

expansion, as she discusses, “was a case study in unfettered exuberance, one that led to reckless exploitation of the land” (p 250).

However, exuberance poses some dangers, as Dr. Jamison points out. “Exuberance becomes dangerous when the goal is reprehensible, the means suspect, or the delight indiscriminate. Enthusiasts may be more interested in the problem being solved than in the ethical issues” (p 256). The book suggests that war provokes such passions, and brings examples of unbridled enthusiasts of war such as Generals George S. Patton and William “Billy” Mitchell. Patton's tactical brilliance and exuberance were legendary, yet at a certain point his intemperate behavior disintegrated into an unpardonable one, when he possibly inflamed soldiers to wanton killing. As Jamison warns us, “normal exuberance can escalate into pathological enthusiasm, anger or even mania” (p 275). Nevertheless, “the juxtaposition of the exuberant and the malignant is potentially dangerous, but a balance between the two can provide ballast and gravitas” (p 286).

Interestingly, at the end of her book, Jamison points out how inherently an *American emotion* exuberance is. She quotes Albert Einstein who once said that America is more capable of enthusiasm than any other country. Americans “see enthusiasm as an advantage ... and they are more likely than people from other countries to favor enthusiasm and ... believe that enthusiasm is a useful and constructive emotion in their lives” (p 296). Interestingly, as Jamison notes, high rates of manic-depressive illness have been observed in American immigrant groups, which suggests that persons with mild forms of this illness but with high energy, exuberant mood and prone to risk taking may have been more likely to immigrate to America. This notion about exuberant people being more likely to come to America provides an interesting complement to Peter Whybrow's book “American mania. When more is not enough” reviewed also on the pages of this journal. Interestingly, Whybrow, a European immigrant, provides a more temperate, yet as insightful, view of the role of mania in American life, while Jamison, an exuberant and enthusiastic American, presents a more positive spin, but does not leave the negative aspects uncovered. Both Jamison and Whybrow provide us with a new, insightful and interesting view of positive emotions in their fullest.

“Exuberance. Then passion for life” is a quite interesting, inspiring and authoritative book on the role of positive emotions, namely exuberance, in our life. It is wonderfully written, in an almost lyrical style, with an abundance of literary quotes and wonderful pearls by the author (some of them I cite in this review). Some may consider it a bit long, but they have to realize that this is prose, not a scientific discourse, written by a woman who, besides being a talented scientist, is also a talented woman of letters.

Richard Balon, MD  
Wayne State University  
Detroit, Michigan

**Powerful Medicines. The Benefits, Risks, and Costs of Prescription Drugs.** By Jerry Avorn, MD.; Alfred A. Knopf, New York, New York; 2004; ISBN 0-37541483-5; \$27.50 (hardcover); 448 pp.

Prescription drugs and pharmaceutical companies are getting a lot of attention lately. The Food and Drug Administration (FDA) has been issuing black box and other warnings right and left. The Congress has been discussing the pricing of medication, re-importation and reimbursement for medications. Physicians have been more and more puzzled about the prescription medication data provided by the pharmaceutical companies, and they keep looking for a more reliable source of information about prescription drugs. The media increasingly criticize the pharmaceutical industry. Finally, the public is just confused and getting angry about prices, warnings and other issues it does not fully comprehend. It is becoming obvious how little we know about the possibly lethal side effects of prescription drugs, and how imperfect the system for the detection of these side effects is. Old medications are increasingly being replaced by newer, supposedly better and safer ones. However, these new medications are frequently hardly any better than the old ones. Many of them are simply “me-too drugs.” Nevertheless, the spiraling costs of these medications place them frequently beyond the reach of many Americans. That all contrasts with lavish, though recently scaled down marketing campaigns and direct-to-consumer advertisement. In the midst of this, we all keep asking, ‘What is going on, and what could be done about it?’

Jerry Avorn, M.D., internist, geriatrician, and pharmacoepidemiologist from the Harvard Medical School and Brigham and Women's Hospital in Boston, in his book “Powerful medicines. The benefits, risks, and costs of prescription drugs”, presents a thoughtful analysis of these issues and also offers an advice how to deal with them. His book is divided into prologue and five parts — I. Benefits, II. Risks, III. Costs, IV. Information, and V. Policy.

The two chapters of Part I, as Dr. Avorn promises, “explore the surprisingly fragile nature of a seemingly simple determination: whether or not a drug works” (p. 18). The rise and fall of hormone replacement therapy clearly demonstrated the importance of randomized controlled trial. The false belief of hormone replacement therapy benefits and lack of risks was based on observations, and not on results of rigorous trials. Rigorous randomized controlled trials discredited these observations. According to Dr. Avorn, a randomized controlled trial is “the single most important development in the revolution of modern therapeutics” (p 53).

However, as we learn from the chapters in Part II, randomized controlled trials do not allow us to get all the necessary information about the long term risks and side effects of medications. That is where the discipline of Dr. Avorn — pharmacoepidemiology — enters the scene. Dr. Avorn cites the famous dictum of Paracelsus that “All medicines are poisons ... the right dose differentiates poison from a remedy”

(p 72). Several chapters of Part II present cases of approved medicines and substances, which were withdrawn from the market due to serious side effects, such as Redux, Rezulin and phenylpropranolamin. Serious side effects could be missed in randomized controlled trials. Pre-marketing randomized clinical trials cannot enroll enough subjects representative of the entire population and follow them long enough to provide a full picture of all possible side effects. However, as the author cautions us, “requiring that drugs on the market be completely ‘safe’ is an impossible goal.” He adds that ‘the real question is whether a drug’s dangers are in some acceptable proportion to the good it does’” (p 102). Pharmacoeconomics, as demonstrated in several chapters, helps in detecting the side effects, and also identifying therapeutic effects, which were mistakenly attributed to prescribed medications. The final chapter of this part also discusses risk stratification and risk management.

Part III provides some explanations for the spiraling costs of medications in the United States. The author rightfully does not blame solely the pharmaceutical industry for the rising costs, but also the regulatory agencies and Congress (as the author suggests in one place, the alliance of industrial greed and political complicity). He points out that the laws originally designed to promote innovation turned into a system that rewards trivial pseudo-innovation even more profitably than important discoveries (the example of “me-too drugs”). The other issues involved in the increasing costs are the impact of the industry on medical education and information provided to physicians, the changing demographics of the American society (older and thus requiring more medications) and the changing habits of our society (everything is treated with medications nowadays). Dr. Avorn also discusses the cost analysis of various medications and its usefulness. Nevertheless, he warns about oversimplification of cost analysis quoting Einstein's observation that not everything that counts can be counted.

The fourth part focused on information “investigates the flow of good data, factoids, and hype that shapes the prescription a doctor writes” (p. 18). It discusses the power of advertising and suggests using industry's own medicine in fighting industry's message. The author brings up interesting concepts such as academic detailing (in opposite to industry detailing), and devising un-ads.

The final part of the book, dealing with policy, presents suggestions of possible solutions to the outlined problems. The author emphasizes that we must figure out how to deliver the most important medical interventions intelligently, equitably, and affordably. His proposed agenda consists of five components: 1) pulling together existing drug information (PDR is clearly not an easy, reasonable and user friendly source); 2) getting that information to prescribers more effectively, safely, and affordably; 3) getting that information to prescribers and patients through an innovative knowledge delivery system; 4) realigning incentives so that only quality and value drive prescribing practices; and 5) tackling the cost problem that makes medicine unaffordable for many. Dr. Avorn suggests that, “the

initial FDA approval of a drug should be seen as the beginning of an intensive period of assessment, not an end” (p 383). He also warns that the growing medical school reliance on industry funding may be a serious hindrance for medical schools becoming the knowledge transfer system in the strategic approach he suggests. Finally, Dr. Avorn argues that the system he suggests is not implausible. On the contrary, he states that, “the current U.S. mode of piecemeal health care delivery, with its all-against-all assumptions, its perverse incentives, its absurdly high costs, its embarrassingly large numbers of uninsured, its tattered patchwork of uncoordinated services, and its frequent denial of care — that is the system that's implausible” (p 415).

This is an important, passionate, though provoking book addressing some very important and central issues of American medicine. It is well written, very informative (a bit too informative at times) and surprisingly entertaining, considering the topic and length. I would recommend it to anybody interested in issues of risks, benefits, regulations, approval and costs of medications we prescribe. I am not sure whether it is good bedtime reading though, as it is a bit disquieting and one might not sleep very well considering all the discussed problems. Thus, maybe read it on weekends or during vacations, but read it.

Richard Balon, MD  
Wayne State University  
Detroit, Michigan

***American Mania. When More Is Not Enough.*** By Peter C. Whybrow; WW Norton Company, New York, New York; 2005; ISBN 0-393-05994-4; \$24.95 (hardcover); 338 pp.

Most Americans keep working more, buying more, being more and more busy, yet being also more dissatisfied, more depressed and anxious, living more and more frantic, fast and faster lives. In his new book, *American mania. When more is not enough*, Peter Whybrow, MD, compares this increasing American frenzy to mania, “a dysfunctional state of mind that begins with a joyous sense of excitement and high productivity but escalates into reckless pursuit, irritability, and confusion, before cycling down into depression” (p 4). Dr. Whybrow is carefully analyzing what he calls a “manic society,” the modern-day America, and its restlessness, ambition, and temperament. His book is divided into three parts with telling titles — I: The American temperament: a mania for prosperity, II: Over the top: prosperity's paradox, and III: More is not enough: prosperity reconsidered.

In the introduction to his book, Dr. Whybrow points out that America is an “unusual nation — it is in many ways a genetic experiment as much as it is a social one — in that the temperament of the migrant has played a unique role” (p 8). The analysis of migrant temperament plays an important role in Whybrow's biological and sociological explanation of what he