Book Review
Experimental and Clinical Neurotoxicology

Peter S. Spencer, Ph.D. and Herbert H. Schaumberg, M.D., eds. Williams and Wilkins (Baltimore:1980)

This text, in both concept and execution, was an ambitious undertaking by its editors Peter S. Spencer and Herbert H. Schaumberg, who also serve as major contributors. To describe this work as over-ambitious would be to imply that it does not reach the rigorous goals it sets for itself. Happily, this reader can report that Experimental and Clinical Neurotoxicology is, by and large, successful in its attempt, according to the editors' prefaced intentions to "encompass the biologist's inquiry into the mechanism of action of neurotoxic chemicals, the clinical problem of toxic neurological disease, the issues associated with neurotoxicants of environmental significance, and the regulator's interest in developing sensitive methods for screening substances for possible neurotoxic effects." The scattered exceptions generally seem to prove the rule. One suspects that when the editors state a little farther on in their preface that "while this book has this broad purview, it is by no means encyclopedic," they are hedging their bets but belying their true intentions. This book does mean to be encyclopedic in the sense that it strives to cover one subject in most if not all of its facets, through the format of numerous short articles authored by a variety of experts in the field. It is a comment on the relative infancy of neurotoxicology as an independent discipline that it is not only feasible but, in fact, useful to attempt an encyclopedic approach to this area of investigation. The editors should feel no embarrassment in undertaking this task, for they are capable of fulfilling it.

Experimental and Clinical Neurotoxicology is divided into five sections: A descriptive introductory series of articles that delineates specific targets of neurotoxic agents; a section that describes a variety of pathways and mechanisms of neurotoxic action with emphasis on current experimental evidence and theoretical implications; a fairly inclusive list of specific neurotoxins; "applied neurotoxicology," covering human epidemiological and clinical studies and animal models; and, finally, the public policy implications of neurotoxicology.

In each of these sections, the editors or authors or coauthors leave their mark on the text. In fact, it would seem almost unfair to expect the other authors in this volume to achieve the same level of clarity and brevity, even while introducing sometimes complicated or unfamiliar material, that Spencer and Schaumberg accomplish on every lucid page under their signature. Particularly noteworthy is their brief article, "Classification of Neurotoxic Disease: A Morphological Approach," which in less than ten pages provides a structural framework with which to conceptualize the disparate modes of action of a variety of neurotoxins. More than any other chapter, it is the heart of this book and its guiding manifesto. This brief article succinctly outlines the basic morphological considerations of somal neuronal disease (e.g., secondary to methyl mercury intoxication); axonal disease, especially the central-peripheral distal ("dying-back") axonopathy which the authors' own original research has been so crucial in elucidating; toxic attack on the myelinating cell body or the myelin itself; and nervous system affects mediated by compromise of the neural vasculature. It should be required reading in any undergraduate medical neurology course.

Their chapter "n-Hexane and Methyl n-Butyl Ketone," co-authored with Daniel Couri, gives a thorough recapitulation of the authors' experimental investigations as well as of the data on the unfortunate human exposure to these hydrocarbon solvents and their common metabolite, 2,5-hexanediol. Even the two chapters consisting of randomly selected neurotoxic drugs and chemicals, none of which in the editors' view merited independent chapters, prove interesting reading and not merely a shopping list of poisons. One wonders, however, if certain of these allocations were made, not because of a lack of widespread human exposure, but rather because of a paucity of good experimental data (or good authors?). This is especially true in the cases of arsenic and manganese, metal intoxicants surely as important as thallium which did merit a separate chapter by William J. Bank. "Selected Outbreaks of Neurotoxic Disease" describes a depressing number of human disease outbreaks caused both by neurotoxins and, as the authors note, "human error, greed, and ignorance." This chapter appears late in the book in the section relevant to public policy, but might have been better placed earlier in an introductory role, for it presents a specter which, as they say, concentrates the mind exceedingly. Spencer's chapter written with M.I. Sabri, on possible biochemical mechanisms of distal axonopathy is the only one authored by an editor that stands out as being weaker than the others. This is not because it does not present stimulating experimental data implicating a variety of axonal neurotoxins in the inhibition of energy metabolism, but because this hypothesis seems to be presented without any real gusto, as if the authors were loath to commit themselves fully.

Spencer and Schaumberg are not alone in writing stimulating, informative, and lucid chapters. Worthy of particular note are chapters by P.K. Thomas on the peripheral nervous system as a target for toxins; Jean Jacobs on vascular permeability and neural damage; John Griffin and Donald Price on proximal axonopathies; and J.W. Olney on excitotoxins, especially glutamic acid and its analogs.

Unfortunately, there are also chapters that disappoint. The chapter on neurotoxins as teratogens should have been re-worked and expanded. As an example, a more detailed discussion of the epidemiology of human neural tube de-
fects is certainly warranted. The chapter on ototoxicity is also weak. The chapter on neurobehavioral testing carries no reference to the abundant Eastern European literature. In fact, a separate chapter on neurotoxins as mediators of psychotic disturbances, e.g., carbon disulfide, manganese, and mercury, would probably have proved interesting reading. The chapter on carbon monoxide, an otherwise thorough review of the subject, fails to mention methylene chloride (CH₂C₁₂), a common industrial solvent metabolized in humans to carbon monoxide. The chapter is also a little too off-handed in its dismissal of the risks of chronic low-level carbon monoxide exposure.

Experimental and Clinical Neurotoxicology also suffers from the shortcomings inherent in any undertaking embarked upon by so many different authors. Although at times these many voices harmonize surprisingly well, at other points the effect is rather cacophonous. To take the most obvious example, lead toxicity is described at various locations in the text as mediating its toxic action primarily through endothelial damage, as the example "par excellence" of a demyelinating neuropathy, and as the cause of a Wallerian type of axonopathy. In a chapter specifically devoted to lead toxicity, some of this confusion is explained if not eliminated by the presentation of the species-dependent rabbit versus guinea pig pathology data. One might wish for a bit more consistency, or at least a more exacting index. The index covers the specific chapter on lead adequately, but most other references to lead toxicity in the text seem to elude it. In terms of internal consistency, the editors of any text with numerous contributors have a difficult task. What is demanded is the scientific equivalent of a Maxwell Perkins in his stewardship of Thomas Wolfe in the literary realm. An editor overly sensitive to the possibility of offending the author may ultimately do him a greater disservice.

In the final analysis, Experimental and Clinical Neurotoxicology cannot and is not all things to all people. I think that it may prove more useful to the neuroscientist and toxicologist than the clinician. For anyone interested in environmental health and occupational disease, it is an invaluable asset to be used as both educational text and reference volume. This work will be an enduring one and an important component of any health sciences library.

Paul Blanc
Class of 1982