

Book Reviews

DARK REMEDY: THE IMPACT OF THALIDOMIDE AND ITS REVIVAL AS A VITAL MEDICINE

By Trent Stephens and Rock Brynner. 228 pp. Cambridge, Mass., Perseus, 2001. \$26. ISBN 0-7382-0404-8.

SOME drugs have become household names — penicillin, insulin, aspirin. Most are known — indeed, revered — as lifesavers. Thalidomide, too, falls into the category of well-known drugs, but for an entirely different reason. As a medicine that maimed rather than saved, it had atrocious effects on the unborn child that make it an object of terror and horror.

Thalidomide appeared in the late 1950s — a decade of optimism about therapies, fueled largely by the success of penicillin during the Second World War. Postwar Western society was essentially at peace with the great infectious diseases, thanks to vaccines and antisera, and the new antibiotics had dramatically reduced the dangers of everyday life. Drugs were being developed for heart disease, kidney conditions, neurologic problems, and skin ailments, among other problems. The appearance of chlorpromazine in the early 1950s revolutionized the treatment of psychiatric disorders, and by the 1960s every facet of life was becoming “pharmaceuticalized,” as the Rolling Stones recognized so acutely in “Mother’s Little Helper.”

Pills for the ill led to pills for the well; about 1 million people in Great Britain were believed to be taking sedatives daily in the mid-1950s, and 1 in 7 people in the United States was believed to be taking barbiturates. Into this highly charged and lucrative medical marketplace came a new sedative in 1956. Originally manufactured by and distributed in continental Europe by Chemie Grünenthal of Germany, thalidomide was licensed to and marketed in Britain and the British Commonwealth by Distillers Company.

Laboratory tests had shown that the drug was astonishingly “safe” because it was impossible to find a dose high enough to kill a rat. Clinical testing in Germany had been scanty — packets of pills distributed to employees, samples given to local doctors — a consequence, Stephens and Brynner conclude, of the medical callousness exhibited by the Third Reich and the distorted view that still prevailed about the acceptability of various testing practices. Because of its low toxicity, the drug was sold openly, over the counter, and was heavily promoted as the safest sedative on the market.

The first baby with malformations was born on Christmas Day, 1956, before the drug went on the market; she was the daughter of an employee of Chemie Grünenthal who had given his pregnant wife some of the free tablets. During the next few years, obstetricians in Germany noted more rare abnormalities in newborn infants, especially the condition of tetra-phocomelia (literally, “four seal’s limbs”) — a condition in which the baby’s arms and legs were shortened to such an extent that the hands and feet were often attached directly to the trunk. At the same time, physicians and neurologists reported an increased incidence of peripheral neuritis in adult patients who were taking the sedative. The connection between these cases and the use of thalidomide, however, was not yet clear.



Dr. Frances Kelsey receiving an award from President John F. Kennedy.

It was in Australia in 1960 that the obstetrician William McBride prescribed the drug for women suffering from morning sickness and then, months later, as he delivered the first Australian babies with malformations, suspected a causal link. The rest of the tragedy is well known — McBride’s growing conviction that thalidomide was responsible, the difficulties of replicating the teratogenic effects in laboratory animals, the initial intransigence of the drug companies that were involved, and the important role of journalists, especially the “Insight Team” of the London *Sunday Times*, in uncovering the scandal and securing proper compensation for the victims. One estimate is that thalidomide caused peripheral neuritis in 40,000 people and malformations in between 8000 and 12,000 infants, 5000 of whom lived to adulthood.

A major issue of immediate concern in countries affected by the tragedy was the safety of other drugs. Regulatory bodies were quickly established to create guidelines for the appropriate, adequate, and effective testing of new remedies, both in the laboratory and in the clinic. Astonishingly, this was the first comprehensive drug-safety legislation in many Western countries. The United States already had a monitoring body, the Food and Drug Administration (FDA), although its working methods and its habit of fraternizing with the pharmaceutical industry made it a less effective agency than it might have been or was to become. Richardson-Merrell of Cincinnati had 10 million tablets waiting to hit the U.S. market in March 1961 when the company

confidently applied for FDA approval to market thalidomide. A newly appointed FDA medical officer, Dr. Frances Kelsey, expressed her dissatisfaction with the medical data and returned it for amplification. At the time, this was the only delaying tactic open to her. Immediately put under immense pressure from the company, its lawyers, and even some of her own colleagues, Kelsey forced the company to resubmit its application half a dozen times. It was while the company was still awaiting approval from the resolute Kelsey that the drug was withdrawn from the German market. The FDA application was soon withdrawn. The United States did not entirely escape the thalidomide tragedy, since some infants and adults were adversely affected as a result of Richardson-Merrell's testing procedures, but by and large Kelsey's vigilance protected the world's largest market from the horrifying effects of the drug.

Thus might the story of thalidomide have ended. A dangerous drug was removed from the market, and important questions were raised and addressed about the practice and ethics of developing, testing, and marketing drugs and about the relationships among industry, medical professionals, and legislators. But in 1964, Dr. Jacob Sheskin was treating patients with leprosy in Marseilles, France. While in despair at his inability to lessen the pain and misery of his patients, he found some packs of thalidomide on the dispensary shelves. Deciding that this sedative might be worth a try in patients in whom other sedatives had failed, he gave two tablets to one of his patients. The man slept, got out of bed the following morning, and after two more pills, his lesions started to heal.

Sheskin's unexpected discovery led to further research on the discredited drug: could it be useful in other inflammatory conditions? For the first time, scientists began studying its mechanisms of action, and they gradually revealed that thalidomide could modify some types of immune reactions and could be effective not only for patients with leprosy but also for those infected with the human immunodeficiency virus and those with a wide variety of autoimmune conditions, such as multiple sclerosis and inflammatory bowel disease. Research on the possibility that thalidomide might act on cancer cells revealed that it could inhibit the proliferation of blood vessels associated with the development of tumors, thus effectively stopping or slowing tumor growth. And here, finally, was a clue to the devastating effects of the drug in utero, for it was shown to interfere with the blood supply to the developing limbs of the fetus.

One of the authors of this book, Trent Stephens, is an embryologist who has been working on thalidomide for nearly a quarter of a century, and much of his own work has focused on unraveling the cellular effects of the drug. His coauthor, Rock Brynner, is a historian and novelist, and together, contributing their different skills and knowledge, they have told a compelling story decisively, with style and clarity. *Dark Remedy* deserves to be widely read.

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EDUCATING FOR PROFESSIONALISM: CREATING A CULTURE OF HUMANISM IN MEDICAL EDUCATION

Edited by Delese Wear and Janet Bickel. 215 pp. Iowa City, University of Iowa Press, 2000. \$42.95. ISBN 0-87745-741-7.

EDUCATING for Professionalism: Creating a Culture of Humanism in Medical Education presents a candid and sometimes painful look at the culture of undergraduate medical education. "We are learning when you least expect it," says an anonymous medical student in the book's epigraph; this may be an alarming notion, given the current state of health care in America. The 13 essays in the book, which were written and edited by a diverse group of respected medical educators, address this notion and offer nothing short of hope for the future.

"How does . . . a commitment to the well-being of others either wither or turn into something barely recognizable?" asks one essayist. The answers, which address all stages of the professional development of physicians, are familiar and are outlined in the first part of the book.

Premedical students develop a one-dimensional, competitive focus that best serves only the admission committees at medical schools. The curriculum they go on to study is strikingly disconnected from the mission statements of the schools; rarely do course objectives include the inculcation of altruism, advocacy, and other forms of moral development. Moreover, although schools provide a formal education and assess performance, it is the unseen transmission of the dominant culture rather than the formal program that may have the greatest impact on the professional development of students. It is within this "hidden curriculum" that students, even as they are learning to care for patients, learn from the faculty the uses of authority, power, and knowledge. But if the members of the faculty are inadequately supported and generally overwhelmed, thus leading too many students to draw negative conclusions, a dangerous downward spiral will start and "academic medicine will have eaten its seed corn." A powerful antidote, the mentor-protégé relationship, is seldom a celebrated part of medical-school culture.

The absorbing essays in the first third of the book are true to its theme of self-reflection as an integral aspect of professional development. They are devoted to understanding the experience of undergraduate medical education, and they challenge the reader to consider the effect of the guiding principles of each institution on the moral development of its students, the crucial role of the hidden curriculum, and the restrictiveness of "professional roles" for those striving for integrity and authenticity. The section ends with a discussion of the conflict between our willful commitment to traditional values of doctoring and our unconscious commitment to traits — fostered by contemporary medical education — that make it difficult to be a caring physician.

The second part of the book offers cause for hope. With the assumption that mentoring relationships, student-initiated activities, and learning to serve stimulate professional growth, this section chronicles the efforts of students, faculty, and their communities in shaping medical education. Wear and Bickel have compiled myriad examples of challenges and opportunities at this intersection of professional development and social consciousness.

In one example, a professor of philosophy, a clergyman, and a medical ethicist have collaborated to write one of the

most vital chapters, entitled “Moral Growth, Spirituality, and Activism: The Humanities in Medical Education.” Andre and colleagues, who define spirituality as “the search for what ultimately gives meaning to life,” which “grounds the deepest thinking about the person — the physician — that one wants to become,” describe the spirituality course at their institution. The authors observe, “Much of the suffering that accompanies serious disease is produced by, and can only be alleviated through, the personal meaning that one attaches to the experience” and note that the “busyness” of daily life can keep physicians from making the critical distinction between the seemingly urgent and the truly important. This essay describes a beautiful and necessary — but often lacking — aspect of the training of the fully developed “professional.”

Maintaining that the mentor–protégé relationship is central to the professional development of students, another chapter offers two new ways of framing the alliance. The writers, all educators and psychiatrists, present schematic representations of professional and personal development and argue strongly that a successful relationship must incorporate both.

The last chapters expand on the central theme that through student-directed community experiences, “the values of service and a fiduciary orientation are internalized most successfully.” These chapters highlight community-based programs that provide students with firsthand experience in attending to the health needs of various populations.

Those directly involved in undergraduate medical education will find this book inspiring. However, it should be required reading for all who believe that irreversible damage would be done to the institution of American medicine if competent, patient-centered physicians were produced only serendipitously. From an optimistic perspective, the transformation outlined in this book could have a ripple effect on its implementers and teachers and ultimately on the wider culture of medicine. But it is hard to imagine such a profound paradigm shift occurring in less than a generation. What of the interim?

Bickel with an answer, perhaps the *raison d’être* of the book:

These perilous times require that each — from student to dean — be ever developing as professionals, as communicators, as leaders. Communities *expect* leadership from physicians. And no wonder. No group is better equipped to champion improvements in the health care system. While competition and restrictions may be mounting, physicians are the ones with the greatest access to knowledge of the human body, to medical technology and resources, and to the respect of those they serve. If courageous and compassionate, each physician has enormous potential for positive impact. This book offers a wealth of ideas on better realizing these potentials. Opportunities do abound.

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TEXTBOOK OF RURAL MEDICINE

*Edited by John P. Geyman, Thomas E. Norris, and L. Gary Hart.
487 pp., illustrated. New York, McGraw-Hill, 2001. \$59.95.*

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TWENTY percent of Americans live outside metropolitan areas in what is collectively called rural America. But rural America is no more homogeneous than the metropolitan areas of Manhattan, Kansas, and Manhattan, New York. Rural America can be distinguished by its lower population density, smaller numbers of services, and fewer kinds of services, but not by a lack of diversity in terms of culture and ethnic backgrounds and the aspirations of its inhabitants. A textbook of rural medicine must reflect that diversity while assessing and describing the health and health care of 51 million people.

The editors approach this task with the combined wisdom of three men who have practiced, taught, and researched rural health care for many years. They call on colleagues from academic centers around the country to expand on an eclectic group of topics designed to profile useful strategies that improve the quality of rural health care. The editors state that their intended audience is rural clinicians, clinician teachers, residents, medical students, other health professionals interested in rural health care, health services researchers, and others interested in rural health policy. To address this broad group on a topic so diverse is a huge, if not impossible, task. The authors make a valiant but not altogether successful attempt.

The first section of the book describes the rural environment, the rural patient, the rural physician, the rural health care team, and the emergence of a federal policy on rural health. The picture seems skewed and harsh and appears to reflect years of personal frustration on the part of the authors. The statistics that health care researchers and policy pundits like to have at their fingertips are there, but the value of these facts to practitioners and students is less clear. The introductory section does give a fascinating view of the evolution of American health care and its effect on rural health care. As described here, the growth of medical specialization and subspecialization changed the focus of medical care and education from care by generalists to the treatment and cure of individual illnesses; the prevalence of rural poverty and the explosion in the number of women in medicine decreased the pool of primary care physicians willing to choose rural practice; and the rapid growth in the number of midlevel practitioners, most of whom stay in urban and suburban settings, has not stemmed the flow of clinicians away from rural practice.

This summary of rural practice seems unlikely to inspire young clinicians to rush to embrace the challenge. But just when all hope seems to be gone, Rosenthal’s chapter on the rural health care team reminds those of us who have practiced rural medicine why we did so. The ability to apply the principles of population-based medicine and public health to daily practice and to solve a medical problem by calling on the resources and resourcefulness of an entire community without task forces, seed money, committee meetings, and planning grants is exciting and satisfying to all involved. This explanation is what might make a student interested in rural medicine.

A few medical problems are singled out for special atten-

tion. The selection seems arbitrary, leaving out preventive care, the care of heart disease, and the treatment of occupational injuries. Some chapters in this section move beyond the usual textbook discussions. For example, the author of the chapter on mental health flatly states that "country people are different than city people." It is this ability to incorporate the qualitative and quantitative view of rural medicine, perhaps on the basis of direct rather than academic experience with rural America, that allows some of the authors to describe rural medicine in a meaningful context. The chapters on both mental health and dental health suggest ways of providing care in smaller, underserved areas. Examples include providing mental health services at primary care sites and teaching the primary care clinicians the basic skills needed to incorporate dental health into well-child visits. It is this type of creative endeavor and energy that may inspire students, nurses, administrators, and rural physicians to accept the challenge of rural medicine.

The section on the organization and management of rural health care accounts for over a third of the book. Perhaps this reflects the expertise of the editors and authors and their views of health care. Or perhaps it reflects the current reality of health care, in which the direct delivery of services accounts for only about one quarter of the expended resources. Several of the chapters are of interest to a limited group of people. Conversely, the short chapter on quality assessment illustrates the value of having a unique rural focus, highlighting the gaps and potential flaws in several studies that purport to compare the quality of care in rural and urban settings. The authors end the chapter with a list of challenges that should be read and addressed by all members of quality-assessment groups who desire to understand and to respond to the medical, cultural, and social needs of people in rural areas.

Who will actually buy and read this book is not clear. Medical students are unlikely to find the time or desire to read the sections on practice management, continuing medical education, and systems integration. Practicing rural physicians will find limited information on solutions to their challenging daily problems. The book will provide urban researchers and policy advisors with statistics, a flavor of rural health care, and an extensive list of challenges.

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BOOKS RECEIVED

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ANESTHESIA AND CRITICAL CARE

Chest Medicine: Essentials of Pulmonary and Critical Care Medicine. Fourth edition. Edited by Ronald B. George, Richard W. Light, Michael A. Matthay, and Richard A. Matthay. 688 pp., illustrated. Philadelphia, Lippincott Williams & Wilkins, 2000. \$89. ISBN 0-683-30667-7.

BIOMEDICAL SCIENCE

- An Atlas of Preimplantation Genetic Diagnosis.** (The Encyclopedia of Visual Medicine Series.) Edited by Yuri Verlinsky and Anver Kuliev. 174 pp., illustrated. New York, Parthenon, 2000. \$149. ISBN 1-85070-760-X.
- Biochemistry Illustrated.** Fourth edition. By Peter N. Campbell and Anthony D. Smith. 218 pp., illustrated. Philadelphia, Churchill Livingstone, 2000. \$39.95. ISBN 0-443-06217-X.
- Biomimetic Sensor Technology.** By Kiyoshi Toko. 211 pp., illustrated. New York, Cambridge University Press, 2000. \$74.95. ISBN 0-521-59342-5.
- Brain Imaging in Substance Abuse: Research, Clinical, and Forensic Applications.** (Forensic Science and Medicine.) Edited by Marc J. Kaufman. 425 pp., illustrated. Totowa, N.J., Humana Press, 2000. \$135. ISBN 0-89603-770-3.
- Cellular Mechanisms in Airways Inflammation.** (Progress in Inflammation Research.) Edited by Clive P. Page, Katherine H. Banner, and Domenico Spina. 362 pp., illustrated. Boston, Birkhauser, 2000. \$169. ISBN 3-7643-5852-1.
- Clinical Bacteriology, Mycology and Parasitology: An Illustrated Colour Text.** By W. John Spicer. 221 pp., illustrated. Philadelphia, Churchill Livingstone, 2000. \$39.95. ISBN 0-443-04365-5.
- Clinical Chemistry.** Fourth edition. Edited by William J. Marshall. 362 pp., illustrated. St. Louis, Mosby, 2000. \$39.95. ISBN 0-7234-3159-0.
- Lysosomal Pathways of Protein Degradation.** (Molecular Biology Intelligence Unit 11.) Edited by J. Fred Dice. 108 pp., illustrated. Georgetown, Tex., Landes Bioscience, 2000. \$119. ISBN 1-58706-003-5.
- Merkel Cells, Merkel Cell Carcinoma and Neurobiology of the Skin: Proceedings of the 1st Symposium of the Japanese Society for Ultrastructural Cutaneous Biology, Tokyo, 24-25 November 1999.** (International Congress Series 1187.) Edited by Hiroyuki Suzuki and Tomomichi Ono. 256 pp., illustrated. Amsterdam, Elsevier, 2000. \$157. ISBN 0-444-50221-1.
- The Pineal Gland and Cancer: Neuroimmunoendocrine Mechanisms in Malignancy.** Edited by Christian Bartsch, Hella Bartsch, David E. Blask, D.P. Cardinali, William J.M. Hrushesky, and Dieter Mecke. 578 pp., illustrated. New York, Springer-Verlag, 2000. \$169. ISBN 3-540-64051-7.
- Tissue Engineering for Therapeutic Use 4: Proceedings of the Fourth International Symposium on Tissue Engineering for Therapeutic Use, Kyoto, Japan, 23-24 September 1999.** (International Congress Series 1198.) Edited by Yoshito Ikada, with Yoshiko Shimizu. 192 pp., illustrated. Amsterdam, Elsevier, 2000. \$118. ISBN 0-444-50293-9.

EDUCATION, HISTORY, BIOGRAPHY, AND PUBLIC PRESS

- Americans with Disabilities: Exploring Implications of the Law for Individuals and Institutions.** Edited by Leslie Pickering Francis and Anita Silvers. 410 pp. New York, Routledge, 2000. \$29.95. ISBN 0-415-92368-9.
- Appleton & Lange's Outline Review for the Physician Assistant Examination.** Edited by Albert F. Simon and Anthony A. Miller. 490 pp. New York, Appleton & Lange, 2000. \$39.95. ISBN 0-8385-0373-X.
- Beyond Six Billion: Forecasting the World's Population.** Edited by John Bongaarts and Rodolfo A. Bulatao. 236 pp. Washington, D.C., National Academy Press, 2000. \$29.95. ISBN 0-309-06990-4.
- British Cardiology in the 20th Century.** Edited by Mark E. Silverman, Peter R. Fleming, Arthur Hollman, Desmond G. Julian, and Dennis M. Krikler. 390 pp., illustrated. New York, Springer-Verlag, 2000. \$49.95. ISBN 1-85233-312-X.
- The Burn Rate Diet.** By Stephen R. van Schoyck. 284 pp., illustrated. New York, HarperCollins, 2001. \$24. ISBN 0-06-019637-8.
- Climb That Mountain . . . One Last Time . . . or Was Jack Keavorkian Right?** By J.J. Van Gasse. 560 pp. Ann Arbor, Mich., Proctor, 2000. \$16.95. ISBN 1-882792-98-X.
- Culture and Subjective Well-Being.** Edited by Ed Diener and Eun-kook M. Suh. 355 pp. Cambridge, Mass., MIT Press, 2000. \$45. ISBN 0-262-04182-0.
- Diagnosis: Heart Disease — Answers to Your Questions about Recovery and Lasting Health.** By John W. Farquhar and Gene A. Spiller. 152 pp. New York, W.W. Norton, 2001. \$25.95. ISBN 0-393-05012-2.
- The Education of Medical Students: Ten Stories of Curriculum Change.** 233 pp. Washington, D.C., Association of American Medical Colleges, 2000. Price not available. ISBN 1-887748-40-7.