Book Review

Prescribing by Numbers: Drugs and the Definition of Disease.

Jeremy A. Greene

(Baltimore: The Johns Hopkins University Press, 2007, 336 pgs.)

Reviewed by Charles Bardes

The year 2008 marks a notable anniversary in the history of medicine. Fifty years ago, in 1958, the pharmaceutical manufacturer Merck Sharp & Dohme launched Diuril—a diuretic for the treatment of hypertension—the first medication ever promoted for the prevention of disease in asymptomatic persons. Previously, a drug was conceived as treatment for a disease—that is, for the relief of suffering. With Diuril, for the first time ever, a drug was newly conceived not to relieve suffering but to avert it. Moreover, this radical redefinition of the role of drugs created a new treatment category that was based not on symptoms (what a patient feels) or on physical signs (clinical observations that, to a physician, indicate the presence of disease), but on a measurement. If your number is wrong, you need medicine.

Jeremy A. Greene has given us a splendid book that probes the large issues related to the numerification of medicine. The core of the book is a set of three paired chapters that explore the careers of three paradigmatic drugs. Diuril was the first well-tolerated treatment for hypertension. Orinase, introduced in 1957, was the first oral medication for diabetes, while Mevacor in 1987 was the first successful drug for reducing cholesterol. The use of paired chapters is ingenious and effective: the first of each pair describes the development of the drug, and the second the evolving concept of the disease it treats. Indeed, one of the author's major points is that these two developments twine about each other and cannot be separated. Interest in a medical condition tends to increase in tandem with the development of its drug, as evidenced by the parallel growths of menopause and Premarin, osteoporosis and Fosamax, and erectile dysfunction and Viagra. The drug transforms a bodily state into a treatment category and then into a disease category.

The author is able both to document his meticulous research and to seek the "big picture." The latter will be of greatest interest to the general reader. Defining disease by a number, such as the blood pressure, the blood glucose, or the blood cholesterol, shifts the focus of medicine from what a patient feels to what a doctor measures. As a consequence, doctors will recommend drugs to many people who feel perfectly well, in essence transforming a person from well to sick. Since the phenomenon occurs across the country and even the world, a huge segment of the population undergoes the transformation from putatively well to putatively sick. The body is essentially sick, and the population is essentially sick. Both need medication. In this "preventive medicine paradox," organized medicine reduces the overt manifestations of disease by expanding the number of people assigned to disease categories.

This expansion is vast. When insulin was the only treatment for diabetes mellitus, the disease was defined by the presence of elevated glucose *and* pathological signs or symptoms. This was equally true for hypertension and hyperlipidemia before the advent of palatable pills to treat them. Once these pills arrived, both treatment thresholds and disease categories shifted—always in the direction of increasing the number of people for whom the pill is recommended. Now, physicians are urged (and implicitly required) to treat not only symptomatic diabetes but asymptomatic diabetes and even a newly conceived category of pre-diabetes. One sees, lurking on the clinical horizon, a still newer notion of pre-pre-diabetes, as witnessed by the rightful concern over obesity in children. Each new definition increases, by many millions, the number of people who "should" be treated.

The stakes in the enterprise are huge. Pharmaceutical companies have everything to gain when a drug is "indicated" not only for the small number of people with symptomatic, severe hypertension, but also for the gargantuan number with asymptomatic, mild hypertension. Medical scientists also stand to gain as their careers advance, their grant-support swells, their professional stature grows, and their specialty concerns push to the front of the biomedical agenda. The clinician, too, sees business grow, for the number-one reason for office visits is now high blood pressure.

Does the public also gain? A man prevented from having a heart attack, a stroke, or an amputation has benefited tremendously, but Greene is well aware that doctors treat many, many people with drugs to prevent a single stroke. Most people treated would never have had the stroke anyway. Might the huge cost of diagnosing and treating people with asymptomatic conditions be better spent on other programs, such as encouraging children to exercise? Does the ease of taking pills divert our attention from the more difficult and possibly more righteous task of improving our dietary and exercise habits? Is it not curious that our diseases of excess consumption, primarily of food and especially unhealthy food, lead us to increase our consumption even more, now in the form of pills?

The author, who is both a physician and a medical historian with a PhD in this field, is currently a fellow in the Department of Social Medicine at Harvard Medical School and a medical resident at Brigham and Women's Hospital. Even at this early stage in his career, Greene shows remarkable skill as a writer. His thinking is lucid, his logic clear, and his sentences graceful. Greene is balanced, asserting that he wishes to avoid "thin narratives of scandal or success." He neither bashes the medical-industrial complex nor lauds its triumphs, presenting instead a fair and nuanced analysis of the enterprise's ramifications.

Authors sometimes slip, and reviewers issue quibbles. Although Greene's turns of phrase are mainly felicitous, his uses of "avatar," "perseverant," and "fungible metrics" are a little off. His etymologies for "pathognomonic" and "polydipsia" are not quite right. A few medical errors scatter themselves throughout the text: methyldopa is not

a centrally active catecholamine blocker; doxazosin does not protect the prostate; drugs have not helped in the prevention of tuberculosis. Still, especially when considering that the author is still a physician-in-training, these mistakes are few and trivial.

The year 2008 is also proving to be a moment when the disconnect between improving numbers and improving health glares across the media. In January, the pharmaceutical companies Merck and Schering-Plough sluggishly announced the results of the "Enhance" trial, which appeared to show that their mutual cholesterol-lowering drug Zetia improved cholesterol values but may actually worsen atherosclerotic disease in the carotid arteries, which provide blood to the brain. That the results of this study, which are highly unfavorable to the drug and to the companies that make it, were first announced nearly two years after the completion of the study and still have not been published, is a matter of grave concern that is already under investigation by the Energy and Commerce Committee of the United States House of Representatives. Like the use of hormone replacement therapy in post-menopausal women and of beta-carotene to prevent heart disease—both of which proved to be more harmful than beneficial in the long run—drug treatment of the population-at-large is a controversy with large implications for the common weal as well as for conceptions of disease and health. Greene has submitted an admirable contribution both to an important chapter in recent medical history and to the understanding of some of the large philosophic issues underlying current clinical practice.

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