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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 Shepard 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.

Reference

1. Luhmann TM: *Of Two Minds: The Growing Disorder in American Psychiatry*. New York, Alfred A Knopf, 2000

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MOOD DISORDERS

Psychodynamic Treatment of Depression, by Fredric N. Busch, M.D., Marie Rudden, M.D., and Theodore Shapiro, M.D. Arlington, Va., American Psychiatric Publishing, 2004, 204 pp., \$32.95 (paper).

In an uncommonly lucid introduction, the authors summarize the existing choices of treatment for depression, the value of combined treatments, and the assets that psychodynamic psychotherapy brings to bear on treating depression. The authors point out that in spite of the fact that there are no placebo-controlled studies demonstrating superiority of the psychodynamic approach, there is good reason to believe that its principles are important and that for selected patients it has great utility. In addition, many of its main beliefs and techniques lend themselves to use in other therapies.

In the introduction, the authors write about a focused treatment, not an open-ended exploration. They describe the patients for whom it is most likely to be helpful and the topics that should be explored with the patient to determine suitability for treatment. The book begins with a review of the different ideas underlying a dynamic explanation of depression and a statement of fundamental principles behind psychodynamic treatment. The last introductory chapter presents a demystified overview of psychodynamic treatment that is exemplary in its clarity and freedom from jargon.

The dominant middle section of the book consists of a series of chapters on the techniques used to treat depression. The approach emphasizes clarity, and the authors are consistent and organized. A chapter on starting treatment includes an excellent discussion of forming a therapeutic alliance as well as barriers to engaging depressed patients. Subsequent chapters expand on the topics introduced earlier in the book, so there are chapters on narcissistic vulnerability and injury, harsh self-judgment and guilt, idealization and devaluation, and the defenses used by depressed people. The chapter on defenses is unusually good. The authors abundantly illustrate their points with cases, which are very helpful and constitute a strong point of the book. Occasionally it seems as if there is an overreliance on cases in situations where more discussion and explanation of what the therapist does might have been in order. There also should have been a few cases of clear-cut treatment failure followed by appropriate discussion, and the case mix tends heavily toward the urban, bright, and talented, but these are minor points.

This section ends with a chapter on termination that contains fairly standard advice. However, the examples are of rather lengthy terminations, sometimes longer than the entire course of many therapies using short-term dynamic approaches. Support for extended termination is not as well presented as the authors' other recommendations.

The book includes a few special topics, including approaches to suicidal behavior and a chapter on the use of psychodynamic psychotherapy with other treatment approaches. This last chapter would be best read with the introductory chapters.

Treating depression will remain a mainstay of psychiatric practice. No treatment fits everyone no matter how skillfully applied. Anything as complicated and pervasive as depression, which, as we know, appears as a universal symptom as well as specific syndromes, can only be seen as having multiple contributing variables. Explanatory models include evolutionary ones in addition to the those we regularly think about in the spheres of endowment and experience. When it comes to treating disorders like depression, there will always be people who need to understand who they are in the present in terms of the experiences they have had in the past. For many such people, treatment that is too formulaic or ritualized does not make sense to them and does not work. For most patients, open-ended exploration of origins of problems leads nowhere. Psychodynamic therapy applied in a focused fashion, combined, if necessary, with other approaches including medication, offers many patients the opportunity to put demons to rest. Success in treatment often hinges on a good fit of patient, psychiatrist, and treatment approach. Having flexibility in choosing and applying the treatment that best meets the patient's needs is ideal.

Although this book deals specifically with the treatment of depression, it actually is an excellent introduction to psychodynamic theory and practice. As such, it would have particular utility in residency training. Residency accreditation requirements include didactic material in psychodynamic theory and clinical experience using such an approach. This book should be ideal in helping meet these requirements.

There are many experienced therapists who would find the focus of this book on depression useful; it has great practical utility either as a modern, clearly explained review of an approach or as a fresh introduction to a way of looking at patients. I tried to imagine reading this book lacking any background in psychodynamic theory and practice. I believe it would still work well because of the lucid, organized approach that remains clinically focused and mercifully free of old-fashioned theory and jargon. The one exception is the traditional psychoanalytic use of the term "genetic." It is time to part ways with using this term in its confusing archaic sense, which has nothing to do with genes. In every situation I can think of, the word "developmental" could be substituted and would represent current, commonly accepted use.

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Pharmacotherapy of Depression, edited by Domenic A. Ciraulo, M.D., and Richard I. Shader, M.D. Totowa, N.J., Humana Press, 2004, 400 pp., \$125.00.

I like this book and found it quite useful. It is somewhat different in that it is not as clinically specific as many "how to" books about treatment of depression. It covers more theory and gives the basis of treatment for both bipolar and unipolar depression, as well as specific targeted areas, such as geriatrics and children. The book also has a "value added E-book/PDA": there is a CD-ROM that has an electronic book version