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BOOK REVIEW

Handbook of Toxicology of Chemical Warfare Agents, First edition, Ramesh C. Gupta, Editor, Academic Press, Elsevier, San Diego, CA, USA, 2009, Hardback, 1147 pages, US$225, ISBN 978-0-12-374484-5.

This book is intended for employees at poison centers such as certified specialists in poison information, pharmacists, toxicologists, and people who work in regulatory and policy-making capacities. It touts itself as the first reference book of its kind in terms of its breadth.

The editors have divided this book into nine sections. Section I is an introduction that gives historical perspective of the use of chemical warfare agents. It primarily focuses on military and terrorist attacks, such as in World War I and the sarin subway attacks in Japan. Other incidents of chemical warfare described include the use of mustard gas by Iraq in its war with Iran and accidental events like the Bhopal, India, methyl isocyanate disaster. These chapters are generally well-written and informative, though overlap of coverage of these events does occur.

Section II describes agents that can be used as weapons of mass destruction. Some of these chapters are good overviews of the subject matter – such as the chapters on thallium, strychnine, and polychlorinated biphenyls, dioxins, and furans. Other chapters suffer from a focus on the basic science and read like scientific journal articles, focusing on the authors' research. The summary of arsenicals does a nice job of covering the different types of toxic arsenic compounds, their clinical effects, and potential treatments. However, it is not complete enough for a clinician to be able to work up a patient with suspected arsenic poisoning. The same holds true for other chapters, and they could have benefited from a more practical, clinical focus. The discussion on superwarfarins even mentions the induction of emesis with ipecac as a treatment, which is an outdated treatment.

The cyanide chapter in Section II does a nice job covering the mechanisms of cyanide toxicity and potential treatments. The carbon monoxide chapter is a good general overview, especially given the limited pages given to a topic that can fill an entire textbook. The chapter on methyl isocyanate and the Bhopal, India, disaster is a fascinating and comprehensive look at the world's worst industrial disaster. The chapter describing chlorine is rather superficial but does highlight important points. Phosgene is treated in a similar manner. The chapter "Other Toxic Chemicals as Potential Chemical Warfare Agents" is somewhat superfluous but does mention some interesting ideas. Ricin and abrin are given a good overview despite our limited knowledge of these toxins. The chapters on trichothecene mycotoxins, cyanobacteria toxins, radiation, and depleted uranium were interesting but lacking in depth and clinical applicability. However, the chapters on botulism and anthrax were very complete.

Section III takes another tack at approaching the issue of chemical warfare agents by focusing on organ systems. The first chapter, which details the nervous system as a target for chemical warfare agents, does a great job giving a general overview of nervous system mechanisms and how selected toxins cause neurotoxicity. The chapter on the behavioral toxicity of nerve agents is weaker, as the evidence is less convincing. The authors do however make some interesting points concerning degeneration of the hippocampus post-exposure to these compounds. The chapter on cardiovascular system is not quite as extensive as the one on the nervous system but still does a nice job covering potential effects of organophosphorous agents, CN, arsenic, and ricin on the heart. The chapter on skeletal muscle focuses more on the basic science and is less useful clinically. The chapter on reproductive toxicity and endocrine disruption does a serviceable job. The chapter on liver toxicity is an adequate overview. The chapter on kidney pathology is interesting but focuses on animal renal toxicity more so than human effects. The discussion of the ocular toxicity of sulfur mustard highlights a topic that is not discussed much by most toxicologists. Despite the documented historical experience, very little evidence appears available for treatment. The chapter on immunotoxicity is a very basic overview, but to be fair to the author, very little is known on the subject. The section on dermal toxicity of sulfur mustard unfortunately relies mostly on cell line and animal studies to make conjectures for treatment.

Section IV deals with special topics and starts off with a chapter on excitotoxicity, oxidative stress, and neuronal injury, which is strong on the basic science but less clinically relevant. The following chapters on neuropathologic effects of chemical warfare agents and molecular and transcriptional responses to sarin exposure have a similar tone, and in the chapter on the effects of organophosphates in the early stages of human muscle regeneration, the authors present their primary research. The chapter "Organophosphate Intoxication: Molecular Consequences, Mechanisms and Solutions" has a similar tenor though they present a broader view of the available genetic research.

Section V covers risks to animals and wildlife and starts off with a chapter titled "Chemical Warfare Agents and Risks to Animal Health." It gives some basic overviews of various chemical warfare agents, and though it tries to focus the topics on animals, known symptoms and treatment options do not vary much compared to humans. A more novel topic is the chapter "Potential Agents that Can Cause Contamination of Animal Feedstuffs and Terror." It is an interesting idea, and the author goes over various scenarios with different

types of chemicals that could be used. Similar scenarios are presented in the following chapter on the risks to animals and wildlife.

Section VI covers toxicokinetics and physiologically based pharmacokinetics. The first chapter discusses these topics related to nerve agents and vesicants. The following chapter then details using a physiologically based pharmacokinetic model rather than the classical, analytical approach, using sarin as an example. The chapter on metabolism of warfare nerve agents then expands on how the human body deals with these nerve agents and its implications for detection (e.g., via protein adducts) and treatment.

Section VII goes on to cover analytical methods, biosensors, and biomarkers. The first chapter in this section covers various devices used to detect chemical warfare agents and describes how they work. The following chapter details detection methods for nerve agents, sulfur mustard, and lewisite. The next chapter covers the use of biosensors for detecting organophosphorous agents via enzymatic reactions. Another chapter then details current methods of detection for organophosphorous compounds and their pitfalls and mentions other potential markers and even treatments via antibodies. A discussion of organophosphorus induced delayed polyneuropathy, its pathophysiology, and potential biomarkers and biosensors follows. The next chapter discusses monitoring of blood cholinesterase activity in workers exposed to nerve gas agents and is a good overview of using different cholinesterase activity for diagnosis. However, its conclusion veers off to discuss a study presumably performed by the chapter's authors.

Section VIII discusses prophylactic, therapeutic, and countermeasures for chemical warfare agents. It starts off with a discussion of the collaboration between National Institute of Health and other agencies in combating potential chemical warfare scenarios with the Countermeasures Against Chemical Threats program. This is followed by a chapter on potential protective measures and treatments following sulfur mustard toxicity, which is nicely summarized by a figure at the end of the chapter. The next chapter discusses medical management of pediatric toxicity. It discusses why children may be more susceptible to certain toxins, goes over various scenarios of different classes of pediatric poisonings, and treatments. Subsequently, there is a discussion of physiologically based pharmacokinetic/pharmacodynamic modeling of interactions with nerve agents. This is followed by a chapter on prophylactic and therapeutic measures for nerve agents, which details the rat studies the authors have performed, and another chapter that discusses agents that can be used against nerve agent poisonings. There is then a chapter on the different pyridinium oximes for treatment of organophosphorus compound poisonings and the evidence behind their use. Afterwards, several authors from the Czech Republic discuss their work in trying to find novel oximes that might have better therapeutic effect. More interestingly, the next chapters detail the existence of the protein paroxonase that naturally hydrolyzes many organophosphorous compounds, and how genetic polymorphisms may effect rate of organophosphorous compounds metabolism and how synthetic, recombinant paroxonase might be useful in the future as a potential treatment. The discussion on carboxylesterases and their metabolism of nerve gas agents is less elegant but again emphasizes potential treatments from the human body's natural mechanisms to deal with these drugs. Investigators from the NIH Countermeasures Against Chemical Threats Program then describe kinetic studies of some bioscavengers for protecting acetylcholinesterease from organophosphates, and lastly, several European researchers discuss the use of recombinant enzymes for detoxification for organophosphorous compounds.

Section IX, the final section of this 72-chapter book, goes over decontamination of chemical warfare agents. The first chapter discusses animal models and materials that can be used for decontamination, including bleach, the M291 skin decontamination kit, the Sandia form, Diphotérine, reactive skin decontamination lotion, an enzyme immobilized polyurethane foam sponge, and immobilized enzyme badges. The penultimate chapter then goes over the detoxification of arsenic and details the many ways that prokaryotic organisms adapt to high arsenic levels and the potential use for arsenic decontamination via these organisms.

Between the last two chapters of Section III, the editor includes some color plates. The diagrams are clear but the images would have been better served in the chapters that they are referenced rather than in the middle of the textbook. At the very least, a heading and a brief description for each figure with brief descriptions would have been helpful. Its positioning between the last two chapters of Section III is obviously a case of expedience. The illustrations within the chapters vary widely in quality – some chapters have none, some figures are less than useful, while others make effective use of tables or photographs.

In summary, the strength of the book is that it covers a multitude of topics, and specifically for those interested in organophosphorous compound/nerve agent poisonings, there are multiple chapters detailing the many aspects of such exposures.

Many of the authors are experts in their fields, either conducting primary research of the topic or representatives of government agencies that study chemical warfare agents.

For its primary audience, it definitely can be helpful, but more as a reference guide than a primary text. The strongest chapters are chapters that take a basic overview of the topic with the authors presenting a concise and clear discussion of the most important topics.

The Handbook of Toxicology of Chemical Warfare Agents definitely has its weaknesses. As each chapter is written by different authors, there is a lot of redundancy. In addition, they are not always consistent with their abbreviations or approach to the chapters. Stronger editorial control would have resulted in a more effective text. The weakest chapters tend to be written by researchers who delve directly into findings from

their laboratories rather than giving a concise and clear overview of the subject at hand

There are not many similar books on the chemical warfare agents, and as such, this text makes an important contribution in being one of the first attempts to be a standard text of the topic. For the most part, the information is impressively up-to-date for a subject that has received lots of attention over the past decades. This is not a must-have text for the practicing toxicologist but is a nice reference to have at a poison center.

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