

REVIEW OF REVIEWS

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CHINESE MATERIA MEDICA

During the past three decades, a tremendous amount of information has accumulated on the pharmacology and therapeutic applications of various plants and animal products. Although the knowledge resulted from investigative activities throughout the world, the data have, in the main, been derived from recent research in China. This is not surprising. When the Communist Party assumed control there in 1949, its leaders, out of both political and practical considerations, promoted a massive program to blend Chinese traditional medicine with Western medicine. An enormous volume of data was generated, and it became essential to systematize the unwieldy mass of information. To fulfill this need, two volumes on the pharmacology and application of Chinese *materia medica*, edited by Chang and But, were published in Chinese. Recently, volume one has been translated into English by Yao, Wang, and Yeung (1).

The editors' task was by no means simple, owing to the inconsistencies in the voluminous literature on many of the drugs, published within and outside of China, confusion regarding the names of many plant products, and the complexities of Chinese herbal remedies, which are usually recipes. For example, when several herbs are used in a prescription, the latter is listed under the principal component drug recognized for its effect by common usage or as specified in the 1977 *Chinese Pharmacopeia*. When different parts of the same plant have diverse clinical applications, either each is described separately as a main drug, or, if used as an adjuvant, treated in an appendix under the description of a main drug. Included in the book are descriptions of 250 natural products, comprising 231 herbs, 18 animal drugs, and one mineral drug. Their selection was based on their general recognition as well as on their extensive recent investigation.

The coverage of each drug includes sections on its pharmacognosy, chemical constituents, pharmacologic activities on various organ systems, toxicity, clinical studies, adverse effects, and an extensive bibliography. Although the authors concede that there may be errors and omissions in their study, and even if it was not possible for them always to be critical, they are to be thanked for providing a highly useful reference volume, as well as some rational basis for the use of the more important natural products indigenous to China.

BOOKS ON PHARMACOLOGY

Solomon Snyder has authored a popular science volume about drugs acting on the brain that is readable, interesting, and sufficiently authoritative (2). Besides providing entertaining and beautifully illustrated descriptions of the behavioral pharmacology of some psychoactive drugs, he attempts to convey an understanding of the scientific processes involved in generating knowledge and of the value of such pharmacologic agents for identifying the roles of different brain sites in physiologic function. Although basic molecular mechanisms are stressed in this work, the reader is not permitted to ignore the integrative processes involved in producing the drug effect. Among the drug categories selected for discussion are the opiates, antipsychotics, stimulants, antianxiety agents, and hallucinogens.

The historical accounts of the drugs add flavor to the presentation, but the author could have spent a little more time on his homework. K. K. Chen did not begin his investigation of ephedrine at Eli Lilly Co. As Chen himself relates (3), his discovery of the sympathomimetic properties of ephedrine, which he isolated from *ma huang*, occurred in 1923, while he was working at the Peking Union Medical College. Chen wasn't hired by Lilly until 1929. By implication, Snyder appears to credit the first synthesis of amphetamine to Gordon Alles. While it is true that Alles needed to prepare amphetamine to carry out his pharmacologic studies, the compound had been made and studied earlier by others. However, Alles' investigations were more thorough, and he was quick to realize the potentials of his findings. His astuteness enabled him to take out a use patent on amphetamine and certain of its congeners, and he became rich from the royalties he received. On the other hand, in discussing the discovery of the antimanic properties of lithium, Snyder is more correct than the Lasker Committee, which awarded its prize to Mogens Schou instead of John Cade. Cade reported his finding in 1949, five years earlier than Schou. However, lithium was not marketed until the mid-1960s because drug companies did not want to spend their resources on a nonpatentable drug. In this instance, loss of benefit to the public should be blamed on industry rather than the Food & Drug Administration, which often take too long to approve useful drugs.

Further, the science in Snyder's book is not always correct. The more rapid "rush" produced by heroin in comparison with morphine is attributed to the increased ability of heroin to dissolve in brain fat because of the addition of two acetyl groups. In actuality, although acetylation does increase the lipophilicity of heroin, the more instantaneous effect of heroin is due to its ability to traverse the blood-brain barrier more readily than morphine, after which the heroin is hydrolyzed to monoacetylmorphine and morphine to produce pharmacologic effects (4).

My criticisms of the book hardly detract from its value, since the author admirably achieves his mission. Scientists who have the ability and the proclivity to tell the lay reader about scientific discoveries are few and far between. Pharmacology is fortunate to have an articulate, gifted spokesman for its cause.

Wang has edited an extensively revised second edition of *Practical Drug Therapy* (5). After three introductory chapters on theory and principles, various drug classes used in treating diseases of the cardiovascular, respiratory, renal, hematologic, gastrointestinal, endocrinologic, and central nervous systems are considered. These are followed by chapters on antimicrobial agents and on miscellaneous disorders in which drugs used for treating the skin and cancer are discussed. Although the chapter on skin seems out of place, its location at the end of the book appears to be dictated by the wide assortment of agents, often discussed earlier in other chapters, that are used for treating this tissue.

When a book has such an organization, however, there can be considerable redundancy in it, with a drug (e.g. steroids) appearing in many chapters; but then no text can escape criticism. Since the book is organized around disease entities, my personal preference would be for the method proposed and followed by my teacher, Chauncey Leake, who taught, in sequence, about drugs for the diagnosis, prevention, alleviation, and cure of diseases.

It is commendable that in most chapters of this book, a rational basis for pharmacologic intervention is provided in a brief introductory consideration of the functional processes of a particular organ system that is modified by disease. However, such pathophysiologic discussions are not always apparent, as in the chapter on digitalis. Other important omissions are also in evidence. It is surprising, for example, that there is no general consideration of dose-response relationships or clinical assessment of drug efficacy, although these subjects are sometimes covered to varying degrees in the discussions of the separate drug classes. The indexing leaves much to be desired. References for a specific drug are by chapter instead of by page. For example, acetaminophen is indexed as appearing on pages 227–246 and 347–368, but in fact there is only a brief paragraph on the drug in the pages listed. On the positive side, the chapters on drugs for the treatment of gastrointestinal disorders contain practical information that is not ordinarily

found in textbooks of pharmacology or medicine. In addition, in the chapter on oral contraceptives there is a fairly detailed discussion of their beneficial effects other than the prevention of pregnancy. After becoming accustomed and conditioned to reading about side effects of drugs and their dire consequences, it is pleasant to learn about their fringe benefits. On balance, the book can be recommended. Primary-care physicians and pharmacists will find the book more useful than pharmacologists, who nonetheless would profit from having it on their shelf.

Rang & Dale have written a paperback entitled *Pharmacology* that appears to be the most articulate yet for examining the pharmacologic basis of drug action (6). The authors define pharmacology broadly as the study of the effects of chemical substances on living tissue, and as a consequence they do not restrict their presentation solely to drugs, which are, of course, emphasized. By necessity, with this approach, many chemical substances, not drugs in the strict sense, are covered in greater detail than in most pharmacology texts. Although many of these substances, such as the neurotransmitters, are traditionally identified as the turf of pharmacology, other native ligands, such as some amino acids, many neuropeptides, and substances intimately linked to inflammatory and immune responses, are also extensively discussed. Thus, when drug responses are explainable in terms of how these endogenous substances are affected, how the drugs act becomes immediately apparent.

The book does not suffer from multiple authorships. It was not edited, but was written entirely by two gifted scientists who demonstrate knowledge in both breadth and depth not only of general pharmacologic principles but also of specific drugs. The fact that I do not always agree with some oversimplified explanations (e.g. of opiate actions via second messengers) does not make the book less valuable. A minor criticism is the splitting of reference citations between the end of each chapter and the end of the book. Also, although the arrangement of the presentations is generally good, the organization of the last two chapters can be faulted. It is difficult to understand why the last chapter, "Harmful Effects of Drugs," is not included in the first section which treats of general principles. In the next-to-last chapter, nicotine, alcohol, and cannabis are accorded special status in a separate discussion under the rubric "Nontherapeutic Drugs." This makes little sense from a pharmacologic standpoint. How one perceives a drug is dependent on the eyes of the beholder. There are always risks to be encountered from legitimate use of a drug, but then there must also be some benefits to be derived from taking risks with addictive substances. The professional sees no therapeutic benefits in tobacco, but the habitual user considers it essential to his well-being because it functions as an antianxiety agent. The same holds true for alcohol and cannabis, but the benefits to be gained from use of these two agents might be questioned less. Moreover, the principal constituent of

cannabis, tetrahydrocannabinol, finds therapeutic application in glaucoma and in sickness resulting from cancer chemotherapy. Although alcohol may not be a prescription drug, wine is certainly a popular over-the-counter item often recommended by physicians to their patients for some cardiovascular conditions.

The book will not satisfy everybody. Teachers in medical and pharmacy schools, as well as practitioners, will find that it contains insufficient detail about specific drugs. This deficiency is less important for pharmacy than for medical students in the United States because instruction in pharmacology given by medical schools is repeatedly subjected to curricular reduction, whereas it has generally been expanded and included in the pharmacy schools under the course name "clinical pharmacy." The book is especially valuable for graduate students in pharmacology and for post-doctoral researchers in the basic biologic and physical sciences who want an easy and interesting way to gain an overall grasp of pharmacology. In particular, molecular biologists with insufficient exposure to the complexities of integrated function in drug action will find the book illuminating. Moreover, the price is right.

HEROIN, AIDS, AND PUBLIC POLICY

A distinguished jurist and author, John Kaplan, has written on heroin and public policy in the United States (7, 8). I should have told you about the book long ago. However, since it has received little attention from the scientific community and is well worth reading, let's consider this to be a review of a well-deserved revival. Moreover, I am calling this book to your attention because the heroin problem is perennial and is now complicated by AIDS. Besides, none of the author's main positions on an important social problem have had to be changed, and I believe they make good sense.

The book provides an academic's scholarly, yet down to earth, analysis both of the criminal justice system in relation to heroin use and of public policies regarding this drug. Kaplan first considers the gravity of the heroin problem as perceived by the general public in contrast to its actual magnitude, for at most, less than one percent of the population is affected. He perceives that the largest costs imposed by heroin are due directly to the use of criminal law to enforce prohibition of the drug, and he provides many instances to document why the legal system in the United States does not appear to be good at enforcing this national policy. To look at the problem from a proper perspective, though, the costs to the nation of heroin addiction should not be considered solely in terms of money. Although many dollars are spent on treatment of addicts and even more in apprehending, trying, and imprisoning those whose offences arise from the use or sale of heroin, the erosion of civil liberties, police corruption linked to attempted enforcement of heroin laws,

generally lowered quality of life, and the pain suffered by addicts and their families are important facets of the total problem that cannot be ignored.

The efforts to enforce the prohibition of the drug are concentrated on the supplier and the user of heroin. However, it is the policies aimed at suppliers that determine most of the characteristics of drug prohibition. Law enforcement concentrates on eliminating the production of heroin, preventing its entry into the United States, and stopping its sale to the user. Kaplan examines in detail the gains and losses resulting from the implementation of this policy. The chapter makes particularly interesting reading.

To understand more about the restrictions on heroin supply, Kaplan examines how the law and its agents go about their task, and why they manage to do as well or as badly as they do. He sees a contest in which law enforcement is pitted against an intelligent, motivated adversary, and in which advances made by one side are countered by changes made by the other. This struggle began following enactment of the Harrison Act in 1914, after which the importation, sale, or possession of opiates, except for medical use, became illegal. This legislation has done little to contain the desire for opiates, although temporary success has sometimes been achieved. Because of the difficulties of smuggling and concealment, more potent opiates, such as heroin, became preferred over morphine and opium, and injection became the favored route of administration. Thus opiate addiction has become more personally destructive and socially costly. Implementation of the act involved legal regulation of the prescribing practices of physicians and their harassment by law officers. As a consequence, patients with severe pain have suffered because of the caution exercised by physicians in prescribing opiates for relief. The price of heroin skyrocketed after passage of the Harrison Act, and the drug spawned a crime industry. Sellers willing to take high risks for lucrative financial gain have engaged in violence to settle disagreements about deliveries, payments, and territorial rights. Users have committed mostly crimes of property to help sustain the high cost of their habit. It seems clear, then, that the costs of heroin prohibition have outweighed the benefits.

As a way of solving the heroin problem, Kaplan considers the option of making opiates available to the known user. The approaches discussed extend from free availability over the counter to restriction of use by making the drug available legally and cheaply only to addicts. Jurisprudential and philosophic arguments are invoked in weighing the advantages and disadvantages, citing history, legal precedents, and analogies to alcohol use, gambling, prostitution, and laws on pornography. The reader cannot but be impressed by the wisdom and logic marshalled in this chapter to argue for decriminalization (not legalization) of the use of heroin.

The enormous amount of resources expended in law enforcement and treatment over the past decade to eradicate heroin addiction have only man-

aged to achieve a stalemate in which heroin's cost to society has been kept relatively constant. Recently, however, this imbalance has been disturbed by the appearance and spread of AIDS. Among heterosexuals, by far the highest incidence exists among heroin addicts who contract the condition through needle sharing or prostitution. Over 50% of addicts in some treatment programs have AIDS antibodies. Kaplan addresses this pressing problem in a sequel to his book. In a newspaper article, he again places the heroin problem in perspective, but this time in connection with AIDS (8). Because long-term opiate maintenance is the most cost-effective treatment for keeping heroin addicts off the street, he recommends, as a temporizing measure until bureaucratic inertia can be overcome, that admission requirements of opiate maintenance programs be lowered. While he concedes the advantages of rehabilitative and psychiatric counseling for drug addicts, he points out that resources for such purposes would be slow in coming, and that the problem is an urgent one requiring immediate action. He counters the common governmental judgment that deprives us of a less satisfactory alternative because there may be better, though more expensive ways, by stating: "It is the idea that since a Cadillac is better than a Chevrolet, those of us who can afford only the latter should walk."

Professional workers in drug addiction research and treatment are already familiar with most of what Kaplan stresses. However, it is a revelation that a nonscientist should make the effort to familiarize himself thoroughly with the scientific, medical, and social aspects of drug addiction before presenting his case.

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