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Chapter 19

Toxicology and Emergency Pharmacology

Deepan Natarajan
JKKMMRF'S – Annai JKK Sampoorani Ammal College of Pharmacy,
Komarapalayam, Namakkal, Tamilnadu. 638 183, India.
Kannan Raman
St. Johns College of Pharmaceutical Sciences & Research, Kattappana, Idukki,
Kerala – 685515, India.
V.M. Raja
JKKMMRF'S – Annai JKK Sampoorani Ammal College of Pharmacy,
Komarapalayam, Namakkal, Tamilnadu. 638 183, India.

Abstract: Toxicology and emergency pharmacology together constitute a pivotal branch of medical sciences that bridges pharmacological principles with acute clinical care. Clinical toxicology focuses on the recognition, diagnosis, and management of poisoning, encompassing both accidental and intentional exposures to chemicals, pharmaceuticals, and biological agents. The discipline integrates toxicokinetics and toxicodynamics to predict systemic effects, guide therapeutic interventions, and prevent morbidity and mortality. Emergency pharmacology underlines the rational and timely administration of antidotes, cardiovascular stabilizers, anticonvulsants, and decontamination measures in acute settings. In recent decades, the epidemiology of poisoning has shifted with increased prevalence of prescription opioid overdoses, emergence of novel psychoactive substances, and frequent household exposures to pesticides and industrial toxins. Organ-specific toxicities such as hepatotoxicity, nephrotoxicity, cardiotoxicity, and neurotoxicity remain significant contributors to adverse outcomes, necessitating precise therapeutic interventions. Modern toxicological practice emphasizes rapid toxicology screening, advanced diagnostics such as liquid chromatography–mass spectrometry (LC-MS), and incorporation of evidence-based antidote use. Beyond clinical management, toxicology extends into legal and forensic domains, addressing workplace drug testing, medicolegal investigations, and forensic laboratory quality control. This chapter provides a comprehensive overview of toxicological principles, common toxic agents, antidotal therapies, organ-specific toxicities, and emergency pharmacological strategies, while also addressing medico-legal and forensic perspectives in toxicology.

Keywords: Clinical toxicology, emergency pharmacology, antidotes, poisoning management, forensic toxicology.

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19.0 INTRODUCTION

Clinical toxicology and emergency pharmacology represent dynamic fields that interface between pharmacological science, clinical medicine, and public health preparedness. Toxicology is traditionally defined as the science of poisons, encompassing the study of harmful effects of xenobiotics, their mechanisms of action, and strategies to counteract adverse consequences. In clinical settings, toxicology is not merely theoretical but a highly practical discipline that aids in the rapid recognition and treatment of poisoning episodes, whether arising from accidental household exposures, occupational hazards, deliberate self-harm, or drug overdoses. Emergency pharmacology focuses on time-sensitive interventions with drugs such as antidotes, cardiovascular agents, and seizure control medications that are essential in acute poisoning care.

Globally, the burden of toxicological emergencies has evolved over the last two decades. While traditional challenges such as pesticide poisoning remain highly prevalent in low- and middle-income countries, high-income regions are witnessing a surge in opioid overdoses, benzodiazepine misuse, and intoxication from designer drugs and novel psychoactive substances [1]. Mortality related to poisoning contributes significantly to emergency department admissions, intensive care utilization, and long-term morbidity. Thus, effective toxicology practice must be multidisciplinary, integrating pharmacologists, emergency physicians, critical care specialists, toxicologists, and forensic experts.

The scope of toxicology today also encompasses preparedness against chemical warfare agents, environmental exposures, and bioterrorism threats. Strategic antidote stockpiling, integration of poison control centers, and deployment of real-time toxicological screening methods are essential elements of modern emergency response frameworks [2]. The subsequent sections of this chapter explore toxicokinetics, common poisoning agents, organ-specific toxicity, antidotes, emergency pharmacology, decontamination strategies, toxicological diagnostics, and medico-legal implications, thereby providing a comprehensive understanding of this discipline.

19.1 Toxicokinetics and Toxicodynamics

The principles of toxicokinetics and toxicodynamics are central to predicting the course of poisoning, determining treatment regimens, and anticipating complications. Toxicokinetics refers to the absorption, distribution, metabolism, and excretion (ADME) of toxic substances, whereas toxicodynamics examines the biochemical and physiological effects of toxins on cellular and organ systems [3]. Absorption in poisoning varies considerably depending on the route of exposure. For instance, ingestion of lipophilic agents like organophosphates results in rapid gastrointestinal absorption, while inhalational exposure to carbon monoxide produces almost instantaneous systemic toxicity due to its high affinity for hemoglobin. Distribution is influenced by factors such as protein binding, lipid solubility, and compartmentalization. Drugs like tricyclic antidepressants exhibit high tissue binding, leading to delayed toxicity despite declining plasma concentrations [4].

Metabolism represents a critical determinant of toxicity, as many xenobiotics undergo bioactivation to more toxic metabolites. Acetaminophen is a classic example, wherein excessive metabolism via cytochrome P450 enzymes generates N-acetyl-p-benzoquinone imine (NAPQI), a hepatotoxic intermediate. Conversely, detoxification pathways such as glucuronidation and sulfation may be overwhelmed in overdose scenarios [5].

Excretion through renal and biliary routes can be impaired in patients with organ dysfunction, thereby prolonging toxic effects. Non-linear kinetics often emerge in overdose situations due to saturation of metabolic pathways, exemplified by ethanol and phenytoin toxicity [6].

Toxicodynamics further explain dose-response relationships, thresholds for toxicity, and receptor-level interactions. For example, opioids exert toxicodynamic effects through excessive μ-receptor activation, leading to respiratory depression, while benzodiazepines enhance GABAergic activity, resulting in profound sedation. Biomarkers, including serum drug concentrations, metabolite ratios, and emerging omics-based indicators, provide valuable insight into toxic exposure and prognosis [7]. Advanced toxicokinetic modeling and physiologically based pharmacokinetic (PBPK) models are increasingly employed to predict overdose behavior and guide individualized therapeutic strategies.

19.2 Common Poisoning Agents

The landscape of toxic exposures encompasses a wide variety of agents, ranging from domestic products and environmental chemicals to prescription medications and recreational drugs. Household and environmental toxins continue to account for a significant proportion of accidental poisonings, particularly among children. Pesticides, especially organophosphates and carbamates, remain leading causes of morbidity and mortality in agricultural communities. Industrial chemicals such as hydrocarbons, solvents, and heavy metals (e.g., lead, mercury, arsenic) also contribute substantially to toxicological emergencies [8].

Prescription drug overdose has become a dominant issue in both developed and developing regions. The global opioid epidemic underscores the catastrophic impact of excessive consumption of agents such as morphine, oxycodone, and fentanyl, which cause life-threatening respiratory depression. Similarly, benzodiazepine overdoses often present with profound sedation, hypotension, and respiratory compromise, particularly when co-ingested with alcohol or opioids. Acetaminophen, while widely used and safe at therapeutic doses, is among the most common agents implicated in intentional overdose due to its ready availability and severe hepatotoxic potential [9].

Recreational drug toxicity has expanded with the proliferation of synthetic cannabinoids, cathinones (“bath salts”), and hallucinogens. Novel psychoactive substances (NPS) are particularly challenging because their constantly evolving chemical structures evade regulatory controls and toxicological screening methods [10]. These agents may cause unpredictable sympathomimetic, serotonergic, or dissociative syndromes, complicating diagnosis and management. The recognition of poisoning agents requires thorough clinical history, corroboration from witnesses, circumstantial evidence, and diagnostic screening. Poison control centers play a crucial role in surveillance, case management, and public health guidance. Recent advances include the use of portable mass spectrometric devices for point-of-care identification of toxins in emergency settings [11].

19.3 Organ-Specific Toxicity

Toxins and drugs in overdose affect multiple organ systems, with organ-specific toxicity often dictating the clinical presentation and prognosis. Hepatotoxicity is a major concern with agents such as acetaminophen, isoniazid, and halothane. Acetaminophen-induced liver injury remains the leading cause of acute liver failure in many countries, necessitating timely administration of N-acetylcysteine [12]. Nephrotoxicity arises from aminoglycosides, amphotericin B, ethylene glycol, and heavy metals, leading to acute tubular necrosis or oxalate nephropathy.

Cardiotoxicity is frequently observed with tricyclic antidepressants, cocaine, and digoxin. Tricyclic overdose manifests as QRS prolongation, arrhythmias, and hypotension due to sodium channel blockade, while digoxin toxicity presents with bradyarrhythmias, visual disturbances, and hyperkalemia [13]. Neurotoxicity encompasses central nervous system effects such as seizures,

coma, and cognitive dysfunction, commonly caused by isoniazid, organophosphates, and synthetic stimulants.

Pulmonary toxicity results from inhalational irritants, hydrocarbons, and paraquat ingestion, which cause acute lung injury and progressive fibrosis. Gastrointestinal toxicity is exemplified by corrosive ingestion of acids and alkalis, producing esophageal perforations and strictures. Hematologic toxicity includes methemoglobinemia from nitrates, aplastic anemia from chloramphenicol, and hemolysis in glucose-6-phosphate dehydrogenase (G6PD)-deficient patients exposed to certain drugs [14]. Dermatologic toxicity includes Stevens-Johnson syndrome and toxic epidermal necrolysis, often drug-induced.

Recognition of organ-specific patterns aids in early identification and targeted therapy. Monitoring biomarkers such as liver enzymes, serum creatinine, cardiac troponins, and neuroimaging results is essential to stratify severity and guide supportive measures [15].

19.4 Antidotes and Reversal Agents

Antidotes represent a cornerstone of emergency pharmacology, offering targeted therapy against specific poisons. Naloxone is a prototypical reversal agent for opioid toxicity, rapidly reversing respiratory depression and central nervous system depression. Its widespread availability as intranasal formulations has been pivotal in addressing the opioid overdose crisis [16]. Similarly, flumazenil acts as a competitive antagonist at benzodiazepine binding sites, although its use is limited due to risks of precipitating seizures in patients with chronic benzodiazepine use or co-ingestion of pro-convulsant drugs.

N-acetylcysteine (NAC) is the definitive antidote for acetaminophen poisoning, replenishing hepatic glutathione stores and detoxifying the reactive metabolite NAPQI. Its timely administration within 8–10 hours post-ingestion significantly reduces the risk of fulminant hepatic failure [17]. Chelating agents such as dimercaprol, succimer, and EDTA are essential for heavy metal poisoning, while fomepizole and ethanol serve as competitive inhibitors of alcohol dehydrogenase in ethylene glycol and methanol intoxication. Hydroxocobalamin provides effective therapy for cyanide poisoning by binding cyanide to form cyanocobalamin, which is excreted renally [18].

Digoxin immune Fab fragments (Digibind) are lifesaving in severe digoxin intoxication, whereas methylene blue is employed in refractory methemoglobinemia unresponsive to conventional measures. Lipid emulsion therapy, though initially developed for local anesthetic systemic toxicity, has expanded to treat various lipophilic drug overdoses [19].

Despite their utility, antidotes are limited by factors such as availability, cost, and narrow indications. In many cases, supportive care remains the mainstay of therapy. Furthermore, antidotes must be administered judiciously, guided by toxicological confirmation and clinical presentation, as inappropriate use may cause harm [20].

19.5 Emergency Cardiovascular and CNS Pharmacology

Acute toxicological crises frequently manifest as cardiovascular or central nervous system (CNS) emergencies, necessitating rapid pharmacological intervention. Advanced Cardiac Life Support (ACLS) guidelines emphasize the use of drugs such as epinephrine, atropine, and amiodarone in poisoning-induced cardiac arrest or arrhythmias. Epinephrine, a potent adrenergic agonist, is indispensable in asystole and pulseless electrical activity, although outcomes are often poorer when cardiac arrest is secondary to massive poisoning due to refractory conduction disturbances [21]. Atropine serves as the first-line agent in organophosphate-induced bradycardia, counteracting

excessive cholinergic stimulation at muscarinic receptors [22]. Amiodarone is often reserved for ventricular tachycardia or fibrillation refractory to defibrillation and is preferred over lidocaine in tricyclic antidepressant poisoning due to its less pronounced sodium channel blockade.

Seizure management in toxicology primarily involves benzodiazepines such as lorazepam or diazepam, which enhance GABA-mediated inhibition. In refractory cases, barbiturates and propofol are used, albeit with caution given their potential for hypotension and respiratory suppression [23]. Specific toxic agents, such as isoniazid, induce seizures resistant to conventional therapy, necessitating pyridoxine supplementation as both a cofactor replacement and antidote [24]. Lipid emulsion therapy has emerged as a rescue modality for severe toxicity from lipophilic drugs, notably local anesthetics such as bupivacaine. The "lipid sink" theory suggests that intravenous lipid emulsions sequester lipophilic toxins, reducing their bioavailability to target tissues. This approach has expanded to manage overdoses involving beta-blockers, calcium channel blockers, and tricyclic antidepressants [25].

High-dose insulin euglycemia therapy (HIET), coupled with dextrose infusion, is increasingly utilized in severe calcium channel blocker and beta-blocker poisoning. Insulin promotes myocardial carbohydrate utilization and exerts inotropic effects, thereby restoring cardiac output [26]. These interventions underscore the integration of pharmacological principles with critical care strategies in managing toxicological emergencies.

19.6 Decontamination Strategies

Decontamination remains a central pillar of poisoning management, aiming to reduce further absorption of toxins from the gastrointestinal tract, skin, or eyes. Activated charcoal is the most widely employed agent, functioning through adsorption of toxins within the gut lumen. Its efficacy is maximal when administered within one hour of ingestion; however, it remains valuable in delayed presentations involving drugs with enterohepatic recirculation or sustained-release formulations [27].

Gastric lavage, historically a mainstay, has declined in routine use due to risks of aspiration, esophageal injury, and limited evidence of improved outcomes. Current recommendations restrict its use to life-threatening ingestions within one hour, under strict airway protection [28]. Whole bowel irrigation using polyethylene glycol electrolyte solution is particularly indicated in cases of sustained-release drug ingestion, iron poisoning, and body packer scenarios where drug packets are concealed within the gastrointestinal tract.

Dermal decontamination, involving copious water and soap washing, is critical for chemical exposures such as pesticides or phenol. Similarly, ocular exposures necessitate immediate irrigation with isotonic saline or water to prevent corneal damage [29]. Enhanced elimination techniques, such as multiple-dose activated charcoal, hemodialysis, hemoperfusion, and urine alkalinization, are reserved for toxins with specific physicochemical properties. For example, methanol, lithium, and salicylates are dialyzable due to low molecular weight and limited protein binding [30]. The choice of decontamination strategy must balance potential benefit against procedural risks and be individualized according to the toxin, timing of ingestion, and patient condition.

19.7 Toxicology Screening and Diagnostics

Timely and accurate identification of toxic agents is essential for guiding therapy. Initial assessments rely on clinical syndromes or "toxidromes" such as cholinergic (organophosphates), anticholinergic (antihistamines, tricyclics), opioid (miosis, respiratory depression), and

sympathomimetic (cocaine, amphetamines). Point-of-care diagnostics, including urine drug screens, are commonly used in emergency departments; however, their specificity and sensitivity are often limited, and false positives from cross-reactivity remain a challenge [31].

Blood and urine toxicology testing remain the mainstay of diagnostic evaluation, providing quantitative insights into exposure. Advanced techniques such as gas chromatography–mass spectrometry (GC-MS) and liquid chromatography–tandem mass spectrometry (LC-MS/MS) represent the gold standard for confirmatory testing, allowing precise identification and quantification of a wide array of xenobiotics [32].

Emerging diagnostic modalities include biosensors, immunoassays, and high-resolution metabolomics, which hold promise for rapid, bedside applications. Postmortem toxicology has a vital role in forensic medicine, often requiring specialized sample handling and interpretation to distinguish ante-mortem exposure from postmortem redistribution [33].

The integration of toxicology data into electronic health records and poison control databases enables real-time surveillance, trend analysis, and informed policy decisions. Artificial intelligence-driven algorithms are being explored to predict toxicological outcomes based on clinical and laboratory inputs, potentially transforming acute care paradigms [34].

19.8 Biothreats and Chemical Warfare

Beyond individual exposures, toxicology extends into public health domains involving biothreats and chemical warfare. Nerve agents such as sarin, soman, and VX are highly potent organophosphorus compounds that irreversibly inhibit acetylcholinesterase, resulting in catastrophic cholinergic crises. Immediate therapy involves atropine, oximes such as pralidoxime, and benzodiazepines to control seizures [35]. Cyanide, encountered in both industrial settings and as a potential bioweapon, exerts toxicity by inhibiting cytochrome oxidase, thereby halting cellular respiration. Hydroxocobalamin and sodium thiosulfate remain essential antidotes.

Ricin, a protein toxin derived from Ricinus communis, causes severe gastrointestinal and multi-organ toxicity following ingestion, inhalation, or injection, and currently has no approved antidote. Radiation exposure from nuclear incidents induces hematopoietic, gastrointestinal, and neurovascular syndromes, requiring both supportive care and specific interventions such as potassium iodide for radioiodine exposure [36].

Preparedness for such threats involves stockpiling of antidotes, establishment of decontamination protocols, simulation-based training, and inter-agency coordination. Strategic National Stockpiles and international frameworks ensure rapid deployment of antidotes during mass casualty scenarios [37]. Advances in biosciences also highlight the role of monoclonal antibodies, bioscavenger enzymes, and RNA-based countermeasures as potential future therapies against chemical and biological threats.

Table 1: Common toxicology screening methods and their applications

Method	Principle	Advantages	Limitations	Applications
Immunoassay (urine/blood)	Antibody-based detection	Rapid, inexpensive, point-of-care	Cross-reactivity, false positives	Initial screening in ED, workplace testing
Gas chromatography–mass spectrometry (GC-MS)	Separation and identification of compounds	High specificity, gold standard	Time-consuming, requires expertise	Confirmatory testing, forensic investigations

Liquid chromatography–tandem mass spectrometry (LC-MS/MS)	High-resolution detection of drugs/metabolites	Ultra-sensitive, broad coverage	Expensive, limited availability	Complex drug panels, postmortem toxicology
Biosensors (emerging)	Real-time detection of analytes	Portable, rapid, minimal sample preparation	Still experimental, limited validation	Future bedside diagnostics

Table 2: Applications of forensic toxicology in clinical and legal contexts

Domain	Purpose	Examples
Medicolegal investigation	Establish cause of death, confirm poisoning	Homicide, suicide, accidental overdose
Workplace drug testing	Ensure safety in sensitive professions	Aviation, defense, transportation
Child abuse/neglect cases	Detect covert exposures	Household poisoning, intentional drugging
Sports anti-doping	Identify prohibited substances	Anabolic steroids, stimulants, EPO
Forensic lab quality control	Ensure reproducibility, accuracy, and chain of custody	ISO/IEC 17025 accreditation requirements

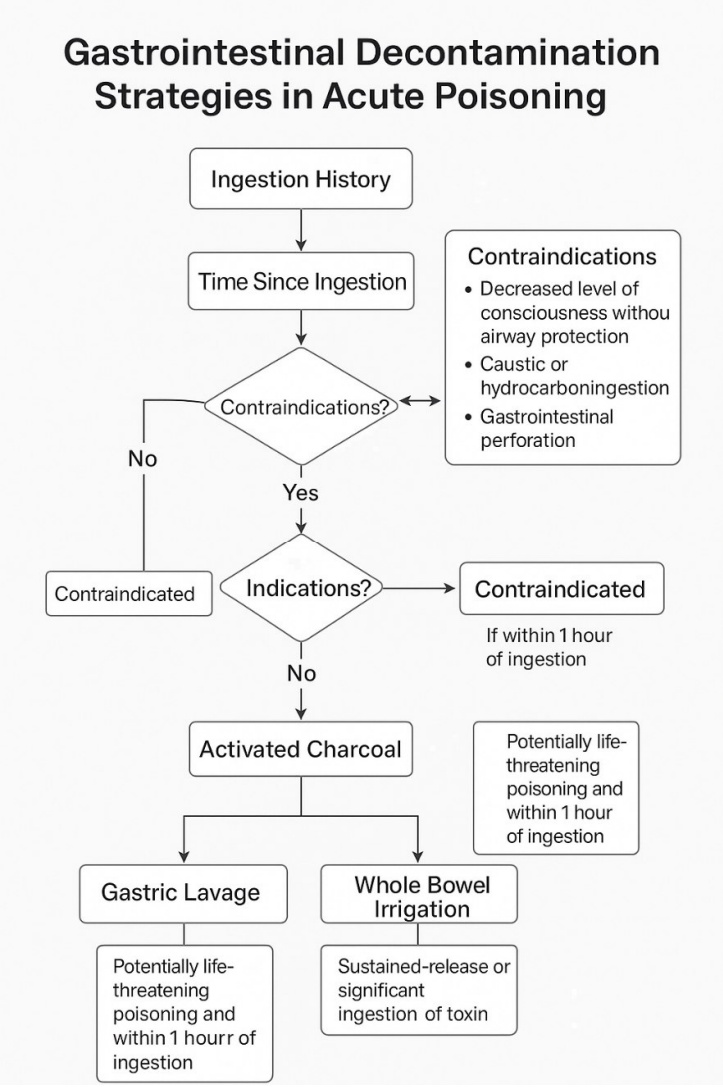

Figure 1: Gastrointestinal decontamination strategies in acute poisoning.

19.9 Legal and Forensic Toxicology

Toxicology also underpins medicolegal and forensic investigations, where accurate detection, quantification, and interpretation of toxic substances influence judicial outcomes. Medicolegal considerations include suspected homicides, suicides, child abuse, workplace accidents, and impaired driving cases [38]. Maintaining chain of custody is crucial to ensure admissibility of toxicology reports in court. Any breach in specimen handling or documentation can invalidate findings. Workplace drug testing is another expanding field, particularly in safety-sensitive industries such as aviation, defense, and transportation. Urine remains the most commonly tested matrix, although hair and saliva testing are gaining importance due to extended detection windows and non-invasive collection [39].

In cases of child abuse or neglect, toxicology aids in identifying covert drug exposures, environmental toxins, or poisoning as a form of maltreatment. Forensic laboratory quality control ensures accuracy, reproducibility, and compliance with international accreditation standards such as ISO/IEC 17025 [40]. The growing complexity of novel psychoactive substances has challenged

forensic laboratories to continually upgrade detection technologies and maintain specialized expertise. Interdisciplinary collaboration among clinicians, forensic experts, and legal authorities is vital for ensuring justice and public safety.

CONCLUSION

Toxicology and emergency pharmacology form the cornerstone of acute poisoning management, integrating fundamental pharmacological principles with life-saving clinical practice. Understanding toxicokinetics and toxicodynamics provides a foundation for predicting toxic effects, while identification of common poisoning agents and their organ-specific toxicities enables targeted interventions. Antidotes and emergency pharmacological measures such as ACLS drugs, lipid emulsion therapy, and high-dose insulin therapy have transformed clinical outcomes. Equally important are decontamination strategies, advanced diagnostic tools, and preparedness for chemical and biological threats. Forensic toxicology extends the relevance of this discipline into the legal arena, ensuring accountability and societal protection. Future directions include the integration of real-time biosensors, AI-driven diagnostic algorithms, and novel antidotal therapies that promise to enhance both individual patient care and public health responses.

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