

TOXICOLOGY

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1 INTRODUCTION

Toxicology is most simply defined as the science of poisons. Using naturally occurring substances—first as foodstuffs and subsequently as drugs—must inevitably have led to the recognition of poisoning as a result of excessive intake or overdose at a very early stage in human evolution. There must also have been recognition that death or other ill effect sometimes followed the intake of very small amounts of a foodstuff or other substance. This would have led to the deliberate use of such substances as poisons and their use on weapons, such as arrows, to paralyze or kill. The use on arrows led to the science of toxicology, derived from the Greek word τοξικον (toxicon) for an arrow poison. Today, the main emphasis of toxicology is on detecting and preventing the unwanted effects of chemical agents, although their use as poisons, especially as pesticides and in chemical warfare, continues.

Toxicology is not a “pure science.” It occupies an interface between chemistry, medicine, and biology and is embedded in legislation that governs what substances may be manufactured and how they are used. Thus, it influences, and is itself influenced by, laws and regulations introduced to protect people from the toxic effects of substances that, like pharmaceuticals, may have been marketed because of their beneficial effects when used properly. As a result, the findings of toxicology can have profound economic effects and whole industries, such as asbestos manufacturing, may collapse if their products are condemned as excessively toxic in normal use.

The main objective of toxicology is to prevent harmful effects of useful substances, including therapeutic agents. For new pharmaceutical agents, extensive toxicity and efficacy data are required, including data from volunteer studies in humans. Pharmaceutical agents, at appropriate dose levels, are expected to have a beneficial effect on patients. Other substances, in normal use, whatever their beneficial effects, should have no biological effects on people. This includes pesticides, which, when used as intended, should produce a biological effect in pests without any effect on humans. Absence of effect of pesticides on people depends partly on differences in biochemistry and physiology between pests and humans and partly on careful application of the pesticides to minimize human exposure.

This chapter on toxicology can give you only a limited idea of all that is involved on the subject and you are strongly advised to refer to one or more of the good general textbooks that are available [1–3].

2 BASIC PRINCIPLES

Three concepts underlie modern toxicology. The most fundamental may be paraphrased as “the dose makes the cure or the poison.” This concept was first recorded by Paracelsus (Theophrastus Phillipus Aureolus Bombastus von Hohenheim, 1493–1541), a Swiss physician and alchemist. In other words, all substances, including pharmaceuticals, are potentially toxic. Defining precisely the therapeutic dose and the toxic dose is, thus,