



**THE MD ANDERSON
MANUAL OF** **MEDICAL**
ONCOLOGY

FOURTH EDITION

**Mc
Graw
Hill**

HAGOP M. KANTARJIAN

ROBERT A. WOLFF

ALYSSA G. RIEBER



The MD Anderson Manual of Medical Oncology

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The MD Anderson Manual of Medical Oncology

Fourth Edition

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Dedication



Emil J Freireich, MD
March 16, 1927 – February 1, 2021

Dedication of the fourth Edition of “The MD Anderson Manual of Medical Oncology” to Emil J Freireich, a Legendary Trailblazer in Cancer and Leukemia Research and Therapy

Emil J Freireich was a founding father of modern cancer research, and leader of the world’s first generation of cancer research pioneers.

Following his medical training at the University of Illinois College of Medicine at Chicago, and internal medicine training at Cook County Hospital and Presbyterian Hospital, he moved to the National Cancer Institute (1955-1965), where he made his first seminal discoveries: the benefit of platelet transfusions in reducing bleeding; the design of the first-ever continuous-flow blood cell separator that extracted platelets from whole blood; the development of multidrug regimens that paved the way for the cure of childhood acute lymphoblastic leukemia (ALL).

In 1965, Freireich moved to Houston and spent the next 55 years at MD Anderson, his real home. He was a founding member of the institution, which owed much of its early success and reputation to his work and that of his mentees. Freireich’s name became synonymous with that of MD Anderson. He created a department of Developmental Therapeutics (DT), dedicated to medical cancer research and to developing novel cancer strategies. Over the next 15 years, he attracted hundreds of cancer researchers from all over the world who, like him, were convinced that cancer was curable and were determined to accomplish this. Many of the early chemotherapy drugs (cytarabine, Adriamycin, cisplatin, others) were developed during this period, and became building blocks for curative combinations. Together with Dr Gerald Bodey, Freireich discovered the association between neutropenia and increased risk of infections and developed the concept of empiric antibiotic therapy to prevent and treat fever and infections in patients with cancer. This, along with platelet transfusions, made cancer care safer and opened the research venues for intensive chemotherapy and stem cell transplantation in hematologic and solid tumors. The pheresis machines he helped to create were later used to collect stem cells for the purpose of transplantation.

In DT, and later as a senior leader at MD Anderson, Freireich trained and mentored hundreds of oncologists, many of whom later created their own legacies and helped hundreds of thousands of patients with cancer. He also created in 1966 the first training fellowship program in cancer and established clinical-translational research and care as a new critical discipline in oncology.

To the hundreds of us who trained under Freireich, he and his stories and education are indelibly cemented in our memories. In recognition of his massive contributions to education in cancer research and care, we dedicate this fourth edition to Emil J Freireich.

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New in this edition is the online-only presentation of clinical cases, *The MD Anderson Manual of Medical Oncology Cases*, for readers to explore, with each case linked to the relevant chapter.

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A Brief History of MD Anderson Cancer Center

Houston's evolution into the fourth largest city in the United States was propelled by four seminal events. First was the Great Galveston Hurricane of 1900, which destroyed the city port of Galveston and led to the realization that Houston could become a viable and safer deep-water port; this led to the widening of the Ship Channel to offer direct access to Houston. Second was the discovery of oil at Spindletop in Beaumont, Texas in 1901. This prompted the development of the oil industry in Texas and transformed Houston from a small town into a large city. Third was (of course) the commercialization of air conditioning in 1950's, which made Houston (and many Southern cities of the United States) more livable. And lastly, the allocation of land for the Texas Medical Center created the largest medical center in the world with one of the highest densities of clinical facilities for patient care, basic science, and translational research. The Texas Medical Center is a major contributor to Houston's economy and growth.

Several additional factors contributed to the creation of The University of Texas MD Anderson Cancer Center in Houston and its development into one of the most important cancer centers in the world. First was the generous philanthropy of visionary Texans such as Monroe Dunaway Anderson (Fig. 1) (his nephew died of leukemia in 1936) and his partner Will Clayton, who founded the charitable MD Anderson Foundation, which helped create the Texas Medical Center in 1945.



FIGURE 1.



FIGURE 2.

The charter of the Anderson Foundation did not specify how the money should be used, but Mr. Anderson's trustees and close friends—Colonel William Bates, John Freeman and Horace Williams—leaned strongly in favor of health care. Soon after taking possession of the estate from its executors, the trustees turned to Dr. Ernest Bertner (Fig. 2) for advice. Dr.

Bertner was a prominent Houston surgeon and gynecologist who was well known to the trustees because of his care for cancer patients, despite inadequate facilities and treatment options (he was later called the “father of the Texas Medical Center”).

The trustees and Dr. Bertner noted that the 1941 Texas legislature authorized the University of Texas to create a hospital for cancer research and treatment, allocating \$500,000 for the purpose. Today, that figure would be approximately \$8 million. The Anderson trustees, with Dr. Bertner's guidance, seized the opportunity and offered to match the \$500,000 legislative appropriation, if the hospital was to be named for Monroe Dunaway Anderson and located in Houston. The legislature accepted their offer. The trustees then purchased 134 acres of mosquito-infested land to create the Texas Medical Center, stating that the new cancer hospital would be located there. They made it known that the new state hospital should be an academic institution. In fact, MD Anderson was the first comprehensive cancer hospital to be associated with a major university as an independent free-standing unit.

In 1942, The University of Texas Board of Regents appointed Dr. Bertner as the director of the new hospital. A 6-acre property near downtown was purchased from the estate of Captain James A. Baker, grandfather of former Secretary of State James Baker III, and became the first campus of the hospital. An empty

carriage house became the office and stables were the research laboratories. Twelve surplus army barracks were procured for patient clinics (Figs. 3A-C). With the addition of 22 leased beds at Hermann Hospital, the dream became reality. A small faculty of physicians and scientists was recruited from the University



FIGURE 3A.



FIGURE 3B.



FIGURE 3C.

of Texas Medical Branch in Galveston, and cancer patients finally had a home. The name proposed in 1941 was the “Texas State Cancer Hospital and the Division of Cancer Research”, which was changed to “M.D. Anderson Hospital for Cancer Research of The University of Texas” (to acknowledge the donation of M.D. Anderson). The name was again changed in 1955 to “The University of Texas M.D. Anderson Hospital and Tumor Institute at Houston” (to avoid the word “cancer” which elicited fear and avoidance). In 1988 the name was finally changed to its current “The University of Texas MD Anderson Cancer Center”.

In 1946, Dr. Bertner persuaded Dr. Randolph Lee Clark, a native Texan, to become president of what was to become The University of Texas MD Anderson Cancer Center. Dr. Clark, a widely recognized surgeon, concentrated on recruiting an excellent surgical faculty and then set upon acquiring all the basic and clinical scientists and clinicians. From the outset, all efforts, whether administrative, clinical or research, were focused on developing excellence in research-driven cancer care. Forty-six patients were receiving treatment in these early quarters when the hospital moved to its current site in March 1954 (Figs. 4A and B).



FIGURE 4A.



FIGURE 4B.



FIGURE 5.



FIGURE 6A.



FIGURE 6B.



FIGURE 6C.

Additional resources to expand the MD Anderson infra-structure (Fig. 5) and research capacities came from several venues: (1) generous donations from the oil industry; (2) the visionary research and administrative leadership under its five presidents, Drs. Randolph Lee Clark (1946–1978) (Fig. 6A), Charles A. LeMaistre (1978–1996) (Fig. 6B), John Mendelsohn (1996–2011) (Fig. 6C), Ronald DePinho (2011–2017) (Fig. 6D), and Peter WT Pisters (2017-present) (Fig. 6E); (3) the recruitment of world-renowned cancer research pioneers (some of the early legends included Drs. Emil J. Freireich, Emil Frei, Gilbert Fletcher, James Butler, Felix Rutledge, Gerald Dodd, and Sidney Wallace); and (4) the relentless research efforts of the cancer experts on the MD Anderson’s faculty.

Today, MD Anderson is one of the largest cancer centers in the world, with more than 21,000 employees and 1800 faculty; serving more than 150,000 patients with cancer in Houston every year; operating a 700-bed cancer hospital; and being ranked as



FIGURE 6D.



FIGURE 6E.

the No. 1 hospital for cancer care by the *U.S. News and World Report* in 11 of the past 14 years. The MD Anderson Cancer Center research has resulted in numerous discoveries that became standards of care across many types of cancers, and that have saved the lives and/or improved survivals and outcomes of millions of patients with cancer around the world.

One component of MD Anderson’s mission is to spread its knowledge about cancer research and discoveries across the globe. This educational mission is furthered by the hematology/oncology fellowship that currently trains more than 40 medical hematology-oncology cancer specialists on its premises.

The MD Anderson Manual of Medical Oncology, created as part of our educational mission, is often written by our fellows as first authors (many of whom later join the MD Anderson faculty) and supported in depth by senior tumor specialty faculty as co-authors. We envision this fourth edition expanding into a continuously updated electronic version that educates and spreads knowledge and discoveries in cancer research and therapy rapidly and widely.

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Foreword

The MD Anderson Manual of Medical Oncology, fourth edition, articulates the personalized, multidisciplinary approach to cancer management pioneered by The University of Texas MD Anderson Cancer Center. Our unique perspective has evolved from decades of clinical practice and research with more than 1.6 million patients turning to MD Anderson for care. We are expanding our reach, making it easier for the patients and communities we serve to access our expertise. We are enabling high-impact discovery and introducing novel therapies through a leading clinical trials network. And we are setting new standards for high-touch, high-value cancer care.

This book is designed to bring a pragmatic approach to cancer management that may serve as a guide for oncologists around the world. The text reflects how MD Anderson currently operates, including many patient care practices that would not have been recognized by practitioners just a decade ago. Since the first edition, MD Anderson's experts have improved our ability to identify biomarkers that are predictive for survival, a major triumph in medical oncology that is demonstrated throughout the text.

Reflecting new advances in our research and our approach to cancer management, the fourth edition of *The MD Anderson Manual of Medical Oncology* features a wealth of new material. The sections on Lymphoma and Myeloma and Gastrointestinal Cancer contain additional chapters focused on recently defined subsets of disease and their treatment modalities. New targeted therapies are described in Lung Cancer. Additional Cancer Topics of Interest chapters detail updated knowledge in viral and fungal infections, for example, as well as oncocardiology and thrombosis. Biostatistics now has its own section, underscoring the

extraordinary wealth of information brought about by big data analytics and its application to influence value-based oncology care. Supportive and Palliative Care content reflects current approaches in advanced symptom management concurrent with a patient's entire cancer journey, starting at diagnosis.

Every chapter includes abundant tables and diagrams, including algorithms and decision trees developed at MD Anderson for specific cancers or disease subtypes; promising novel therapy targets and the latest clinical trial phase of drugs targeting them; and new molecular therapies recommended to overcome resistance to previously effective therapies.

Emphasis on safety is even more relevant now than in prior editions of this book. MD Anderson's core value of Safety drives our colleagues each day, and this was especially highlighted during the COVID-19 pandemic when we came together with diligence, determination and evidence-based protocols to ensure the safest possible environment for our immunocompromised patients. Additionally, we remain laser focused on survivorship, as advances in cancer care have increased the number of people who are cancer free or who are living with cancer as a chronic condition rather than a fatal one. We remain dedicated to our bold aspiration of maximizing our impact on humanity through research-driven patient care, education, prevention and science that contribute to Making Cancer History®.

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