The American Psychiatric Publishing Textbook of Psychopharmacology, 3rd ed., *edited by Alan F. Schatzberg, M.D., and Charles B. Nemeroff, M.D., Ph.D. Arlington, Va., American Psychiatric Publishing, 2004, 1,248 pp., $178.00.*

This is the third edition of the textbook that has set the standard for knowledge and wisdom regarding psychopharmacology as practiced in the United States. Extensively revised from the 1998 edition, it includes 17 new chapters, 180 additional pages, and 138 distinguished contributors, many new to this volume. As in the previous edition, subject matter is logically organized, with 65 chapters divided among four major sections.

The first of these sections, Principles of Psychopharmacology, brings readers up-to-date on the basic (e.g., molecular biology and genomics) and clinical (e.g., statistics, brain imaging) sciences forming the foundations of psychopharmacology. These chapters vary in breadth, depth, and complexity, but all are suitable and understandable for psychiatric clinicians, residents, and medical students.

The second section, constituting about half the book, covers virtually all psychotropic medications used in U.S. psychiatry (and a few not yet introduced), giving most agents their own separate chapters. A basic structure is imposed on these chapters: each covers the same areas (pharmacokinetics, mechanism of action, indications, etc.) in the same order, easing the reading of and comparisons among chapters. However, this format also leads to some unnecessary repetition of content (for example, each individual selective serotonin reuptake inhibitor [SSRI] chapter discusses mechanism of action).

The third section delves into current knowledge of the neurobiology of seven broadly defined psychiatric disorders (e.g., schizophrenia, mood disorders, and personality disorders). More uneven in approach and substance than the other sections (e.g., schizophrenia receives nine pages and mood disorders 46 pages), the writing of the individual chapters is clear and the information current.

The fourth section is targeted at practicing clinicians with chapters devoted to treatment of the major categories of psychiatric disorders (schizophrenia, bipolar disorder, etc.), a few specific symptoms (agitation, insomnia), and special populations (children, the elderly, and pregnant women). Although these chapters have some overlap with the second section regarding discussions of specific drugs, the approaches are sufficiently different for both to be useful.

Given the comprehensive nature of the book, I would have liked other areas covered that are relevant to current practice, such as management of pain and the importance of the placebo effect in psychopharmacological treatment. Obviously, choices had to be made, and no book can contain every relevant subject. However, there are several overlapping chapters such as the four on geriatrics-related topics that could have been combined, leaving room for alternatives.

The book has many strengths and a few areas that might deserve attention in future editions. Physically, although hefty, it is put together well with a strong binding, clear readable type, and freedom from annoying grammatical and spelling errors. It is exceptionally well referenced through 2002 with several references extending into 2003. The 85-page index is serviceable and useful. The writing is of high quality with a few exceptions. Many of the chapters on specific drugs and treatments are rigorous in their approach, considering only or mainly double-blind controlled studies as guidelines for recommendations; others freely include case reports and open-label studies in their guidance. A consistent standard set by the editors as to what would constitute suitable data across all chapters may have been preferable. Tables and graphs are placed generously and usefully in a number of the chapters, add little or even confuse in other chapters, and are very sparse or absent in most. Perhaps more defined instructions to contributors regarding the use of such material would enhance future editions.

A few of the authors had notations at the beginning of their chapters on specific drugs indicating that a pharmaceutical company had "provided data and support for editorial assistance in the development of this chapter." The companies mentioned are the manufacturers of the specific drug. The meaning of "support for editorial assistance" is not clear but may represent a worrisome trend. In a similar vein, there is little discussion of the influence of the pharmaceutical industry on research, education, and clinical practice, although the listing of 57 contributors' relationships to commercial supporters, including pharmaceutical companies, is welcome. Only an occasional comment relates to this influence, e.g., "Later randomized, controlled trials that compared tricyclics with SSRIs were invariably supported by the pharmaceutical industry, which had no desire to compare their new compound against optimal tricyclic treatment" (p. 1087).

Occasional factual oversights occur, but not many; for example, lithium's benefit in preventing suicide is not mentioned, fenfluramine is discussed as a therapeutic option without noting that it has been withdrawn from the U.S. market, and methamphetamine is not mentioned in the chapter on substance-related disorders, which also gives only two sentences each to Ecstasy and PCP.

In summary, this book competently and accurately reflects the current and best of psychopharmacological practice in the United States with its realistic optimism based on rapid advances in the neurosciences. However, many issues that cast a shadow on the future promise of this practice are given less or no attention. For example, genuine progress in applied psychotherapeutics is mixed at best. Of the multiple new drugs introduced in the past 15 years, none (with the possible exception of clozapine) offers a major efficacy advance over the medications serendipitously discovered 40 years ago (although offering advances in relief from adverse effects). Given this track record, both the reasons for this deficiency and the place of new and expensive medications in the allocation of scarce resources to psychiatric patients are issues in a debate yet to be fully engaged. In a similar vein, the clinical and economic consequences of the manner in which drugs are developed, marketed, and used are widely recognized but hesitantly confronted. More broadly, the need to reassess current methods of classifying disorders and symptoms as the basis for therapeutics is only beginning to be explored. It is perhaps unfair to expect this or any textbook of psychopharmacology to address these issues. However, the future of the field of psychotherapeutics may rest on an open and vigorous debate of these and similar issues. Until such time as decisions are made regarding the place of such issues in the education of psychiatrists, this book will deservedly continue

to set the standard for comprehensive knowledge in psychopharmacology.

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Drug Interactions Casebook: The Cytochrome P450 System and Beyond, *by Neil B. Sandson, M.D. Arlington, Va., American Psychiatric Publishing, 2003, 313 pp., $35.50 (paper).*

The development of psychoactive drugs in the 1950s gave psychiatry a new way to treat many of its most challenging patients. Although the new medications were initially rejected by the then regnant Freudians, devotees of the new generation of drugs considered them so benign as to be almost "miraculous." The enthusiastic and sometimes irresponsible application of these new compounds generated an unanticipated epidemic of neurological disorders and other serious side effects. For psychiatrists these ill effects brought new ethical and legal considerations and a focus on the precept of "risk-benefit ratio," not formerly promulgated widely for any psychiatric treatment.

The newly dominant role of pharmacotherapy brought psychiatry back into the mainstream of medicine from which the Freudians had alienated it, but it also reminded psychiatrists that they would have to learn some of the old-time principles of doctoring from which they had excused themselves for about 40 years. Learning how and why drugs are absorbed, metabolized, and excreted; how they interact with food and with other drugs; how they activate, suppress, enhance, and antagonize endogenous agents; and how they open or close channels to therapeutic work became the responsibility of the people whose job it was to prescribe them. T.M. Luhrmann's seminal but unflattering study of the profession's mastery of the tools of its trade (1) exposed the poor quality of therapeutics practiced by (and presumably being taught to) some of the psychiatric house staff she studied as recently as the turn of the millennium.

Dr. Sandson, Director of Education and Training at Sheppard Pratt Hospital, has centered his book on the cytochrome P450 system and other enzymes found primarily in the liver, with small concentrations in the intestinal wall and other tissues. Their important role is to help rid the body of toxins, including the medications we psychiatrists go to so much trouble to introduce. Through a process of oxidative metabolism and conjugation, these enzymes render lipid-soluble drugs water soluble so that they can be excreted through the kidneys. Not all of the P450 enzymes act on all drugs, but each acts on many. When one enzyme is acting on two or more concomitantly prescribed medications at the same time, conditions are ripe for an unanticipated drug interaction. These interactions can include one drug's slowing another's excretion, causing it to accumulate until it reaches the clinical equivalent of an overdose, or the first drug can expedite excretion of another, reducing its therapeutic action.

There are many more mechanisms of interference, some less important, some very important. Dr. Sandson has chosen to expound on them at book length because, although many psychiatrists prescribe multiple drugs simultaneously, not many have enough basic clinical pharmacology at their fingertips to predict and work around the interactions they create.

Dr. Sandson opens with a section titled Core Concepts, an array of brief but pertinent explications of ground-level pharmacology in drug-drug interactions. Read it; it will help you to understand and appreciate the rest of the book. Seven chapters explain specifics of phase I (primarily the cytochrome P450 subgroups) and phase II (mainly glucuronidation) drug metabolism. The case reports are cleverly titled to help take some of the weight off. A lot of the featured interactions can be mid-therapy surprises, when a drug added or subtracted for fine-tuning of a nicely progressing case causes changes in medication blood levels to which a patient has become well accommodated. Interactions like this can seem threatening and mysterious, precisely because they are unanticipated, hard to recognize, and tough to treat. They can also be discouraging to fragile patients and hazardous to a critical therapeutic relationship.

"Cranky and Crampy" is about how an additional drug slowed metabolism of an acetylcholinesterase inhibitor, causing higher blood levels and the miserable abdominal cramping side effects common to these drugs at high doses; naturally, the physician who was prescribing the medication at a standard dose couldn't understand where things had gone wrong. "Nauseated Nanny" is about how an angiotensin-converting enzyme inhibitor slowed renal excretion of lithium and raised the ion's blood level to toxicity. There is also a case of a drug interactively decreasing another's blood level, with attendant sacrifice of therapeutic effect.

Another case illustrates caffeine's combination with a prescribed medication and is intended to alert us to the potential dangers of interactions between drugs that we do not necessarily think of as drugs. For example, when cigarettes, potent P450 inducers, are withdrawn, an index drug's blood value can rise to toxic levels. You might well encounter this kind of problem (so-called reversal of induction) when you've admitted a patient maintained on clozapine to the hospital, where smoking is not permitted. Even though the patient may be in acute exacerbation of psychotic symptoms and your natural predilection would be to increase the antipsychotic dose, the smoking cessation retards the patient's P450 production and clozapine is being excreted more slowly. Thus, the patient is accumulating higher blood levels. If you raise the dose you could very well precipitate a toxic overload.

Dr. Sandson and his colleagues have included three useful appendixes, and I would recommend that you take a good look at each so you will know where to return when you have a sick patient and have to look up a specific interaction. The appendix titled "P450 Tables" groups the drugs that induce and inhibit these enzymes; those titled "Phase II Glucuronidation Tables" and "P-Glycoprotein Table" contain extensive listings of relevant psychotropic and medical pharmaceuticals regularly encountered in clinical practice.

This is an attractive and genuinely useful reference book. Certainly not the first to be published on drug interactions, it is nevertheless among the more readable and entertaining, with the feel of a classic English who-done-it in the mystery enfolding nearly every case. I highly recommend it as a much-needed contribution that is likely to improve the medication management skills of everyone who reads it.