PREFACE

Neurotoxicology is a broad and burgeoning field of research. Its growth in recent years can be related, in part, to increased interest in and concern with the fact that a growing number of anthropogenic agents with neurotoxic potential, including pesticides, lead, mercury, and the polytypic byproducts of combustion and industrial production, continue to be spewed into and accumulate in the environment. In addition, there is great interest in natural products, including toxins, as sources of therapeutic agents. Indeed, it is well known that many natural toxins of broadly differing structure, produced or accumulated for predatory or defensive purposes, and toxic agents, accumulated incidentally by numerous species, function to perturb nervous tissue. Components of some of these toxins have been shown to be useful therapeutic agents and/or research reagents. Unfortunately, the environmental accumulation of some neurotoxicants of anthropogenic origin, expecially pesticides and metals, has resulted in incidents of human poisoning, some of epidemic proportion, and high levels of morbidity and mortality. Furthermore, an increasing incidence of neurobehavioral disorders, some with baffling symptoms, is confronting clinicians. It is not clear whether this is merely the result of increased vigilance and/or improved diagnostics or a consequence of improved health care. In any case, the role of exposure to environmental and occupational neurotoxicants in the etiology of these phenomena, as well as neurodegenerative diseases, is coming under increasing scrutiny and investigation.

Recognition and utilization of environmental (in the broadest sense) information comprise the currency of life. Therefore, the effects of perturbation of these critical capacities deserve thorough investigation. The acquisition of information, and its processing, storage, retrieval, and integration leading to functional outputs, are fundamental nervous system functions. It should not be surprising, then, that structural, functional, and evolutionary research has revealed that even "simple" nervous systems are immensely complex. On the systems level, the intact nervous system is an exquisite example of integration within the context of a continuously evolving, apparently infinitely programmable and regulatable hierarchical input/output system of complex chemical structure. However, as the complexity of nervous systems has increased, so has their vulnerability to chemical and physical insult. In part, this is a consequence of loss of regenerative capacity.

Living systems have evolved to function within relatively narrow ranges of environmental conditions. Perturbation beyond the limits of the range of a given system can result in irreversible damage manifested as loss of function or viability. Also, the nervous tissue of more highly evolved organisms is particularly refractory to regeneration. But, with complexity has come an increased capacity for compensability. Albeit often limited and difficult to achieve, through learning and recruitment, compensation can bypass irreversible damage allowing, to varying degrees, recovery of function. The developing brain, in particular, is endowed with immense plastic potential. Unfortunately, the efficiency of both homeostatic and compensatory mechanisms progressively diminishes as a function of aging. Indeed, a large body of literature indicates that humans generally lose memory with age and the magnitude and rate of loss are highly variable among individuals. In addition, data obtained through the medium of testing protocols, and supported by evidence obtained from functional neuroimaging studies, indicate that not all types of

memory are affected equally. Depending on the task, such studies show that, compared with younger adults, older adults can display greater or lesser activity in task-associated brain areas. Conceivably, the increases in activity may be the result of the input from compensatory mechanisms. In any case, age-related diminished mental capacity is a complex function of the interaction of genetic constitution and environmental factors. The type, magnitude, duration, and period of exposure in the life cycle to the latter can impact the functional status of the aging nervous system. Major windows of vulnerability occur during development, when target sizes are small and defense mechanisms immature, and in post-maturity, following decline of the functioning of compensatory and defense mechanisms along with increased duration of exposure.

Intellectually, we may appreciate that thermodynamics dictates that, as a function of population size, environmental pollution will increase. However, do we appreciate that, in the short-run, if a connection between environmental pollution and nervous system damage exists, the incidence of nervous system damage will increase as the population increases? Likewise, as life span increases, exposure to neurotoxicants will increase and, it is not unreasonable, therefore, to predict that the incidence of neurodegenerative diseases also will increase. Are these phenomena self-limiting? If not, can we estimate the magnitude of these problems that ensuing generations will have to face? With time, sufficient funding, and manpower, it may be possible to solve many of these problems. Indeed, we must. If not, the consequences border on the Orwellian.

With an eye to the future, the *Handbook of Neurotoxicology* has been developed to provide researchers and students with a view of the current status of research in selected areas of neurotoxicology and to stimulate research in the field. Obviously, the field is enormous and all areas of interest could not be covered. However, if the *Handbook of Neurotoxicology,* volumes 1 and 2 prove useful, other volumes will be forthcoming. Therefore, we invite your comments and suggestions.

Edward J. Massaro

http://www.springer.com/978-0-89603-796-0

Handbook of Neurotoxicology
Volume II
Massaro, E.J. (Ed.)
2002, XVI, 594 p. 32 illus., 11 illus. in color., Hardcover
ISBN: 978-0-89603-796-0
A product of Humana Press