Medical Toxicology: A Distinct Medical Subspecialty Sprouting from Ancient Roots

Yedidia Bentur MD

Israel Poison Information Center, Rambam Health Care Campus, and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Key words: toxicology, poisoning, toxin, intoxication

IMAJ 2008;10:747–748

The term "toxicology" is derived from the Greek words *toxikos* or *toxa* ("bow") and *toxicon* ("the poison in which the arrows were dipped"). Today this term is used to define the science of poisons – their source, chemical composition, effects, tests and antidotes. Recognition of the potential toxic effects of various substances is probably as old as mankind, dating back 18,000 years to the prehistoric Masai hunters of Kenya who used poison arrows. The historic poisons were plant extracts, animal venoms and minerals. They were used for hunting, in wars, for executions and in religious rituals. Currently abused agents were also known in antiquity: cannabis in China (2200 B.C.), the hallucinogenic mushroom *Amanita muscaria* – "soma" in India (2000 B.C.), opium in Egypt (1500 B.C.), and cocaine in South America (at least 300 B.C.). Only as late as the 19th century did the danger of opiate addiction become recognized, followed by cocaine, sedative hypnotics, hallucinogens and stimulants (the current drug epidemic). The first toxicologists were in fact magicians, sorcerers and religious figures.

Ancient non-medical references to the use of poisoned arrows can be found in the Indian text *Rig Veda* (12th century B.C.), in the *Odyssey* by Homer (850 B.C.) and in Aristotle's scripts (384–322 B.C.). Historical medical texts dealing with toxicology include the *Ebers Papyrus* (about 1500 B.C.), *Materia Medica* (Dioscorides 40–80 A.D.), the *Book of Poisons* which combined contemporary science, magic and astrology (Ibn Wahshiya, 9th century), and the *Treatise on Poisons and their Antidotes* (Moses Maimonides, also known as the Rambam, 1198) who differentiated the hematoxic (hot) from the neurotoxic (cold) effects of poisons.

Paracelsus (1493–1451) established the important concept of dose-response: "What is there that is not poison? All things are poison and nothing is without poison. Solely, the dose determines that a thing is not a poison." In the 18th and 19th centuries the magical and mythological poison mystique was gradually replaced by an increasingly rational, scientific, experimental and analytical approach. Toxicology developed as a separate scientific discipline, distinct from clinical medicine and pharmacology.

World War II was followed by enhanced industrialization and technological progress. The wide availability of medicinal and non-medicinal products in the home, workplace and environment has led to increasing numbers of exposures and poisonings. At the same time, suicide has been recognized as a leading cause of death, including by poisoning. Clearly, despite the ever-expanding information on poisons and poisonings, a serious medical problem has been created due to the lack of awareness to potential hazards on the part of the public, as well as physicians' inability to keep pace with the growing amount of information and their limited training in toxicology. All these factors prompted the medical community to establish poison information (or control) centers, first in the Netherlands in the late 1940s and in 1953 in the United States (Chicago). The initial goal of these poison centers was to provide product information to health care providers (health management organizations, hospitals, and emergency health services). In Israel, the Ministry of Health founded the Israel Poison Information Center in 1964. The current concept and objectives of poison centers are: to serve as a reliable information source on product ingredients, provide first aid and triage advice to the community, advise health care providers on rational and updated poisoning management, prevent unnecessary referrals to health care facilities and hospitalizations, collect epidemiological data on the incidence, characterization and severity of poisoning, educate health care professionals and offer information on prevention. Therefore, the current operation of poison centers such as the Israel Poison Information Center involves clinical toxicological consultations, academic activities, updating the commercial products database, laboratory service, teaching, research and advising governmental and non-governmental agencies. These activities have been expanded due to the increased awareness to environmental health problems (since the 1960s; e.g., Minamata disease, the Bhopal disaster), the growing issue of medication errors (since the 1990s) and the recent profound changes in preparedness for chemical terrorism (e.g., the sarin incident in 1995) [1-3].

Despite thousands of years of knowledge, decades of intense research and huge analytical progress, Medical Toxicology has not developed to the same extent as most other medical specialties. This is probably best illustrated by the very small number of antidotes (only two) approved by the U.S. Food and Drug Administration for clinical use in the past 20 years: fomepizole and hydroxcobalamin [4,5]. There are several possible explanations for this anomaly. Poison lore is sometimes still based on myths, and rational scientific research (including descriptive) is often required to debunk such myths. Knowledge acquired by one generation can be forgotten or discarded inappropriately by subsequent generations. Performing adequate randomized clinical trials is often not possible. This could be due to an inability to recruit large number of patients as well as the inability to standardize and ascertain exposure and ethical issues as we are often dealing with life-threatening situations. Poison center databases have been used as a reliable source for large-scale clinical information, but attention should be drawn to possible confounders such as retrospective design and reliance on second-hand information. *In vitro* and animal experiments are extensively done but extrapolation to humans is neither simple nor straightforward, especially regarding mass poisonings and extreme populations (i.e., young children and the elderly, and those with underlying lung and heart diseases). Pharmaceutical companies tend not to provide significant grant awards since the potential return on development costs of therapies for toxic exposure is not worth the investment. Finally, government support is also limited, often due to lack of resources and allocation priorities. One consequence of this situation is the reliance on consensus guidelines or position statements issued by the major U.S. and European Medical Toxicology organizations.

This issue of the *Israel Medical Association Journal* includes a section dedicated to Medical Toxicology. The subjects covered are: poisoning in Israel (a comprehensive annual report using the database of the Israel Poison Information Center); a similar report from the recently established Palestinian Poison Control and Drug Information Center; a response algorithm to mass toxicological incidents (industrial, transportation or terror); organophosphate poisoning which is hazardous in both individual and mass exposures; medication errors reported by physicians; the prevalence of viral diseases (hepatitis C and B and human immunodeficiency virus) among drug abusers and their ethnic propensity; adolescent ethanol and drug abuse encountered in a pediatric emergency department; a survey on marine injury/poisoning along the coast of Israel; scombroid fish poisoning which is mainly caused by consumption of tuna and resembles allergic reaction; the use of brain magnetic resonance imaging in experimental manganese poisoning; ingestion of cylindrical batteries; an organophosphate-like poisoning caused by the fungicide fenarimol; and the use of available modern online communication techniques to facilitate rapid identification of poisonous plants.

It is our hope that Medical Toxicology will become a certified subspecialty in Israel, that reporting of poisoning and medication errors as well as of toxic exposures to over-the-counter products will become mandatory, that a national poisoning registry be established in the national poison center, and that poisoning consultations provided to all health care providers by the national center not be charged. It is suggested that all these activities be adequately supported by the Ministry of Health and probably also by the industry, as in the U.S. and many European countries.

References

1. Clark RF. The practice of medical toxicology. In: Dart RC, ed. Medical Toxicology. 3rd edn. Philadelphia: Lippincott Williams & Wilkins, 2004:3–6.
2. Wax PM. Historical principles and perspectives. In: Flomenbaum NE, Goldfrank LR, Hoffman RS, Howland MA, Lewin NA, Nelson LS, eds. Goldfrank's Toxicologic Emergencies. 8th edn. New York: McGraw-Hill, 2006:1–17.
3. Shannon MW. The history of toxicology. In: Shannon MW, Borron SW, Burns MJ, eds. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose. 4th edn.: Philadelphia: Saunders Elsevier, 2002:3–11.
4. Brent J, McMartin K, Phillips S, et al. Fomepizole for the treatment of ethylene glycol poisoning. Methylpyrazole for Toxic Alcohols Study Group. *N Engl J Med* 1999;340:832–8.
5. Borron SW, Baud FJ, Mégarbane B, Bismuth C. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. *Am J Emerg Med* 2007;25:551–8.

Correspondence: Dr. Y. Bentur, Director, Israel Poison Information Center, Rambam Health Care Campus, P.O. Box 9602, Haifa 31096, Israel.
Phone: (972-4) 854-2725; Fax: (972-4) 854-2092
email: d_bentur@rambam.health.gov.il