

TOXICOLOGY AND THERAPY OF INTOXICATION

Subcommittee

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Introduction to Toxicology and Therapy of Intoxication

A medical pharmacology course should be primarily concerned with three aspects of toxicology: adverse effects of therapeutic agents, acute intoxications, and chronic poisoning/environmental toxicology. The adverse effects of drugs should be taught along with the pharmacology of individual drugs or groups of drugs.

The discussion of acute intoxications should constitute a short, but important, part of the pharmacology course and should deal with the techniques and procedures used in dealing with the effects of exposure to acutely toxic materials. Lectures dealing with chronic intoxications should emphasize environmental toxicology and risk assessment.

Principles of Toxicology

Recommended Curriculum Equivalent: 1 hr

Learning Objectives

Describe how toxicants are influenced by the basic pharmacokinetic and pharmacodynamic processes such as absorption, distribution, biotransformation, excretion and cellular targets.

Explain the principles of bioactivation of chemicals to toxic species.

Describe the concept of dose-response curves and how it can be helpful in the management of acute and chronic poisonings.

Explain the concepts of threshold levels for toxicity.

Describe measures for determining the safety of a drug or non-therapeutic chemical (e.g. therapeutic ratio).

Explain how toxicogenetics can alter responses to chemicals

Priority Toxic Chemicals	
Recommended Curriculum Equivalent: 2 hr	
Drugs and Chemical Toxicants	Antidotes
ACETAMINOPHEN	N-ACETYL-L-CYSTEINE
AIR POLLUTANTS	ACTIVATED CHARCOAL
ALCOHOLS (ETHANOL, METHANOL, ETHYLENE GLYCOL)	ATROPINE/2-PAM
BENZODIAZEPINES	ETHANOL
CARBON MONOXIDE	FLUMAZENIL
HEROIN, MORPHINE	METHYLENE BLUE
IRON	METAL CHELATORS (EDETATE, 2,3-DIMERCAPTOSUCCINIC ACID, DIMERCAPROL, DEFEROXAMINE)
LEAD	NALOXONE
MERCURY	SODIUM BICARBONATE
PESTICIDES (ORGANOPHOSPHATES AND CARBAMATES)	fomepizole
SALICYLATES	glucagon
beta-blockers	oxygen
cyanide	sodium or amyl nitrite/sodium thiosulfate
Learning Objectives	
<p>Explain how exposure to the primary and secondary toxicants can occur.</p> <p>Describe the signs and symptoms of a toxic exposure induced by each of the toxicants.</p> <p>Describe the mechanism of toxicity of the primary and secondary toxicants.</p> <p>Compare and contrast the toxicity induced by various metals.</p> <p>Compare and contrast the toxicity induced by the neurotoxic pesticides.</p> <p>Describe the antidote and/or treatment for each toxicant.</p>	

Management of Acute Intoxications

Recommended Curriculum Equivalent: 1 hr

Learning Objectives

This section can be case-based to follow up on the identification of priority toxicant poisoning and the therapeutic aspects of treating intoxications. Alternatively, lectures can be provided to teach the “decision-tree” approach to the treatment of acute intoxications using examples such as acetaminophen overdose.

Explain the basic principles of managing an acute intoxication from a drug or non-drug. Describe how decisions are made to determine how an acute intoxication should be handled.

Define what is a toxidrome and know the main signs and drugs/toxins that are associated with the anticholinergic, sympathomimetic and cholinergic toxidromes.

Describe common intoxications and their management.

Define a Poison Control Center and services and information it can provide to physicians.

Clinical Pharmacology

Polyelectrolyte lavage solution has become the standard of care for poisoning by modified release dosage forms. Administration must be titrated to prevent induction of nausea and vomiting and is continued until the presence of a clear rectal effluent. This intervention is only to be used in conscious patients.

For salicylate overdose, acetazolamide is only to be considered as an intervention with failure to alkalinize the urine after intravenous doses of bicarbonate. CAUTION: Serum potassium must be carefully monitored to limit the potential for cardiac arrhythmias. Glucose is also to be administered to counter the uncoupling of mitochondrial oxidative phosphorylation by circulating salicylic acid.

Syrup of ipecac is no longer recommended as a home remedy for pediatric intoxications, since its emetic action is not effective to remove clinically relevant amounts of dosage forms in the time period after the ingestion when it is likely to be administered. Its acute sedative effect may increase the risk of aspiration pneumonia.

Activated charcoal is not effective as an antidote for drug overdose in patients appearing at Emergency Departments, since its efficacy has only been demonstrated within 2 hours of the toxic ingestion. Almost no overdose patients ever appear for treatment within this time interval.

Environmental Toxicology/Risk Assessment	
Recommended Curriculum Equivalent: 1 hr	
Learning Objectives	
<p>Explain the concept of risk versus dose and methods for risk assessment.</p> <p>Describe the concept of pre-carcinogens, proximate carcinogens and ultimate carcinogens.</p> <p>Describe bioactivation pathways for carcinogens.</p> <p>Describe mechanisms of chemical carcinogenesis.</p> <p>Differentiate between mutagenicity and carcinogenicity.</p> <p>Describe chemical preventive mechanisms from carcinogenicity.</p> <p>Describe how toxicogenomic studies may be used to identify potential modes of action and/or bioactivation for a chemical and determine across species for use in risk assessment.</p>	
Relevance	
<p>USMLE topic General Principles – Pharmacodynamic and pharmacokinetic processes</p>	<p>Principles of therapeutics Mechanisms of action and use of drugs for treatment of toxic overdose</p>
<p>AAMC Medical School Objectives Project Report X Patient Safety – Table 1</p>	<p>Topic B: Principles of clinically important pharmacokinetics</p> <p>Topic C: Drug treatment of common conditions</p> <p>Topic D: Management of less common but severe medical conditions and emergencies</p>