BOOK REVIEWS

Fiduciary Disorders

Medicine, Money, and Morals. Physicians' Conflicts of Interest. MARC A. RODWIN. Oxford University Press, New York, 1993. xx, 411 pp., illus. $25 or £22.50.

As Marc Rodwin demonstrates in his admirably researched and cogently argued book, conflict of interest is now a problem of epidemic proportions in medicine. He is not the first to discover that many prescriptions are written to gratify financial interests; at least a dozen published papers document how profoundly economic incentives distort physician practices. Rodwin builds on these findings by using court cases, congressional hearings, and medical company and hospital solicitations and presents us with the fullest catalogue of the forms that physician conflict of interest may take. Although he can be frustratingly repetitious, the evidence is daunting. His findings and recommendations must be pondered by everyone concerned with quality in health care.

The "maze of financial incentives" begins with kickbacks, or fee-splitting, by which physicians receive a percentage of the fees from referrals. He or she may also obtain kickbacks from laboratories and hospitals (in one documented case $70 in return for each admission, in another a $75,000 "loan" that could be paid off by patient referrals), from drug companies (sometimes disguised as a research grant), or from supply companies (one physician received nearly a quarter of a million dollars over a four-year period from two pacemaker manufacturers).

The financial incentives to physicians include gifts, particularly from drug companies. A 1992 Department of Health and Human Services survey of nearly 1000 doctors found that in one year 82 percent received at least one offer of a gift or payment from a pharmaceutical house, at an average value of $727 per physician. Still other doctors supplement their incomes by personally dispensing drugs or selling medical products. One advertisement from a pharmaceutical repackaging company enticed physicians with the slogan: "How to Earn $52,000 This Year with No Investment." Another counseled: "Every time you sign a prescription, it's like writing a check to the pharmacy. . . . Why not write that check to your practice instead?"

However sleazy these arrangements, conflict of interest is still more significant in physician self-referrals and in the incentives provided by hospitals and other health care facilities. Rodwin adeptly explains the myriad of deals that can be struck, all of which may subvert the commitment of the physician to the patient's well-being. Doctors invest in diagnostic laboratories and nursing home facilities and then to ensure profits send their patients to them. In Florida, for example, "over 80 percent of the direct owners of health care facilities . . . are physicians." Moreover, hospitals lend physicians money to start their practices and provide income guarantees or, in the case of for-profit facilities, stock in the enterprise, all in return for patient referrals. Legal handcuffs are not necessary—as one hospital official explained, "the physicians 'owe us.' We haven't been disappointed yet."

Rodwin is among the first to recognize that conflict of interest is entering a novel and still more intractable stage. Traditionally, financial incentives have inflated the amount of medical treatment by encouraging needless tests and procedures. Now there are incentives for physicians to decrease services. The controlling influences are not drug companies or device manufacturers but hospitals, government regulators, and health maintenance organizations that want physicians to reduce the costs incurred in referrals, diagnostic tests, and therapies.

Under Medicare's prospective payment reimbursement program, hospitals have a critical stake in doctors' treating patients quickly and efficiently, thereby maximizing turnover and reducing length of stay, and they are hiring and promoting physicians who meet this standard. HMOs are profitable to the extent that employee physicians see many patients and keep down treatment bills, and many of the organizations (estimates are between 20 and 60 percent) use incentive payments to shape physicians' behavior. Indeed, since the federal government seems likely to rely upon HMO-type organizations in its projected national health care program, the pattern of rewarding doctors for *not* treating are likely to become more entrenched. As Rodwin astutely notes, managed care means that both the patient and the doctor are managed.

What can be done to curb physician conflict of interest? The record of past attempts is not impressive. Despite their illegality, kickbacks continue; ethical guidelines notwithstanding, drug companies still dispense gifts, and regulations to eliminate self-referrals and hospital-provided incentives have demonstrated little efficacy. The reasons for failure are numerous and discouraging. State medical licensing boards pay the issue almost no attention; even when an organization like the American Medical Association condemns a practice it has no enforcement mechanisms; peer review of patient care only compensates for overtreatment after the fact; government agencies enforce prohibitions sporadically; physician disclosure of a conflict of interest to patients (for example, of ownership of shares in the nursing home the physician is recommending) provides little protection; and federal regulations include so many "safe harbors" exclusions that hospitals and HMOs have more than enough latitude to seek their own ends.

The problems are more profound in clinical practice than in other areas. In clinical research, for example, the National Institutes of Health had recognized by the mid-1960s that conflict of interest undermined the relationship between investigator and human subject; the researchers wanted to develop new knowledge and advance their own careers, not to cure their subjects. This formulation led directly to the creation of institutional review boards and to the unprecedented emphasis on informed consent. To be sure, neither the NIH nor the universities have resolved the emergent dilemmas of researchers' financial conflict of interest, but deliberations and the initial codes are far more extensive for the laboratory than the examining room.

Moreover, Rodwin is surely right in insisting that medicine lags behind other professions in regulating conflict of interest. Law firms are almost obsessed with the subject, perhaps because the law has a built-in policeman, in the person of the presiding judge, who monitors breaches. Stockbrokers know they must account ultimately to the Securities and Exchange Commission and politicians to the voters. Not that conflict of interest is eliminated, but it is more effectively restrained.

All this conceded, the prospect for medicine's catching up is not bright. Not only are HMOs, government regulators, and hospital officials likely to influence physician practice patterns to suit their own agendas, it is considerably more difficult to monitor undertreatment than overtreatment. Payoffs for referring patients at least may show up on income tax returns. Short of a comprehensive and effective quality-assurance program, which would be exceptionally difficult to administer, it will be almost impossible to know whether the doctor should have ordered a CAT scan or called in a specialist. And to the degree that the forthcoming national health plan curbs

malpractice suits, penalties for undertreatment will decline further.

With due modesty Rodwin urges changes on three fronts. First, physicians both individually and collectively must contemplate the nature of fiduciary relationships as thoroughly as lawyers, pension officers, and corporate directors have done. Medicine does have important lessons to learn from them. Second, federal and state authorities must be more consistent in prohibiting conflict of interest and more aggressive in policing it. Finally, Rodwin favors making medicine still more of a regulated industry. He wants auditing czars reviewing hospital financial records and conflict-of-interest review boards setting institutional policies.

It takes a strong heart to call for yet more bureaucracy and regulation in medicine, and it is entirely possible that such remedies may be worse than the disease. A noble profession would lose not only its appeal to present and future practitioners but its very sense of honor. On the other hand, one must respond to the dismay that a well-respected patient provoked at a recent medical meeting when she told her audience that she trusted her lawyer more than her doctor.

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Vignettes: Hard Words

You are always *busy*. You have a finger in every pie. . . . It gets you nowhere. It gets nothing done. You are the Mad Hatter of the Scientific World.

—*H. G. Wells* to Julian Huxley, as quoted by Krishna R. Dronamraju in *If I Am To Be Remembered: The Life and Work of Julian Huxley* (World Scientific)

I do not mean to be harsh, but your very versatility and you[r] polemical cleverness make it necessary for some older people to tell you bluntly where they think the trouble lies. Otherwise you might go on through life doing half-baked work which wins applause from the uncritical and the unsophisticated, working hard and sincerely, and thus never realizing that your work was superficial. . . . You have very unusual experimental ability; you have exceptional drive; you write well; your enthusiastic personality will make you a stimulus to others; you think clearly when your drive does not carry you away. The only flaw in this gem is that [you are] too clever always to be thorough . . . [and you] believe . . . that tricky sophistical argument is justified if the end is justified.

—*Edwin G. Boring* to B. F. Skinner, as quoted by Daniel W. Bjork in *B. F. Skinner: A Life* (Basic Books)

Practical Proteins

Protein Structure. New Approaches to Disease and Therapy. MAX PERUTZ. Freeman, New York, 1992. xiv, 326 pp., illus. $44.95 or £33.95; paper, $34.95 or £22.95.

The dramatic impact that knowledge of the three-dimensional structure of protein molecules is now having on efforts to develop new therapies for disease is the occasion for this enticing book by Max Perutz. Rich in autobiographical recollection, the book captures the excitement that accompanied selected discoveries with which Perutz has been familiar. The book is not a textbook or an attempt to review the entire field; rather, Perutz has selected favored examples of protein structures to focus on some larger issues in biology and the prospect of using the structural knowledge to therapeutic advantage.

There is something in the book for everyone. In addition to Perutz's own recollections there are accounts of important discoveries that herald the 21st century in molecular medicine—Bernal and Crowfoot's discovery in 1934 that protein crystals, if maintained in a hydrated state, could reveal protein structures; Lwoff's discovery that bacteriophage transformed cells; Levi-Montalcini's discovery of a factor that could accelerate differentiation in nerve fibers. These add to the excitement and convey a sense of the process of discovery. For a graduate student the book can be an enchanting eye-opener to the prospects of using macromolecular structure determination for therapeutic purposes. For the medical student and undergraduate it should be an important supplement to biochemistry texts. A strong point is the demonstration of the connections between structure and function at the appropriate level, whether stereochemical or cellular.

Beginning with Waldmann, Winter, and colleagues' discovery that a rat anti-T cell antibody, modified in two cycles of protein engineering based on crystal structures, could induce prolonged remission in human leukemia patients, Perutz discusses work on molecules important to immunobiology. Focusing on the structure of chymotrypsin determined at the Medical Research Council laboratory of which he was the head, Perutz points out how the structures of serine proteinases validated the classic 1948 prediction of Linus Pauling that enzymes enhance reaction rates by their complementarity to transition states. Structures of proteins that regulate transcription and of DNA-binding anti-cancer drugs show how they function. Perutz's own major research focus, the structures of hemoglobin, provided the first insight into the exact molecular basis of a disease, sickle cell anemia. Perutz uses hemoglobin structure as the exemplar for showing how small-molecule "drugs" interact with protein molecules—affecting in this case oxygen affinity and cell sickling—and later for analyzing effects of genetic variants.

The book introduces iterative structure-based design of drugs to "fit" target sites on specific proteins by describing studies from the University of California at San Francisco of compounds that inhibit action of HIV protease and so shut down the HIV infective cycle. Initial insights were generated by computational "docking" of all the known three-dimensional structures of small compounds into the enzyme functional site. Structures of the resulting complexes as determined by crystallography showed how the compounds could be improved and were then used to iteratively improve efficacy. The principles of structural complementarity are underscored in the book by structural analyses of other antiviral agents, discovered by serendipity rather than by computational screening, that show how they too evoke their effects by complementarity to their target sites.

The structural analysis of human growth hormone attached to the soluble form of its cell surface receptor, as developed by Wells, deVos, and Kossiakoff, has opened tremendous new possibilities for understanding and manipulating the human response to growth hormones and cytokines more generally. Surprisingly, the structures show that a single growth-hormone molecule functions by drawing two recep-