marrow for the absence of cancer cells have improved much over the years.

Detecting Tumor Cells in Bone Marrow

On the horizon are new laboratory techniques to assure that the bone marrow is free of cancer cells. Two of these were developed by Mary Jean Hodges, Ph.D., and Christopher L. Reading, Ph.D., both researchers in the Bone Marrow Transplantation Center.


Dr. Mary Jean Hodges

Hodges works with Joel Bressler, Ph.D., of the Department of Clinical Immunology and Biological Therapy to develop for clinical practice a method by which oncogenes are used to detect abnormal, and therefore cancerous, gene expression in bone marrow cells.


Dr. Christopher L. Reading

"We are at the point at which we do this routinely in the lab with bone marrow samples from patients," Hodges said. "We can detect any gene or any virus we want to look at, and we hope that the technique will be applicable whenever one needs to detect disease that may be present in only a small proportion of cells."

One drawback of the methods available now, she said, is low sensitivity. "With current methods, we can tell whether a particular gene is being expressed in tissue, but it has to be present at fairly high levels. With the method we are developing, with oncogenes as probes, we can detect one abnormal gene in a million cells if we need to."

In Reading's laboratory, the researchers use monoclonal antibodies that react specifically with different cell types in the bone marrow.

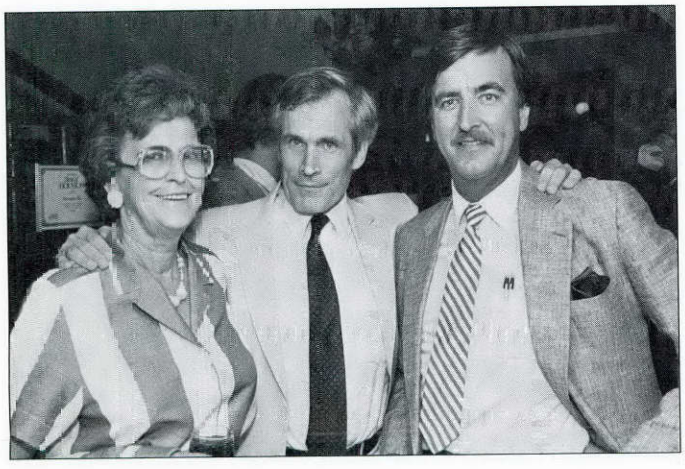
In 10 years, 700 patients received bone marrow transplants at UT MDAH.

After treatment with the monoclonal antibody, Reading explained, cells are treated with a magnetic-affinity colloid, a reagent he developed. This colloid binds to the antibody-reactive cells. The cell mixture is then passed through a column of screens magnetized by a sammarium cobalt magnet. The positive cells are retained in the steel screen and the negative cells flow through and into a syringe.

The procedure, Reading said, "has worked consistently well. The system can be used to remove antibody-reactive cells, and it can be used to deplete bone marrow of mature T cells in allogeneic transplantation or to purge tumor cells from autologous bone marrow. After six years of development, this magnetic removal of tumor cells is ready for clinical use."

Improved Results in Leukemia Patients

For the short term, last year's ABMT program achieved good results for patients with acute myelogenous leukemia.



Dr. Karel Dicke (center) with Mariam Young of Clarksville, Tenn., who came to reunion of bone marrow transplantation patients with her son, Dr. Morris Young.

"Among 17 patients, the projected 18-month disease-free survival is 75%," Dicke said, "although patient selection might be one of the reasons for this promising result." The study was not truly randomized, he explained, because patients needed to volunteer for it and the volunteers turned out to be patients in good condition.

"Selection is a difficult problem," Dicke said. "We tried to do it as a randomized study, but at that time the patients did not want to enter the transplantation program. Now it is the other way around—patients like to have transplantation, now that they see the remissions it can produce."

Transplantation results for patients with acute lymphocytic leukemia have also improved, he said, "because the normal chemotherapy that precedes the high-dose program has become excellent. At the time the marrow is collected, therefore, the leukemic cell count may be very low, so that few leukemic cells are reinfused into the patient."

At UT MDAH, he said, the most effective high-dose chemotherapeutic program for patients with acute leukemia has turned out to be CBV, a combination of cyclophosphamide, BCNU (carmustine), and VP-16-213 (etoposide). In some cases, it is administered twice to strengthen and lengthen the patient's remission. Then, three months after the patient has undergone the first high-dose chemotherapy program and ABMT, Dicke explained, another high-dose chemotherapy regimen is administered. "In our hands," Dicke said, "CBV seems to be very active in acute leukemia."

For patients who have relapsed with Hodgkin's disease, the MDAH team has a collaborative program with a University of Nebraska team headed by James Armitage, M.D. "We have treated 60 patients among whom the complete remission rate is 47%," Dicke said. "Our first results with 30 patients were published in the *Annals of Internal Medicine* early this year. Since then, we have treated 30 more patients with ABMT, and the results are holding."

International Collaborations

The international symposia are tightening connections between bone marrow specialists everywhere. Dicke and the Nebraskans are working with physicians in France and the Netherlands—Thierry Philip, M.D., of Lyons and Ton Hagenbeek, M.D., of Rotterdam—to study the effect of high-dose chemotherapy in patients with non-Hodgkin's lymphoma who have relapsed but are responding to normal-dose chemotherapy. One aspect of the program, just beginning, is "involved-field irradiation," which means that, instead of the whole body, primary areas of disease involvement—usually the mediastinum or abdomen—are irradiated before transplantation.

Results for patients with acute lymphocytic leukemia have also improved.

New Breast Cancer Protocol

For patients with stage IV breast cancer who respond to normal-dose chemotherapy, Dicke is studying a new protocol that consists of bone marrow removal, high-dose chemotherapy, bone marrow transplantation, a repeat course of high-dose chemotherapy, and a second ABMT procedure. "We did this for lung cancer patients with little success," he said, "but it is new for patients with breast cancer. We have treated 10 patients so far and have seen good responses, but we have no idea how long the responses will last. It is encouraging, though, to have patients come in with nodules of the skin and to see these disappear."

Dicke stressed that the breast cancer high-dose chemotherapy and transplantation program is useful only for patients who respond to normal chemotherapy. Nonresponding patients are not likely to gain anything from such risky treatment.

"We have to look at the benefit-risk ratio for all our patients," Dicke said. "It is crucial for us to ask: what does a patient gain from a high-dose program to be worth the suffering that high doses of chemicals often cause? If we can change the natural history of the disease with chemotherapy, and in some cases with radiotherapy—and use bone marrow transplantation to protect the patient's hematopoietic mechanisms—that makes it worth the pain these patients often experience."

Physicians who desire additional information may write Karel A. Dicke, M.D., Section of Bone Marrow Transplantation, Department of Hematology, Box 55, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030.

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Management

Endoscopic examination and surgical intervention are the main techniques designed to eliminate the risk of colon cancer in patients with a defined hereditary syndrome. Because cancers usually arise from adenomatous polyps in these patients, the cancer risk is related to the number of polyps present. A few polyps can be endoscopically removed, but most patients will require surgical removal of the colon at the time of diagnosis. For patients with this syndrome, the surgical options, depending on the number of polyps in colon and rectum, include abdominal colectomy with ileorectal anastomosis, abdominal colectomy with mucosal proctectomy and reservoir ileoanal anastomosis, or total proctocolectomy with an ileostomy.

Colon cancer ranks second as a cause of cancer death.

Molecular Genetic Studies

Since the identification of people who have a genetic predisposition to colon cancer provides an opportunity for prevention, basic research is being done to identify genetic markers associated with hereditary colon cancer. Staff members of the Section of Cellular Genetics analyze chromosomes of cells isolated from these patients, hoping to identify a specific chromosomal defect associated with the disease. Other researchers in the section study the susceptibility of cultured lymphocytes to mutagens to detect possible chromosomal instability in these patients.

My research involves the use of molecular biologic methods to try to identify a chromosome that contains a major gene associated with the inherited predisposition to colon cancer. One study, performed in my laboratory by David Wildrick, Ph.D., involves analysis of DNA isolated from normal and colon cancer tissues by Southern (DNA) blot hybridization to determine whether heterozygous gene loci on a specific chromosome are reduced to homozygosity in the tumor. If tumor-specific loss of heterozygous loci were detected, this would suggest that the chromosome to which these loci are mapped might contain a major gene associated with colon cancer.

In another of our laboratory projects, normal and malignant cells from hereditary colon cancer patients are cultured, and molecular methods are used to clone a complementary DNA library from mRNA isolated from these cell cultures. We plan to use differential gene screening to detect possible gene loss or gene activation in the colon carcinoma cells compared with that in normal colonic epithelial cells.

If we succeed in detecting a genetic marker associated with the hereditary predisposition to colon cancer, it should be useful for genetic counseling, including carrier detection and prenatal diagnosis in high-risk families. Moveover, identification of the chromosome that harbors such a gene could eventually lead to the successful cloning of a colon cancer gene.

The molecular characterization of the gene and its protein products is likely to provide insight into the mechanisms of colon carcinogenesis and thus lead to possible strategies for therapeutic intervention.

Physicians who desire additional information may write Bruce M. Boman, M.D., Ph.D., Section of Gastrointestinal Oncology and Digestive Diseases, Box 68, The University of Texas M.D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030.