CHAPTER 101

Poisoning: Kinetics to Therapeutics

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OBJECTIVES

This chapter will:
1. Review the fundamentals of pharmacokinetics and toxicology.
2. Present an overview of therapeutic management of poisoning by conventional and extracorporeal circulatory methods.
3. Describe the role of supportive treatments.

Accidental or premeditated ingestion of poisons is a significant health problem worldwide and is a frequent cause of admission to emergency departments and intensive care units (ICUs). Reflecting the necessarily urgent nature of the clinical response to poisoning, however, the research and testing often does not involve human subjects for the "no harm principle."[2] Randomized controlled trials evaluating the effectiveness of methods often are lacking, and evidence-based information on the management of poisoning is scarce.

Clinical trials in toxicology are often hard to carry out: The framework conditions are hardly ever the same from one case of poisoning to another, and, as a result, the assessment of any particular intervention may be problematic. The available data on various types of treatment have been taken into consideration in the position papers issued by the medical societies.

After entering the body, a drug is eliminated by excretion and by metabolism. Although elimination can occur through a variety of different routes, most drugs are cleared by the kidney or by metabolism in the liver. The study of

drug absorption, distribution, metabolism, and excretion requires the application of mathematical techniques, or modeling (pharmacokinetics or pharmacokinetic modeling). A variant of this approach is toxicokinetics, which relates to the absorption, distribution, and elimination processes of compounds that produce toxic effects in the body. However, almost all substances are toxic under the right conditions. As Paracelsus (1493–1541), the father of modern toxicology, said, "Only dose determines the poison" (translation).[3]

Epidemiology of Poison Ingestion

Worldwide, the acutely poisoned patient remains a common problem for doctors working in emergency medicine. The causes of acute poisoning change over time. Some substances that were once very common causes of poisoning are now only rarely so, including barbiturates, older types of rodenticide (thallium compounds), and alkyl phosphate insecticides such as parathion. Newer medications, illegal drugs, and poisoning always have been a part of human life. The further scientific understanding of technical products such as cleaning agents and cosmetics such as cleaning agents and cosmetics and new consuming habits (intentional and unintentional) also have changed the overall picture substantially.[4]

Within the United States, since 1983, the American Association of Poison Control Centers has compiled data covering 63 poison centers, which for 2014 reported a total of 2,617,346 cases. Children younger than 3 years were involved in 35.6% of these cases, and 47.7% occurred in children younger than 6 years. A male predominance is found among poison exposure victims younger than 13 years, but the sex distribution is reversed in teenagers and adults. Approximately 93.5% of exposures occurred at home, 1.7% at the workplace, 1.3% at school, 0.3% at healthcare facilities, and 0.2% at restaurants. A total of 1173 fatalities were reported, with analgesics, antidepressants, stimulants and street drugs, sedative-hypnotic-antipsychotic agents, and cardiovascular drugs being the most common agents responsible. Although involved in a majority of poisoning reports, children younger than 6 years incurred just 1.4% of the fatalities; 45.9% of poisoning fatalities occurred in persons 20 to 49 years of age; 24.1% of fatal cases involved two or more drugs or products. The majority of human exposures were acute (55%) or acute on chronic (20.5%). The vast majority (74.7%) of poison exposures were unintentional; a suicidal intent was identified in 11.7% of cases. Therapeutic errors accounted for 12.6% of exposures, with unintentional nonpharmaceutic product misuse accounting for another 5.8% of exposures.[5]

SOME BASIC PRINCIPLES OF PHARMACOKINETICS

Pharmacokinetics is a branch of pharmacology dedicated to the study of the time course of drug and metabolite concentrations or amounts in biologic fluids, tissues, and excreta, and also of pharmacologic response, and construction of suitable models to interpret such data. Pharmacokinetics involves what the body does to a drug, including the processes of absorption, distribution, metabolism, and excretion (ADME), and how long these processes take.[6] The principles of pharmacokinetics first were described in 1937 by a Swedish physiologist and biophysicist, Torsten Teorell, who is regarded as the "father of pharmacokinetics." He introduced the concepts of compartmental modeling in physiologic systems in which to describe the ADME of a drug. The term "pharmacokinetics" was first introduced by F.H. Dost in 1953 and is derived from the Greek word *pharmakon*, meaning drug or poison, and the physics term *kinetics*, which describes change in terms of time.

Absorption

Absorption is the process of drug movement from the administration site to the systemic circulation. Drug absorption is determined by physicochemical properties of drugs, their formulations, the physiologic characteristics of the person taking the drug, and routes of administration. When given by most routes, a drug must traverse several semipermeable cell membranes, which act as a lipid barrier with small holes throughout located in various tissue, muscle, or gastrointestinal (GI) epithelium before reaching the systemic circulation. Drugs may cross these membranes selectively by passive diffusion, facilitated passive diffusion, active transport, or pinocytosis. Bioavailability is the most important term used to describe the rate and maximum amount of drug available to the body after its absorption. Drug solubility is a major factor in determining the bioavailablity. Area under the concentration curve, the best measure of bioavailability, is the integrated space under the curve of a plot of concentration of drug versus time. Peak serum level is important to know and will sometimes correlate with symptoms of drug exposure.

Distribution

Drug distribution refers to the movement of drug to and from the blood and various tissues of the body (e.g., fat, muscle, and brain tissue) and the relative proportions of drug in the tissues. Factors that influence distribution include blood perfusion, membrane permeability, plasma protein binding (PPB), regional pH gradients, and accumulation in fat and tissue reservoirs. The one-compartment model assumes rapid distribution, but it does not preclude extensive distribution into various tissues.

Many different plasma proteins such as albumin, various lipoproteins, and α_1-acid glycoprotein interact with various drugs primarily by electrostatic interactions. Only unbound drug is thought to be available for passive diffusion to extravascular or tissue sites where pharmacologic effects occur. PPB influences distribution and the apparent relationship between pharmacologic activity and total plasma drug concentration.

Apparent volume of distribution (V_D) is a measurement of the apparent space in the body containing the drug. V_D is an artificial concept and depends partly on the lipid/water solubility properties of drugs. It is of value in describing whether a drug is predominantly to be found in blood or at other tissue sites. Drugs that bind strongly to plasma protein tend to have lower V_D.

Metabolism

Drug metabolism is the chemical alteration of a drug by the body. The liver is the principal, but not the sole, site of most drug metabolism in the body. The cytochrome P-450 enzyme system is particularly important because many different drugs also can induce or inhibit these enzymes, resulting in changing efficiency of the system in metabolizing drugs,

which may enhance toxicity or diminish efficacy of the drug. "First-pass effect," an important term of metabolism, refers that some drugs are metabolized in the liver immediately after absorption and then are excreted in the bile, leaving less active drug available to the site of action.

Phase I reactions of drug metabolism involve oxidation, reduction, or hydrolysis of the parent drug, resulting in its conversion to a more polar molecule. Phase II reactions involve conjugation by coupling the drug or its metabolites to another molecule, such as glucuronidation, acylation, sulfate, or glicine. The substances that result from metabolism may be inactive, or they may be similar to or different from the original drug in therapeutic activity or toxicity.

Excretion

Drug excretion is the removal of drugs from the body, either as a metabolite or unchanged drug. There are many different routes of excretion, including urine, bile, sweat, saliva, tears, milk, and stool. By far, the most important excretory organs are the kidney and liver. In kidney, excretion of drugs depends on glomerular filtration, active tubular secretion, and passive tubular absorption. Urine and blood pH and the physical characteristics of the drug molecule are important in determining whether the drug is excreted in the urine or remains in the circulation. Drugs appearing in bile will enter the intestines and may be reabsorbed resulting in enterohepatic circulation. Biliary excretion eliminates substances from the body only to the extent that enterohepatic cycling is incomplete. Drugs with a molecular weight (MW) exceeding 300 daltons and with polar and lipophilic groups are more likely to be excreted in bile. Clearance is a measure of the ability of the body to eliminate a drug. The elimination behavior of a drug is described most simply by its half-life, the time needed for the drugs concentration to be halved.

DIFFERENCES BETWEEN PHARMACOKINETICS AND TOXICOKINETICS

Pharmacokinetics has played an ever-increasing role in discovery and development during the last 40 years and is now a critical and highly interactive discipline, contributing to knowledge regarding drug distribution and activity throughout preclinical and clinical drug development. On the other hand, toxicokinetics is of far more recent orgin and represents a unique expansion of pharmacokinetics detailing the impact of toxins on normal body-drug interactions. Understanding a poison's toxicokinetics provides the clinician with the tools necessary for rational therapeutics. Toxciokinetics may thus be different from pharmacokintics in some of the following principles.[7]

Exposure Doses

The major difference between pharmacokinetics and toxicokinetics is the different exposure doses. It has been known for 500 years that toxicity is a matter of concentration. Paracelsus (1493–1541), the father of toxicology, stated, "All substances are poisons, there is none which is not a poison. The right dose differentiates a poison from a remedy."[8] This is known as the dose-response relationship, a fundamental concept of toxicology. It therefore would be unrealistic to assume that the body could handle administered compounds and their metabolites from these very high doses in a way similar to therapeutic or pharmacologic doses.

Solubility

Solubility may occur in the GI tract at toxicologic doses. This could give rise to drug precipitation in biologic fluids and in organs and tissues giving rise to toxicity that may not be associated with the intrinsic pharmacologic or toxicologic effects of the poison.

Bioavailability

Normal absorption behavior and hence normal bioavailability of a drug may change drastically in overdose situations. For example, ethanol and salicylates may paralyze the pyloric sphincter and delay their own absorption, especially when taken in large doses. This can be beneficial because gastric lavage (GL) can be employed long after ingestion when the drug would be expected to have been absorbed already. The overdose behavior of drugs is therefore difficult to predict, and laboratory results will be difficult to interpret because of unusual absorption behavior.

Plasma Protein Binding

PPB is generally reversible and always saturable at toxicologic doses. Measurement of the free fraction is often preferable clinically, especially for drugs with high degrees of PPB. This can in turn influence Vd and penetration into such tissues as the nervous system. It may give rise to different plasma concentration-effect relationships at toxicologic doses compared with pharmacologic doses.

First-Pass Effect

Hepatic clearance of drug during absorption is an enzyme-dependent process and enzymes responsible for first-pass metabolism may become saturated by toxicologic doses. This results in a higher-than-usual fraction of the drug reaching the intended receptors and may be manifested in more toxicity than expected. The metabolic pathways and metabolic effiency may differ at toxicologic doses relative to pharmacologic doses.

Renal Excretion

Renal excretion comprises satuable and nonsaturable mechanisms. It can be influenced dramatically by circulating drug concentrations, giving rise to changes in renal excretion effciency and clearance of drug from the body. This is particularly true for any compound that is actively excreted wholly or partially by the proximal renal tubules.

Physiologic Feedback

Because the toxicologic doses may be toxic to the host, depending on the site and nature of toxic events, this also

may have a traumatic effect on physiologic feedback that may affect the ADME processes of drug.

Drug Interactions

Drug interactions are frequently concentration dependent, and different types of interactions may occur in poisoning, particularly in patients exposed to more than two poisonous drugs or products.

Saturability

Saturable processes in some way or another, even though they directly involve only passive drug transport, may affect most toxicokinetics processes in the body. These may affect the toxicokinetics and toxicity profile of an administered poison. In overdose, protein saturation may be 100%, so free drug/poison exists that is amenable to removal.

MANAGEMENT OF POISONING

The overall mortality from acute poisoning is less than 1%. The challenge for clinicians managing poisoned patients is to identify at an early stage those who are most at risk of developing serious complications and who therefore potentially may benefit from specific measures (GI decontamination, enhancement of elimination, pharmacologic antidotes), in addition to general supportive care and to avoid unuseful and potentially dangerous interventions in others.

Gastrointestinal Decontamination

The vast majority of poisoning cases observed in emergency departments occur by ingestion: decontamination procedures intend to limit absorption and toxicity thus may be indicated. Methods to prevent absorption can be classified in three categories: gastric emptying (induction of emesis, GL), adsorption in situ (administration of activated charcoal [AC]), expulsion of GI content (cathartics, whole-bowel irrigation [WBI]). Much controversy remains regarding the roles of emesis, GL, AC, WBI, and the use of cathartics in GI decontamination.[9] In view of this, the American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT), the world's two largest clinical toxicology societies, have published guidelines on GI decontamination on the basis of consensus and evidence based position statements in 1997. They are well accepted by the rest of the world, and it is important to understand the advances in understanding and changes in practice that come from the guidelines, although the evidence base for them is still limited.

Administration of Activated Charcoal

Activated charcoal is a highly porous form of carbon with a surface area of 950 to 2000 m^2/g that is capable of adsorbing poisons with a molecular weight of 100 to 1000 daltons. The poison adsorption may be limited by the administration of activated charcoal either as a single dose or in multiple doses. The multiple-dose administration of activated charcoal also may enhance the elimination of a toxic substance. It will be discussed later in the chapter.

The activated charcoal can prevent poison systemic adsorption to some extent. It is a considerably lower risk method than lavage and emesis. However, two recent large studies did not find single-dose activated charcoal to be beneficial in overdose.[10,11] The pharmacodynamics and pharmacokinetic studies suggest that single-dose activated charcoal may decrease drug exposure for some drugs, but this does not translate to clinical benefit. Although activated charcoal may not be clinically beneficial in severe poisoning overdose patients, the benefits will outweigh the low risk of administration.[12] The decision to admit activated charcoal should be based on toxicity and properties of ingested drugs and potential benefit of charcoal, balanced against the willingness of the patient and the risk of complications.

Activated charcoal adsorbs many substances such as alkaloids, vitamin K antagonist, and acetaminophen, but many other kinds are not adsorbed. Therefore it is not suggested to administer activated charcoal before knowing the properties of the ingested substance. The position statement also recommends that single-dose activated charcoal should not be administered routinely in the management of poisoned patients and may be considered only if a patient has ingested a potentially toxic amount of a poison (which is known to be adsorbed to activated charcoal) up to 1 hour previously.[13] However, the approach remains widely used despite the fact that many overdose patients present at least 2 hours after taking a medication. Nevertheless, if absorption has been delayed or gastrointestinal motility is impaired, activated charcoal may reduce the final amount absorbed. Activated charcoal often is given in an insufficient dose according to the poison center's experience; the 0.5 to 1 g/kg body weight is recommended. Particularly in medications that have a delayed pharmacologic effect, the sufficient administrated dose of activated charcoal is important.[14]

Activated charcoal administration is contraindicated whenever the respiratory tract has not been protected (by intubation). The main risk is aspiration. It also is contradicated after ingestion of corrosive substances such as acid or base, liquid hydrocarbons, or surfactants.[15]

Gastric Lavage

GL also commonly is called stomach pumping or gastric irrigation. After insertion of a large-bore tube (32- to 40-French [Fr] in adults, and 16- to 28-Fr in children), GL is accomplished with 100- to 200-mL aliquots of normal saline or water with the intent of removing toxic substances present in the stomach.

The clinical benefit of gastric lavage has not been demonstrated unequivocally. A system review of 56 controlled studies from China showed that the lavage may be useful as a treatment of organophosphorus pesticide poisoning even more than 60 minutes after the ingestion. However, the study potentially suffer from significant methodologic flaws that threaten their reality.[16] There are some severe complications that have been observed in the controlled studies, including hypoxia, aspiration, pneumonia, perforation, and laryngospasm.[15] Therefore the indications for limiting the absorption of poisonous substances have been restricted.[17] In a relevant position paper dated February 2013, it is recommended that GL should be administered only by an experienced physician.[18]

The position statement recommends that GL should not be used routinely in the management of poisoned patients. It may be considered only in a patient who has ingested a potentially life-threatening amount of toxin within

60 minutes, or if the ingestant was an agent that delays gastric emptying (e.g., tricyclic antidepressants) or a drug not adsorbed by activated charcoal (e.g., ferrous sulfate, lithium).[18] Contraindications include ingestion of corrosive substances such as acid or base, low viscosity hydrocarbons such as gasoline, and loss of the protective airway reflexes.

Emesis

Enhancement of gastric emptying, or emesis, relies on the use of emetics, such as ipecac, prepared from the dried rhizome and roots of the *Cephaelis acuminata* or *Cephaelis ipecacuanha* plant and administered in the form of syrup.

Ipecac syrup induces vomiting in a high percentage of patients. The resultant decrease in the gastrointestinal absorption of ingested substances will be time dependent. It is documented effective only in a limited number of drugs in preventing the adsorption. Furthermore, the effectiveness is reduced substantially if ipecac syrup is given more than 90 minutes after ingestion of toxic.[19] Furthermore, potentially severe contraindications and adverse effects may be associated with its administration, including reduced effectiveness of charcoal, delayed administration of oral antidotes, aspiration pneumonitis, and other complication of prolonged emesis.

Although ipecac syrup has been used for years to provoke vomiting after toxic ingestions, it is no longer recommended an appropriate routine measure.[14] The AACT-EAPCTC position statement states that syrup of ipecac should not be administered routinely in the management of poisoned patients. The ipecac syrup is not available in more than 83.3% of emergency departments in United States. There is no evidence available from clinical studies to suggest that it would eliminate some portion of the poison and thereby reduce morbidity and mortality among poisoned patients.[20]

Laxatives and Cathartics

Cathartics (e.g., sorbitol, magnesium citrate) frequently are used to shorten gastrointestinal transit time, thereby shortening the period of absorption. Laxatives, such as sodium sulfate, and sorbitol were given earlier to treat acute poisoning. However, their use is no longer recommended, because it led to volume depletion and electrolyte disturbances; the efficacy remains largely unproved. The doses used are mainly empiric. The position statement says that on the basis of available data, the routine use of cathartics and laxatives is not endorsed. Furthermore, if these agents are used, their application should be limited to a single dose to minimize adverse effects.[17,21] Besides, the simultaneous administration of laxatives and activated charcoal lowers the efficacy of both.[22]

Whole-Bowel Irrigation

In WBI, a solution of polyethylene glycol (PEG) is given orally or by nasogastric tube (1.5–2.0 L/hr for adolescent and adult, 0.5–1.0 L/hr for a child up to 12 years) until the rectal effluent becomes clear (usually after 2 to 6 hours). The PEG solutions are not absorbed and do not cause major electrolyte shift or imbalance.[18]

The whole-bowel irrigation is not recommended to be used routinely in the poisoned patient. Although it is an option for the treatment of ingestion of sustained-release or enteric-coated drugs, or for the toxins with the high morbidity and no other availale effective gastrointestinal decontamination options (e.g., lithium), WBI is a considerable method. It also is considered for those patients presenting later than 2 hours after drug ingestion and activated charcoal is less effective. However, controlled data clinical outcome are still lacking.

WBI is contraindicated in patients with ileus, perforation, or bowel obstruction, and in patients with unprotected airways or hemodynamic instability. WBI should be administered cautiously in unstable patients. The simultaneous administration of AC and WBI may decrease the charcoal effectiveness.[23]

Enhancement of Elimination

Techniques used to increase the elimination of poisons include urine alkalinization (UA), multiple-dose activated charcoal (MDAC), and some kind of extracorporeal therapies (ECT).

Urine Alkalinization

UA is a treatment regimen that enhances the elimination of poison by the administration of intravenous sodium bicarbonate to increase urine pH over 7.5.

The ionized poison is not reabsorbed from the renal tubular lumen back, and the ionization of a weak acid is increased in an alkaline environment, manipulation of the urine pH potentially can enhance renal excretion and toxin elimination. Because dissociation constants (pKa) is a logarithmic function then, theoretically, a small change in urine pH could have a disproportionately larger effect on clearance. For each change in urine pH of one unit there is theoretically a 10-fold change in renal clearance, whereas at best the renal clearance of a reabsorbed drug varies directly with the urine flow rat.[24]

Urine alkalinization increases the urinary elimination of chlorpropamide, 2,4-dichlorophenoxyacetic acid, diflunisal, fluoride, mecoprop, methotrexate, phenobarbital, barbiturate, salicylate and so on. For the patients with severe salicylate poisoning who do not meet the criteria for hemodialysis, urine alkalinization is considered to be first-line treatment.[25,26] Urine alkalinization is no longer recommended for barbiturate poisoning because the AC administration is an better option. It is also no longer recommended for patients with methotrexate poisoning, who instead are treated with folinic acid or glucarpidase.[27]

Multiple-Dose Activated Charcoal

MDAC therapy involves the repeated administration (more than two doses) of oral AC to enhance the elimination of poisons already absorbed into the body. It enhances the elimination of poisonous substance by interrupting the enterohepatic circulation and lowering the concentration of free toxic substance in the intestinal lumen. In fact, the intestinal wall functions as a dialysis membrane of removing the toxic substance via the gastrointestinal tract.

Multiple (two or more) doses of activated carbon can be used to enhance the elimination of poisons with a small distribution volume, low pK_a, low plasma protein binding, and prolonged elimination half-life is enhanced by the administration of multiple doses of activated carbon. Clinical

trials have shown the benefit of repeated administration of activated charcoal in life-threatening cases of poisoning of a small group of medications (barbiturate, carbamazepine, theophylline, dapsone, phenobarbital, quinine).[28,27]

Multiple doses of activated charcoal should be considered only if a patient has ingested a life threatening amount of drugs indicated by experimental and clinical studies, such as barbiturate, carbamazepine, dapsone, phenobarbital, quinine, or theophylline.[29] The appropriate, effective administration of activated charcoal to enhance elimination requires a good knowledge of the properties of the toxic substance.

Extracorporeal Therapy

Extracorporeal methods have a key position in the enhancement of removal of a variety of poisons and drugs, and all rely on the use of diffusion, convection, or adsorption to enhance removal from the blood. The common extracorporeal methods include hemodialysis, hemofiltration and hemodiafiltration, hemoperfusion (HP), therapeutic plasma exchange, continuous renal replacement therapy, peritoneal dialysis (PD), and albumin dialysis. Although such methods are widely applied, randomized controlled trials relating to their efficacy and to resulting modulation of mortality and morbidity are lacking, which limits the interpretation of the effect of extracorporeal treatments. Furthermore, their use frequently superimposes additional complications and difficulties on those invoked by the poison, such as vascular instability arising from fluid removal and the need to maintain adequate levels of anticoagulation, as well as to provide access to the patient's circulation. The Extracorporeal Treatment in Poisoning (EXTRIP) Workgroup was founded in 2010 to perform systematic reviews on the use of ECTRs in various poisonings and to provide clinical recommendations on the use of extracorporeal methods in poisoning, including criteria for indication, cessation, and choice of extracorporeal methods.[30]

Hemodialysis

Hemodialysis (HD) is a process during which solutes move across a semipermeable membrane from the higher concentration side to the lower. Hemodialysis has a good clearance of small-molecular-weight toxins, as well as correcting the abnormalities of electrolyte and acid-base. of electrolyte abnormalities.

HD is the most common extracorporeal modality in acute kidney injury (AKI), end-stage renal disease (ESRD), and poisoning patients.[31] Hemodialysis has a relatively lower cost and complication rate when compared with hemofiltration, hemoperfusion, therapeutic plasma exchange, and albumin dialysis. HD can treat concomitant metabolic disorders and has a significant clearance capacity for a wide spectrum of xenobiotics.[23] Furthermore, it is available even in developing countries and is familiar to doctors. Therefore the time to organize HD in a poisoned patient would be minimized compared with other extracorporeal methods, which is crucial for the clinical outcome. Over the last three decades, the improvements in the HD dialyzers allowed larger molecules and highly protein-bound poisons such as carbamazepine and phenytoin[32,33] to be removed by HD.

Dialysis may be considered in life-threatening toxicity from lithium, salicylates, theophylline, methanol, boric acid, valproate, metformin, and ethylene glycol and for heavy metal chelation in patients with renal failure. In metformin poisoning, the lactic acidosis that arises with intoxication can be treated concomitantly.[34] Ideal characteristics of poisons removable by dialysis are a low volume of distribution (V_D), a low percentage of protein binding, and a molecular weight (MW) below the cutoff of the dialysis membrane, as determined by its pores' size.[35] Efficiency of removal is governed not only by physicochemical characteristics but also by procedural factors such as the blood flow rate, dialysate flow rate, dialyzer surface area, and pore structure of the chosen membrane.

HD usually is administered for 4 hours in AKI and ESRD patients. Its duration can be prolonged in poisoning patients depending on the clinical context. The dialysate also can be tailored to the specific patient. A poisoned patient may have a different metabolic profile, namely regarding serum potassium, phosphate, and bicarbonate.[36]

Hemofiltration and Hemodiafiltration

Hemofiltration (HF) is a technique based mainly on convection, whereas hemodiafiltration (HDF) combines convection and diffusion. Convection is the process during which solutes and solvent move according to the pressure gradient. During the hemofiltration, an ultrapure replacement fluid is reinfused to the patient to keep volume homeostasis. The efficacy of convection is mainly dependent on the size of the dialyzer membranes pores.

Hemofiltration and hemodiafiltration have similar properties as hemodialysis regarding the distribution volume and protein-binding percentage. Furthermore, hemofiltration and hemodiafiltration have a higher molecular cutoff level than hemodialysis,[37] while conserving comparable clearance for small molecules.[38] Although this makes high-efficiency convective techniques suitable for poisonings, reports of their use in poisoned patients remain limited because of their greater technical requirements and lesser availability.[39]

Continous Renal Replacement Therapies

The term *continuous renal replacement therapy* (CRRT) is used commonly to describe all continuous modalities of hemofiltration, including continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous arteriovenous hemodialysis (CAVHD). CVVH is the most commonly used CRRT modality. In continuous venovenous hemodiafiltration (CVVHDF), diffusive transport of molecules is combined with convective removal to improve the solute clearance.[40]

The main advantage of CRRT is its applicability in hemodynamically unstable patients. Besides, the membranes of CRRT are typically more permeable than the membranes of hemodialysis. Substances such as myoglobin, vancomycin, and heparin therefore are better removed by CRRT.[41] Another advantage of CRRT is the ability to avoid rebound. Slower clearance rates by CRRT lead to less dramatic decreases in plasma drug levels and are not associated with marked increases in plasma levels. However, the lack of rebound with CRRT is testimony to the relatively low clearance. Still unclear is whether CRRT is less beneficial than a faster, rebound-associated HD.

The major disadvantage of CRRT is the significant lower clearance rate when compared with other extracorporeal methods. In a patient with acute poisoning, it requires more rapid and immediate effective therapy. The CRRT also requires more intensive anticoagulation treatment with the risk for bleeding and electrolyte disturbances. Finally,

CRRT is not available at some small hospitals, possibly because of the high cost of equipment, training, and staffing.[38]

The application of continuous therapies is indicated in hypotensive and unstable patients. Besides, CRRT is suited for the poisonings associated with redistribution in tissues when removed from the plasma, such as lithium, valproic acid, or theophylline. CAVHDF and CVVHDF provide good and gradual clearance of lithium without an apparent post-treatment rebound.[42] However, there is still a lack of good evidence from numerous case reports and small case series with varying techniques and outcomes to guide therapy. The efficacy and effectiveness of CRRT in the treatment of most kinds of poisons still remain uncertain. In most cases, hemodialysis remains the first choice among modalities of extracorporeal removal with CRRT reserved for patients who truly cannot tolerate hemodialysis.[43]

Hemoperfusion

In hemoperfusion (HP), blood perfused a column made up of either AC or synthetic anion exchange resin. Protein-bound substances bind to the adsorptive material in the column and are removed from circulation. If effective, the hemoperfusion will decrease the blood concentration of the poison, then decrease the severity of toxicity.

The hemoperfusion was more effective and less limited by protein binding than hemodialysis, especially for poisons for which antidotes were not available, such as barbiturates, theophylline, and paraquat.[44] The developments of HP technology, including modifications to adsorbants (such as the coating of charcoal to reduce complications) and newer resin columns, improved its effectiveness and efficiency. Hemoperfusion also was administered for vasculitis, hepatic failure, and autoimmune diseases.[45]

However, the rate of complications in hemoperfusion is greater than hemodialysis,[46] and the cost is significantly higher.[47] With the new development of the membrane and material, the newer high-flux, high-effciency hemodialysis showed comparable results for removing theophylline and carbamazepine to hemoperfusion.[48] There were also several examples of misapplication of hemoperfusion in several settings (e.g., use in poisons with large volumes of distribution).[43] Hemoperfusion is not available in some smaller hospitals; it is now difficult to obtain a hemoperfusion cartridge in a timely manner.[49]

In a nutshell, hemoperfusion has been used effectively to enhance elimination of theophylline, phenobarbital, phenytoin, carbamazepine, paraquat, and glutethimide[50]; however, hemoperfusion has substantial adverse effects. Most complications occur because of nonspecific adsorption of biologic components to the column. The commonly reported adverse reactions are thrombocytopenia, leukopenia, hypocalcemia, hypophosphatemia, hypoglycemia, and a decrease in fibrinogen.[51] The application of hemoperfusion is to treat the poison that cannot be treated satisfactorily in other ways (e.g., by dialysis).[51]

Therapeutic Plasma Exchange (Plasmapheresis)

Plasmapheresis involves removal of the patient's plasma with substitution by crystalloid solution or fresh frozen plasma. Because therapeutic plasma exchange (TPE) can remove all substances from plasma, including proteins, it is particularly the best option to eliminate very large or highly protein-bound poisons that are not removed effectively by either HD or HP.[52] However, the clearance capacity of TPE is much lower than other extracorporeal methods.[38,53] Because most poisons are small or middle sized, TPE seldom is used in poisoning. In fact, there are no well-established clinical indications for the use of TPE in the treatment of the poisoned patient, although there is some support in treating the mushroom *Amanita phalloides,*[48] thyroxine,[54] vincristine, and cisplatin.[55] TPE should be considered only when alternative extracorporeal methods are useless or unavailable, because of the high cost and the risk of complication.[56]

Therapeutic plasma exchange is the option available to remove poisons that are very large or highly protein bound and therefore will not be removed effectively by hemodialysis or hemofiltration.[57–61] Its rationale for use must be confirmed in each type of intoxication by evidence of effective clearance.[59,62] As mentioned earlier, there is some support for it in exposures to the mushroom *Amanita phalloides*, thyroxine, and so on. However, the data on the application of plamapheresis are limited.[63] TPE should be considered only when alternative ECTRs are useless or unavailable.

Albumin Dialysis

Albumin dialysis, namely extracorporeal liver assist devices (ELAD), include the Molecular Adsorbent Recirculating System (MARS), the Prometheus Fractionated Plasma Separation and Adsorption System,[64] and Single-Pass Albumin Dialysis (SPAD).[65]

In albumin dialysis, blood is passed through a membrane against a solution containing albumin. Protein-bound poisons then are cleared by diffusion and eliminated bound to albumin. The effluent then is run through charcoal and anion-exchange resin to cleanse the albumin, enabling it to recirculate.[66] MARS and Prometheus are similar in that they both have a secondary circuit that regenerates the dialysate. SPAD is similar to CRRT but uses a dialysate supplemented with fresh albumin.[67]

Albumin dialysis has the potential advantage of removing a wide range of drugs with high albumin binding from blood.[68] MARS has been described effective in elimination of paracetamol and amatoxins in patients with liver failure and removal of phenytoin, lamotrigine, theophylline, and calcium channel blockers in patients without liver failure.[69] The Prometheus system also has been adminstrated in treatment for amanita poisoning as well as for cerebral edema and hyperammonemia in cocaine overdose.[70]

However, there are limited data about the effective comparison of elimination against other techniques. The available prelimary data also do not show any superiority of albumin dialysis in the treatment of theophylline, valproic acid, or phenytoin than other alternative extracorperal methods.[71,72] In addition, the experimental studies showed that clearance of several drugs rarely exceeds 40 mL/min, even at a high blood flow rate, which is lower than other extracorporeal treatment. Furthmore, it is an expensive and invasive procedure with potential complications, such as hypoglycemia, coagulopathy, and thrombocytopenia.[73]

Because of its limited availability, high cost, risk of complications, and unpredictable effectiveness for many xenobiotics, the role of albumin dialysis in poisonings is still unclear.[74]

Peritoneal Dialysis

PD allows the diffusion of poison from the mesenteric capillaries across the peritoneal membrane into the dialysis

solution within the peritoneal cavity. Drug or poison with low MW, small V_D, low PPB, and good water solubility may be removed by PD.[55]

The clearance rate is much lower with PD than other extracorporeal methods. For example, clearances for theophylline are 10 mL/min with PD compared with 85 mL/min with HD. Therefore PD is not recommended for poisoning because of the low clearance rate.[75] However, in patients already on PD and with minimal effects of the poison and no other available alternative method, PD is considered an option.[76] It also can be administrated in the cases of children who are too small to undergo hemodialysis in centers that do not dialyze children routinely.[77] In conclusion, PD has limited benefit in poisoning and is not recommended in treatment of poison unless the patient is already receiving PD for ESRD, or the poisoning effects are minimal and no other treatment option is available.[31]

Antidotes and Chelating Agents

An antidote is a special pharmacologic or toxicologic antagonist that can alter favorably the toxic effects of a poison. Some antidotes are toxic and therefore should be used with caution.[78] Although some effective and well-tolerated antidotes are considered the ideal treatment of poisoning, such as acetylcysteine for paracetamol intoxications, dimethicone for surfactant ingestions, and fomepizole for poisoning with methanol or glycols. Fomepizole inhibits alcohol dehydrogenase[79] and has replaced ethanol as an antidote with substantially higher toxicity.

As a consequence of recent improvements in symptom oriented intensive care medicine, the use of certain antidotes that carry the risk of severe complications must be reevaluated. The physician using such antidotes needs to have detailed knowledge of the substances used (e.g., antisera, chelators) and their clinical effects. A list of historical and current antidotes and their clinical uses can be found, for example on the GIZ-Nord website.[80]

Recently introduced antidotes include glucarpidase for methotrexate overdoses, icatibant for ACE-inhibitor induced angioedema, uridine triacetate for fluorouracil overdoses, and deferasirox as a new chelator for iron overload.[81]

GENERAL SUPPORTIVE TREATMENT

Serious clinical effects occur in less than 5% of acutely poisoned patients and the overall in-hospital mortality rates are less than 0.5%.[29] The aim of the supportive treatment is to preserve the vital organ functions until detoxification is accomplished and the patient resumes normal physiologic homeostasis.[25]

Respiratory Complications

Hypoventilation, hypoxia, and pulmonary edema occur commonly because most poisons that depress consciousness also impair respiration. Emergency procedures should be directed at maintaining a patent airway and providing respiratory support with immediate access to suction equipment, oxygen, or mechanical ventilation if it is necessary. The loss of an effective airway and inadequate ventilation are the most common causes of serious morbidity and death in poisoning.

Cardiovascular Complications

Patients may have hypotension or hypertension, bradyarrhythmias or tachyarrhythmias. The pathogenesis of hypotension varies and may include hypovolemia, myocardial depression, cardiac arrhythmias, and systemic vasodilation. Treatment should be individualized, but an initial strategy of rapid IV normal saline solution infusion is indicated in most instances. Vasopressors may be required for refractory hypotension.[14] Arrhythmias should be treated depending on the toxin involved and the type of dysrhythmia. Echocardiogram monitoring is also advisable.

Neurologic Complications

Depression of consciousness, seizures, cerebral edema, and peripheral nerve injuries may be included. Therapy consists of correction of arterial blood gas and metabolic abnormalities and hypotension, reduction in intracranial pressure, hyperventilation, elevation of head, and fluid restriction. Seizures may occur because of metabolic disturbances and cerebral hypoxia and direct toxic effect. Treatment includes intravenous (IV) diazepam/phenobarbitone or infusion of thiopentone.

Hypoglycemia

Significant hypoglycemia should be treated initially with a bolus of intravenous 50 mL 50% dextrose in water. However, after initial euglycemia is achieved, administration of oral carbohydrates should be followed in treating hypoglycemia induced by sulphonylurea or meglitinide.[29] Continued hypoglycemia should be treated using octreotide (initial dose of 50 mg, repeated two to three times per day), which decreases intravenous dextrose requirements and therefore minimizes the risk of glucose-stimulated insulin release.

Hypothermia and Hyperthermia

Hypothermia (<35°C) may develop in comatose patients and may be missed by the unwary clinician. Passive rewarming, IV fluid warming, and warm water humidifier in artificial ventilation should treat it. Patients with hyperthermia (>39°C) should be treated aggressively with cool IV fluids and active cooling measures. IV benzodiazepines are appropriate treatment in hyperthermic patients with evidence of excessive sympathetic stimulation such as that associated with cocaine overdose and amphetamines. Patients with resistant hyperthermia may benefit from peripherally acting muscle relaxants (dantrolene), centrally acting serotonin antagonists (cyproheptadine), or general anaesthetic sedation.[29]

Metabolic Complications

Hepatic and renal function, electrolytes, blood glucose, arterial blood gas, and urine samples should be checked routinely.[25] Renal failure may be due to tubular necrosis because of hypotension hypoxia or the direct effect of poison on tubular cells. Hemoglobinuria or myoglobinuria may precipitate renal failure further. Patient should be catheterized to maintain a urine output of 0.5 mL/kg/hr. Metabolic acidosis is encountered frequently, and sodium bicarbonate may be needed if pH falls below 7.1.

EXTRACORPOREAL LIFE SUPPORTIVE TREATMENT

Extracorporeal life supportive treatment (ECLS) includes extracorporeal membrane oxygenation (ECMO), emergency cardiopulmonary bypass (ECPB), intraaortic balloon pumps (IABP), and left ventricular assist devices (LVAD). ECMO is the most frequently used ECLS therapy in poison treatment. There are two major types of ECMO: venovenous ECMO (VV-ECMO), which provides only pulmonary support, and venoarterial ECMO (VA-ECMO), providing pulmonary and circulatory support.[82]

VV-ECMO and VA-ECMO use cannulae, centrifugal, and pumps to produce an extracorporeal circulation for venous blood oxygenation.[83] Although ECMO cannot enhance the elimination of poison, it acts as a bridge to recovery in the unstable patients with cardiovascular or pulmonary failure not responding to conventional medical therapies. ECMO has been used successfully to support patient overdose of tricyclic antidepressants, carbamazepine, chloroquine, and calcium channel or beta blockers.[84,85] The complication for ECMO includes bleeding, stroke, and intracranial hemorrhage. Because the technical complexiety and risk of complication, ECMO should be administrated for severely ill patient refractory to conventional medical therapies with a high risk of death.[86]

Development of Other Potential Poisoning Therapies

The development of pharmacogenomics and pharmacokinetics may open new possibilities for poisoning therapy. Some animal studies indicated that the PTSK gene expression may be related to the pathogenesis of Paraquat poisoning–induced lung damage. Some research also indicated that the aberrant hypomethylated STAT3 may be a potential biomarker of chronic benzene poisoning. This may open new paths for prevention against chronic benzene poisoning through epigenetic pharmacologic interventions. In addition, drugs to downregulate the cytochrome P450 enzyme and slow metabolism of acetaminophen to its toxic metabolites could work much like fomepizole, which blocks the enzymatic metabolism of volatile alcohols.[59]

CONCLUSION

The judicious decision to use which kind of measures in the treatment of poisoning should be based on a rational understanding of poison properties, toxicokinetic principles, and the clinical condition of the patient. Although there has been significant progress in the clinical management of the poisoned patient over the past several decades, provision of meticulous supportive care, identification of patients requiring treatment with an antidote, and the appropriate choose of methods limiting poison absorption or increasing its elimination remain the cornerstone of management. We have summarized the basic pharmacokinetic data and the current treatments for 282 drugs or poisons into an index table listed alphabetically (Table 101.1). According to the limited evidence-based medicine data, many of the traditional management interventions do not really improve patient outcome and sometimes subject the patient to a certain degree of risk. The potential benefit of using any therapeutic method should be assessed prudently for each individual patient. However, it remains controversial whether it is better to use a treatment that may have some benefit but definitely has some risk or not to use a treatment that has any risk unless there is proven benefit. It is time for evidence-based toxicology.

Text continued on p. 629

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
A								
Acebutolol[87,88]	336.4	11%–25%	1.4–3	Lipophilic	8 hr	<10%	?	CV toxicity, CNS manifestations
Acarbose	643.6	?	?	Hydrophilic	2 hr	<2%	?	GI symptoms, flatulence, pharyngitis
Acetazolamide[89,90]	222.2	80%–92%	0.2	Hydrophilic	4 hr	Mostly	Yes	GI disturbances, electrolyte imbalance
Acetic acid[91,92]	60	?	?	Hydrophilic	?	?	Yes	Acidosis, hemolysis, DIC, hepatotoxicity
Acetohexamide	324.4	90%	?	Hydrophilic	1.3 hr	?	?	Hypoglycemia, GI, dermatologic, miscellaneous symptom
Acetonitrile[93,94]	41.1	?	Large	Lipophilic	?	?	?	See cyanide
Acetaminophen	151.2	25%	0.8–1.0	Lipophilic	1–2 hr	?	?	Hepatotoxicity, skin reactions, asthma
Aconitine[95,96]	645.8	?	Large	Hydrophilic	?	Little	?	GI symptoms, neurotoxicity, cardiotoxicity
Acyclovir[97]	225.2	9%–22%	0.8	Hydrophilic	2.5 hr	14%	Yes	Hepatotoxicity, hematotoxicity, neurotoxicity, skin rashes
Ajmaline[98]	326.4	61%–76%	6.17	Hydrophilic	1.5 hr	4%	Yes	GI symptoms, cardiac and CNS toxicity, hepatotoxicity

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Allobarbital	208.2	?	?	?	?	25%–30%	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Alprazolam[99]	308.8	70%–80%	1	Lipophilic	6–12 hr	20%	?	CNS depression
Alprenolol	249.3	80%–85%	3.3	Lipophilic	2–3 hr	Little	?	CV toxicity, respiratory and CNS symptoms
Aluminum	27	80%–95%	Very large	?	Longer	Little	a	Multisystem toxicity
Amanita phalloides[100–102]		Very low	Very small	Hydrophilic	12 hr	90%	Yes	GI symptoms, fatal hepatic failure
Aminocaproic acid	131.7	Low	Large	Hydrophilic	1–3 hr	64%	Yes	GI symptoms, cardiotoxicity, acute muscle necrosis
Amiodarone[103]	681.8	95%	9–20	Lipophilic	5–7 hr	Little	?	Hepatotoxicity, cardiotoxicity, pulmonary toxicity
Amitriptyline[104,105]	277.4	95%	6–36	Lipophilic	12–24 hr	5%	?	Cardiotoxicity, coma, seizures, hyperthermia, urinary retention, ARDS
Amlodipine[106,107]	408.6	97%	2	Lipophilic	36 hr	5%	?	CV toxicity
Amobarbital	226.3	55%–60%	0.9–1.4	Lipophilic	15–40 hr	10%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Amoxapine	313.8	High	Large	Lipophilic	8 hr	Little	?	Coma, repiratory depression, cardiotoxicity, seizures, hyperthermia
Amphetamines[108,109]	135.2	15%–35%	3–33	Lipophilic	10 hr	5%–50%	Indirect	CNS symptoms, CV symptoms, hyperthermia
Aniline[110]	93	?	?	Hydrophilic	?	?	?	Relaxation of smooth muscle, production of methemoglobin
Aprobarbital	210.2	35%	0.6–0.7	Lipophilic	14–34 hr	13%–25%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Arsenic[111,112]	74.9	60%	Large	?	?	22.4%–57.9%	Yes	Hepatotoxicity, cardiotoxicity, CNS toxicity, hematotoxicity
Arsine	77.9	?	Large	Lipophilic	7 hr	20%	Yes	Neurotoxicity, hemolytic anemia, cardiotoxicity, hepatotoxicity
Aspirin	180.2	99.5%	0.2~0.5	?	3~9 hr	Little	Yes	Tinnitus, abdominal pain, hypokalemia, hypoglycemia, pyrexia, CNS symptoms
Astemizole[113]	458.6	97%	Large	Lipophilic	24 hr	5%–6%	?	CNS toxicity, dry mouth, GI symptoms, cardiotoxicity
Atenolol[114,115]	266.3	3%	0.7	Hydrophilic	6 hr	Mostly	?	CV toxicity, CNS manifestations
Atropine[116,117]	289.4	40%–50%	2–4	Lipophilic	2–3 hr	33%–50%	?	Symptoms of vagal stimulation, brain stem depression with respiratory and circulatory failure
Azalea		?	?	Hydrophilic	?	?	?	GI symptoms, neurotoxicity, cardiotoxicity, respiratory paralysis
B								
Baclofen[118]	213.7	30%	0.8	Lipophilic	3.5 hr	80%	?	CNS inhibit, respiratory depression, cardiotoxicity, hypothermia
Barbital	184.2	<5%	0.4–0.6	Hydrophilic	48–65 hr	60%–90%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium

Continued

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Barium[119,120]	137.3	?	Large	Lipophilic	?	7%	?	Stimulation of cardiac, smooth, and skeletal muscle; hypokalemia; hypertension
Benzydamine[121]	309.4	15%–20%	3	Lipophilic	8–13 hr	50%	?	Auditory, visual hallucination, GI symptoms
Bismuth[122]	209	?	?	Lipophilic	?	2.50%	Yes	CNS toxicity
Boric acid[37]	61.8	0%	Large	Hydrophilic	5–21 hr	90%	Yes	GI symptoms, skin signs, CNS symptoms
Bromates[123,124]		?	?	?	?	?	Yes	GI symptoms, deafness
Bromazepam[125]	316.2	70%	1.2	Lipophilic	15 hr	<1%	?	Intoxication rare
Bromides	79.9	?	0.4	Lipophilic	12 days	Little	?	Neuropsychiatric, der;atologic, and GI symptoms
Bromisoval	233.1	?	?	Lipophilic	?	Little	Yes	CNS toxicity, respiratory and cardiac toxicity, hepatotoxicity
Brotizolam	393.7	90%–95%	0.6	Lipophilic	4–8 hr	1%	?	CNS depression
Buflomedil[126,127]	364.4	25%–80%	0.5–1	?	2–3.5 hr	Little	?	CNS toxicity, cardiorespiratory arrest
Buprenorphine[128]	467.7	95%–98%	Large	Lipophilic	1.2–7.2 hr	15%	?	Little information on its toxicity
Butabarbital	212.2	26%–50%	?	Lipophilic	34–42 hr	10%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Butalbital	224.3	?	?	?	?	<10%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
C								
Cadmium	112.41	Low	?	?	10–30 yrs	Little	Yes	Respiratory toxicity, CV toxicity, hepatotoxicity
Caffeine[129,130]	194.2	35%–40%+C51	1	Hydrophilic	3–6 hr	1%	?	CNS, CV, and GI symptoms
Camphor[131]	152.2	61%	2–4	Lipophilic	167 min	Little	?	GI toxicity, CNS toxicity
Carbamates[132,133]		?	?	?	?	?	?	Cardiotoxicity, GI symptoms
Carbamazepine[134–138]	236.3	65%	0.8–1.8	Lipophilic	18 hr	1%–2%	Indirect	Anticholinergic symptoms, hepatotoxicity, hyponatremia
Carbon monoxide	28	?	?	Lipophilic	?	?	Yes	Brain, heart, and almost every organ
Carbon tetrachloride	153.8	?	?	Lipophilic	?	?	Yes	CNS toxicity, hepatotoxicity
Carbromal	237.1	?	?	Lipophilic	?	Little	Yes	CNS toxicity, respiratory and cardiac toxicity, hepatotoxicity
Carisoprodol[139]	260.3	?	?	Lipophilic	?	Mostly	?	CNS depression
Carvedilol[140]	406.5	98%	115	Lipophilic	7–10 hr	42%	?	Asthenia, fatigue, CV, CNS, GI symptoms
Chloral hydrate[141,142]	165.4	0%	Large	Lipophilic	4–14 hr	Little	Yes	CNS depression, cardiotoxicity, hepatotoxicity
Chlorambucil	304.2	99%	?	?	1.5 hr	<1%	?	Corrosive action, neurotoxicity
Chloramphenicol	323.1	50%	0.9–1.4	?	4 hr	5%–10%	?	Bone marrow toxicity, peripheral neuritis, GI symptoms
Chlorates[143]		?	?	Hydrophilic	?	95%	Yes	Hematotoxicity, GI symptoms
Chlordiazepoxide[144]	299.8	95%	<0.4	Hydrophilic	15 hr	1%	?	CNS depression
Chlorine and chloramine	70.9	?	?	Hydrophilic	?	?	?	Respiratory symptoms, headache, dizziness, nausea
Chlormezanone	273.1	0%	?	?	20–24 hr	1%–2%	?	CNS depression
Chlorophenoxy compounds		?	?	?	?	?	?	GI symptoms, respiratory symptoms, CNS toxicity

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Chloroquine[145–148]	319.9	50%–60%	93.6	Lipophilic	50 hr	40%–70%	Indirect	CNS, CV, GI, eyes, blood, hepatic+I77, skin toxicity
Chlorpheniramine[149,150]	274.8	72%	?	?	21–27 hr	?	?	Convulsion, coma, tachycardia, fever, and fatigue
Chlorpromazine	318.9	91%–99%	20	Lipophilic	18 hr	1%–6%	?	CNS toxicity, cardiorespiratory toxicity, hypothemia
Chlorpropamide[151,152]	276.7	?	?	Lipophilic	36 hr	80%–90%	?	Hypoglycemia, GI, dermatologic, hematologic, endocrinic symptom
Chlorprothixene	315.9	99%	11–23	Lipophilic	8–12 hr	5%	Indirect	CV toxicity, CNS toxicity, hepatotoxicity
Cinoxacin	262.2	60%–80%	?	?	1.5 hr	60%	?	GI, CNS symptoms, hypersensitivity
Ciprofloxacin[153–156]	331.3	20%–40%	?	?	4 hr	40%–50%	Yes	GI, CNS symptoms, hepatic injury, rash
Citalopram[157–159]	324.4	50%	12	Lipophilic	35 hr	10%	?	Asthenia, GI symptoms, dizziness, insomnia, somnolence, agitation
Clobazam	300.7	90%	1.4	Lipophilic	50 hr	1%	?	CNS depression
Clomipramine[160,161]	314.9	97%	12	Lipophilic	17–28 hr	3%	?	Drowsiness, ataxia, seizures, respiratory depression, cardiotoxicity, and coma
Clonazepam	315.7	47%–82%	3.3	Lipophilic	23–36 hr	1%	?	Intoxication rare
Clonidine[162–165]	230.1	30%–40%	3–5.5	Lipophilic	5–13 hr	50%	?	Respiratory depression, CNS depression, hypotension, bradycardia, hypothermia
Clorazepate	332.7	?	?	Hydrophilic	36–100 hr	?	?	See oxazepam
Clotiazepam	318.8	?	2–3	Lipophilic	?	Little	?	CNS depression
Cocaine[166–168]	303.4	?	1.2–1.9	Lipophilic	1 hr	5~10%	Indirect	CNS stimulation, sympathomimetic effects, "body packer" syndrome
Codeine	299.4	7%–25%	3.5	?	3–4 hr	Little	?	Respiratory depression, CV, dermatologic and GI symptoms
Colchicine[169–172]	399.4	0–50%	1.4–3.0	Lipophilic	20 min	20%	Yes	GI symptoms, multiorgan failure, hypothermia
Cresol	108	High	Large	Lipophilic	?	?	Indirect	Corrosive effects, CNS depression, hemolysis, Heinz bodies
Cyanide/hydrogen cyanide[173–177]	27.04	?	Large	Lipophilic	1 hr	Little	?	Respiratory, CV, CNS symptoms
Cyclobarbital	236.3	25%	?	Lipophilic	8–17 hr	7%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Cyclobenzaprine[178]	275.4	93%	?	?	1–3 days	<1%	?	Symptoms of central and peripheral cholinergic blockade
Cyclopentobarbital	234.1	?	?	?	?	?	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Cycloserine	102.1	<2%	0.6	Hydrophilic	10 hr	60%	?	Extremely rare; headache, dizziness, abnormal behavior, ataxia, pyramidal signs
D								
Dapsone[179,180]	248.3	80%	1~2	Lipophilic	20–40 hr	15%	?	Methemoglobinemia, hemolysis, damage in various organs due to hypoxia
Desipramine	266.4	70%–95%	40	Lipophilic	25 hr	5%	?	Intoxication is rare
Dextromoramide	392.5	?	?	?	?	Mostly	?	?

Continued

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Diacetylmorphine	369.5	20%–39%	Large	Lipophilic	<1 hr	Little	Yes	CNS and CV toxicity, GI symptoms, infections, immune dysfunction, leukoencephalopathy Heroin lung, rhabdomyolysis, "body packer" syndrome
Diazepam[181]	284.8	98%	1.1	Lipophilic	30–45 hr	<1%	?	Tiredness, sleep, stupor, respiratory depression, CV symptoms
Diazoxide[182]	230.7	90%	0.2	?	28 hr	50%	?	Tachycardia, headache, vomiting, nausea, hyperglycemia, hypotension
Dibenzepin[183]	295.5	96%	Large	Lipophilic	4 hr	Little	?	Cramps and arreflexia, severe tachycardia, cardiac insufficiency, bronchospasm
Dichloroethane[184,185]	98.96	?	?	Hydrophilic	?	?	Yes	See carbon tetrachloride
Dicyclomine	310.5	?	?	?	?	?	?	Drowsiness, irritability, respiratory symptoms
Dieffenbachia[186]		?	?	?	?	?	?	Pain, inflammation, swelling of lips, dysphagia, edema, contact dermatitis, respiratory arrest
Diethylene glycol[187,188]	106.1	?	?	Hydrophilic	?	?	?	Metabolic acidosis, edema, GI and pulmonary bleeding
Digitalis[189–192]	764.9	90%–97%	0.6–0.8	Lipophilic	180–220 hr	60%	?	GI and neurologic symptoms, visual disturbances, cardiac manifestation, electrolyte abnormalities
Digoxin[193,194]	780.9	20%–30%	5–12	Lipophilic	30–50 hr	70%	?	GI and neurologic symptoms, visual disturbances, cardiac manifestation, electrolyte abnormalities
Dihydrocodeine[195,196]	301.4	?	1	?	20 min	13%–22%	?	Respiratory depression, miosis, hypothemia, CV depression
Diltiazem[197,198]	414.5	80%	5	Lipophilic	2 hr	0.2%–4%	?	CV toxicity
Dimenhydrinate[199]	470	98%	Very high	?	4–7 hr	Little	?	CNS depression, anticholinergic stimulation, sedation
Dinitrophenol	184.11	High	Large	Lipophilic	?	?	Indirect	Corrosive effects, hemolysis, CNS depression, respiratory and CV symptoms
Dinitro-o-cresol	198.13	High	Large	Lipophilic	?	?	Indirect	Corrosive effects, hemolysis, CNS depression, respiratory and CV symptoms
Diphenhydramine	255.4	90%–98%	3–7	?	4–10 hr	2%–4%	?	Peripheral and central anticholinergic symptoms, rhabdomyolysis
Disopyramide[200]	339.5	<5%	0.5–1.2	?	5–9 hr	42%–62%	Indirect	Anticholinergic effects, cardiac toxicity, hypokalemia, metabolic acidosis, hypotension
Dothiepin[201,202]	331.9	80%–90%	10	?	20 hr	<0.5%	?	Intoxication is rare, see amitriptyline
Doxepin[203]	279.4	75%	20	?	16 hr	Little	?	See amtriptyline
Doxorubicin	543.5	74%–76%	20–30	?	0.6 hr	4%–5%	?	Cardiac toxicity
Doxylamine[204]	270.4	?	2.6–3.2	?	10 hr	60%–85%	?	Dry mouth, headache, tachycardia, dizziness, GI symptoms, rhabdomyolysis

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
E								
Encainide	352.5	70%	Large	Lipophilic	4 hr	Mostly	?	Seizures, hypotension, marked QRS widening
Enoxacin	320.3	40%	?	Hydrophilic	3–6 hr	>40%	?	GI, CNS symptoms, hepatic injury, rash
Ergotamines[205]	581.6	?	2	?	2 hr	<5%	Indirect	Hemorrhagic vesiculation, pruritus, nausea, vomiting, peripheral nervus symptoms
Erythromycin	733.9	90%	?	Lipophilic	1.5 hr	<5%	?	Abdominal pain, diarrhea, nausea, vomiting
Escitalopram[206]	324.4	56%	12	Lipophilic	27–32 hr	8%	?	Somnolence, tremor, dizziness, ejaculation failure, mouth dry, GI symptoms
Esmolol	331.8	55%	?	Hydrophilic	9 min	Little	?	CV toxicity, CNS manifestations
Ethchlorvynol	144.6	35%–50%	4	Lipophilic	10–25 hr	10%	Yes	Respiratory depression, hypothermia, cardiac toxicity, GI symptoms, hemolysis
Ethinamate	167.2	?	?	?	2.3 hr	2%	No	CNS depression, respiratory depression, nausea, hyperthermia
Ethyl alcohol	46	?	?	Hydrophilic	?	2%–10%	?	Neurologic symptoms, abdominal pain, hypoglycemia, metabolic acidosis, hypothermia
Ethylene glycol[207,208]	62.4	0%	0.7–0.8	Hydrophilic	3 hr	25%	Yes	Severe metabolic acidosis, neurologic, cardiopulmonary manifestations
F								
Fenfluramine[209]	231.3	30%	8–10	Lipophilic	8 hr	10%–30%	?	CNS toxicity, cardiac toxicity, hepatotoxicity
Fentanyl[210,211]	336.5	80%–85%	1–5	Lipophilic	1.5–6 hr	6%–10%	?	Respiratory depression, CNS and CV toxicity, dermatitis, hypothermia
Flecainide[212–214]	414.4	48%	9–10	Lipophilic	7–23 hr	27%	?	Cardiovascular toxicity, vertigo, blurred vision, headache, nausea
Flunitrazepam[215]	313.3	80%	3–4	Lipophilic	15 hr	1%	?	CNS depression
Fluorine and fluorides[216]		0	?	Hydrophilic	2–9 hr	50%	Yes	Respiratory and cardiac toxicity, neurologic disturbances
Fluoxetine[217,218]	309.3	94%	20–45	?	2 day	11%	?	Nausea, agitation, vomiting, hypomania, insomnia, tremor
Fluoxetine[219]	349	94.5%	?	Hydrophilic	2–4 day	80%	?	Nausea, headache, nervous, sedation, insomnia, dry mouth
Flurazepam[220]	387.9	15%	22	Lipophilic	2–3 hr	1%	?	CNS depression
Fluvoxamine	318.3	77%–80%	25	Lipophilic	15.6 hr	2%	?	Diarrhea, fatigue, anxiety, sexual dysfunction, anorexia
Formic acid	58	?	?	Hydrophilic	45 min	?	Yes	High causticity, cytotoxicity
G								
Gatifloxacin	375.4	20%	1.5–2.0	Hydrophilic	7–14 hr	>70%	?	Nausea, conjunctivitis headache, dizziness, diarrhea
Gemifloxicin	389.4	60%–70%	4.18	Hydrophilic	5–9 hr	36%	?	Rash, diarrhea, urticaria, vomiting, headache, dizziness
Germanium[221,222]	72.6	?	?	?	?	Mostly	Yes	Hepatotoxicity, muscle and CNS toxicity
Gliclazide[223]	323.4	?	?	?	11 hr	?	Yes	Hypoglycemia, respiratory, GI, musculosketetal symptoms

Continued

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Glimepiride	490.6	>99.5%	8.8	Lipophilic	5 hr	60%	?	Hypoglycemia, dizziness, asthenia, headache, nausea
Glipizide	444.5	98%–99%	11	?	2–5 hr	<10%	?	Hypoglycemia, GI, dermatologic, miscellaneous symptom
Glutethimide	217.3	50%	Large	Lipophilic	40 hr	0–2%	?	Profound and prolonged coma, respiratory and CV toxicity
Grepafloxacin	359.4	50%	4–6	Hydrophilic	12–18 hr	<10%	?	GI, CNS symptoms, hypersensitivity
H								
Halazepam	352.7	95%		Lipophilic	35 hr	Little	?	CNS depression
Haloperidol	375.9	90%	20–30	Lipophilic	20 hr	1%	?	Severe extrapyramidal reactions, hypotension, sedation, cardiotoxicity
Heptabarbital	250.3	?	?	?	10 hr	Little	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Hexachlorophene	407	92%	Large	Lipophilic	24 hr	?	Indirect	Neurotoxicity, GI disturbances
Hexobarbital	236.3	20%	1.0–1.2	Lipophilic	2–7 hr	<10%	?	CNS depression, respiratory depression, suppress skeletal smooth and myocardium
Hydralazine	160.2	87%	7–8	Hydrophilic	3–4 hr	3%–14%	?	Cardiovascular toxicity, headache, skin flashing
Hydrochloric acid	36.5	?	?	Lipophilic	?	?	Yes	High causticity, cytotoxicity
Hydrocodone	299.4	?	?	?	4–8 hr	?	?	Neurologic effects, dizziness, diaphoresis
Hydromorphone	285.3	?	1.2	?	2–5 hr	<10%	?	Respiratory depression, somnolence, progressing stupor or coma, hypotension, bradycardia
I								
Imipramine[224–226]	280.4	76%–95%	20–40	?	9–20 hr	1%–3%	?	See amitriptyline
Iron[227–231]	55.8	?	?	?	?	Little	Indirect	Phase of GI, relative stability, circulatory shock, cell necrosis, gastric scarring
Isocarboxazid[232]	231.3	?	?	?	?	Little	Indirect	CNS, CV, hepatic toxicity
Isoniazid[233–235]	137.2	30%	0.6	Hydrophilic	2–3 hr	4%–20%	?	Recurrent seizures, metabolic acidosis, hepatic dysfunction
Isoprenaline	?	?	?	?	?	?	?	Headache, cardiotoxicity
Isopropyl alcohol[236,237]	60	0	0.6–0.8	Lipophilic	7.6–26 hr	10%–30%	Yes	GI sign and hemorrhage, CNS effects, cardiac depression and hypotension
L								
Lactic acid	90.1	?	?	?	?	?	Yes	High causticity, acidosis, hemolysis, DIC, hepatotoxicity
Lead[238–241]	207.2	?	?	?	?	?	Indirect	Gastrointestinal symptoms, hematologic effects, CNS and neuromuscular effects
Levofloxacin	741.8	24%–39%	?		6–8 hr	Mostly	?	Transient decreased vision, fever, headache, ocular pain, pharyngitis
Lidocaine[242,243]	234.3	40%–80%	1.5	?	6–15 min	5%–10%	?	CNS, cardiovascular, GI tract toxicity
Lithium	6.94	0	0.6–0.9	?	24 hr	95%	Yes	CNS, GI, CV, hematopoietic system toxicity
Lofepramine	419	32%–96%	Large	Lipophilic	44–76 hr	Little	?	See amitriptyline
Lomefloxacin	351.3	10%	?	Hydrophilic	8 hr	65%	?	Headache, GI symptoms, photosensitivity, dizziness
Lorazepam	312.2	80%	?	Lipophilic	<10 hr	3%	?	CNS depression

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Lorcainide[244]	370.9	75%–85%	8~10	?	7.7 hr	2%	?	CNS, cardiac toxicity, GI symptoms
Lormetazepam	335.2	85%	4.6	Lipophilic	9–15 hr	<1%	?	CNS depression
M								
Mannitol	182.2	7%	0.18	?	1.5–3 hr	Mostly	Yes	Severe fluid overload, CNS disturbance, hyponatremia, hyperosmolality
Maprotiline	277.4	88%	23	Lipophilic	30 hr	Little	?	CV, psychiatric, neurologic, hematologic toxicity, GI disorders, anticholinergic activity
Medazepam	270.8	100%	?	Lipophilic	2 hr	<1%	?	Intoxication is rare
Mephobarbital	246.3	40%–60%	2.6	Hydrophilic	48–52 hr	?	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Meprobamate	218.3	15%–20%	0.7	?	8–12 hr	10%	?	CNS, CV toxicity
Mercury[245–248]	200.6	>90%	20	?	40 day	Mostly	Yes	Neurologic, GI symptoms, cardiac, hepatic, endocrine, immune system toxicity, metabolic changes
Metformin[249–253]	165	0	1–5	Hydrophilic	6.2 hr	Mostly	Yes	Hypoglycemia, diarrhea, nausea
Methadone[254–256]	309.5	8%–44%	4–7	Lipophilic	2–3 hr	Little	Yes	Respiratory depression, hypotension, hypothemia, miosis, bradycardia, vomiting, euphoria
Methaqualone	250.3	70%–90%	2.5–6	Lipophilic	2–6 hr	1~3%	Indirect	CNS depression, pulmonary edema, increased mascle tone and motor activity
Methohexital	262.3	73%	1.1	Lipophilic	1–2 hr	1%	?	CNS depression, respiratory depression, supress skeletal smooth and myocardium
Methotrexate[257–264]	454.4	35%	1	Hydrophilic	2 hr	90%	Yes	GI and bone marrow toxicity
Methotrimeprazine	328.5	50%–60%	20–40	Lipophilic	16–31 hr	1%	?	Intoxication is extremely rare
Methsuximide	203.2	0	?	?	2.6–4 hr	1%	?	Delayed onset of stupor and coma
Methyl alcohol[265]	32.04	0	0.6–0.7	Hydrophilic	8–28 hr	2~5%	?	Systemic acidosis, CNS depression, neurotoxicity, blindness
Methyldopa	211.2	0–20%	0.5	?	0.2–0.5 hr	50%	?	Hepatotoxicity, CNS depression
Methylphenobarbital	246.3	20–45%	?	Hydrophilic	?	Little	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Methyprylon	183.2	60%	Large	?	3–6 hr	<3%	?	CNS depression, pulmonary, GI tract, CV manifestation
Metoprolol[266,267]	267.4	12%	5.6	Hydrophilic	3–4 hr	5%	?	CV toxicity, CNS manifestations, acute shoulder-syndrome
Mexiletine[268,269]	179.3	60–75%	5.5–12	?	5–15 hr	10%	?	Prolongation of ventricular depolarization, motor seizures
Mianserin	264.4	90%	40–50	Lipophilic	17 hr	4~7%	?	Cardiac arrhythmias
Midazolam[270]	325	95%	1.7	Lipophilic	2 hr	<1%	?	CNS depression
Minoxidil[271,272]	209.3	0	3–5	?	4 hr	90%	?	Skin rashes, polymenorrhea, headache, hypertrichosis

Continued

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Monochloroacetic acid[273,274]	94.5	?	?	Hydrophilic	?	?	Indirect	Malaise, vomiting, CNS, CV, hepatic toxicity, metabolic acidosis, hypokalemia
Morphine	303.4	35%	3–4	?	3.5 hr	10%	?	Coma, respiratory depression, miosis
Moxifloxacin[275]	401.4	50%	?	?	11.5–15.6 hr	?	?	CNS, GI symptoms, conjunctivitis, dry eyes, keratitis, ocular hyperemia
N								
Nadolol	309.4	20%–30%	2.5	Lipophilic	14–24 hr	70%	?	CV toxicity, respiratory and CNS symptoms
Nalidixic acid	232.2	93%	?	?	1.1–2.5 hr	85%	?	CNS, GI, allergic symptoms
Nateglinide[276]	317.4	98%	10	Lipophilic	1.5 hr	16%	?	Upper respiratory tract infection, headache, back pain, sinusitis, diarrhea
Nifedipine[277,278]	346.3	99%	0.6–1.2	?	4 hr	<1%	?	CV toxicity, flushing
Nitrazepam	281.3	87%	1.9–2.4	Lipophilic	20–50 hr	1%	?	CNS depression
Nitric acid	63	?	?	Hydrophilic	?	?	Yes	High causticity, acidosis, hemolysis, DIC, hepatotoxicity
Nitrites and nitrates	191.1	<4%	?	?	5 hr	Little	?	Methemoglobinemia, CV, respiratory and CNS toxicity
Norfloxacin[279]	319.3	10%–15%	?	Lipophilic	3–4 hr	26%–32%	?	Dizziness, GI symptoms, headache, asthenia
Nortriptyline	263.4	High	Large	?	36 hr	?	?	See amtriptyline
NSAIDs		90%–99%	0.1–0.17	?	?	Little	Yes	GI, CNS, CV, hepatic, neuromuscular activity symptoms
O								
Ofloxacin	361.4	32%	?	?	9 hr	65%–80%	?	Nausea, insomnia, headache, dizziness, diarrhea, rash, pruritus
Oleander/Oleandrin[280–285]	576.7	?	Large	?	?	?	?	Irritation of mucosa, GI symptoms, CV symptoms
Orciprenaline	?	?	?	?	?	?	?	Headache, cardiotoxicity
Organochlorines		?	?	Lipophilic	?	?	?	Tremor, seizures, CNS and GI symptoms, arrhythmias, metabolic acidosis
Organophosphates[286,287]		?	15–27	?	?	?	?	Stimulations of autonomic nervous system muscarinic receptor, nicotinic receptors, cholinergic receptor in CNS
Orphenadrine[288]	269.1	20%	?	Hydrophilic	10 hr	8%	?	CNS, CV, hepatic toxicity
Oxaflozane[289]	273.3	?	?	?	2 hr	?	?	Seizures, mydriasis, tachycardia, coma
Oxalic acid	90	0%	33	Hydrophilic		Mostly	Yes	Corrosive effects, hypocalcemia, hematemesis, petechial bleeding, diarrhea, CNS symptoms
Oxazepam	286.7	97%	1	Lipophilic	12 hr	<1%	?	Intoxication is extremely rare
Oxprenolol	265.3	70%–80%	1.3	Lipophilic	2 hr	<5%	?	CV toxicity, respiratory and CNS symptoms, hypokalemia
Oxycodone	315.4	?	?	?	2–3 hr	?	?	See codeine
P								
Paracetamol[290–292]	151.2	15%–20%	0.9–1	Lipophilic	8 hr	1%–4%	Yes	Hepatotoxicity, CNS and cardiac toxicity, respiratory symptoms
Paraphenylenediamine[293,294]	108.1	?	?	?	?	?	Yes	Dermatitis, asthma, anemia, cardiac and CNS toxicity, hepatitis, vasculitis

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Paraquat[295–297]	257.16	0%	1.2–1.6	Hydrophilic	5–84 hr	7%–8%	Yes	Hepatocellular necrosis, cerebral and adrenal hemorrhage, mycocardial necrosis, pulmonary fibrosis
Pargyline	152.9	?	?	?	?	<1%	Indirect	CNS, CV, and I199 hepatic toxicity
Paroxetine	329.4	95%	Large	Hydrophilic	24 hr	2%	?	CNS, GI symptoms, asthemia, ejaculation failure
Pefloxacin[298]	333.4	20%–30%	?	Hydrophilic	8.6 hr	?	?	Peripheral neuropathy, nervousness, agitation, anxiety, phototoxic events
Pentachlorophenol[299,300]	266.4	?	Large	Lipophilic	10–35 hr	80%	Yes	Central, peripheral and vegetative system effects, bone marrow injury, hepatomegaly
Pentobarbital[301]	226.3	65%	0.8–1.0	Lipophilic	20–30 hr	1%	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Phencyclidine	243.4	65%	6	Lipophilic	21–24 hr	<10%	Yes	CNS, respiratory and CV symptoms, hyperthermia
Phenelzine	136.2	?	?	Hydrophilic	1.2 hr	<2%	Indirect	CNS, CV, and hepatic toxicity
Phenobarbital	232.2	15%–45%	0.5–0.6	Hydrophilic	48–144 hr	25%	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Phenol and derivatives[302]		High	Large	Lipophilic	?	?	Indirect	Corrosive effects, hemolysis, CNS depression, respiratory and CV symptoms
Phenylbutazone[303]	308.4	88%–98%	0.17	?	70 hr	1%	Yes	Toxic hepatitis, gastric ulceration, acidosis
Phenytoin[304–306]	252.3	90%–95%	5~6	Lipophilic	24–230 hr	5%	?	Respiratory depression, CV and CNS symptoms, hepatotoxicity, hyperglycemia
Philodendron	?	?	?	?	?	?	?	Pain, inflammation, swelling of lips, dysphagia, edema, contact dermatitis, respiratory arrest
Phosphoric acid	98	?	?	Hydrophilic	5–11 hr	?	Yes	High causticity, acidosis, hemolysis, DIC, I209 hepatotoxicity
Phosphorus	31	?	Large	?	?	?	Yes	GI and CNS symptoms, hepatotoxicity
Pindolol	248.3	60%	2	Lipophilic	3–4 hr	40%	?	CV toxicity, respiratory and CNS symptoms
Pioglitazone	356.4	>99%	0.22–1.04	Lipophilic	3–7 hr	Little	?	Upper respiratory tract infection, headache, back pain, sinusitis, diarrhea
Platinum[307]	195.1	?	?	?	?	?	?	Gastroenteritis, hypovolemia, fever, muscle cramps
Potassium permanganate[308,309]	158	?	?	Hydrophilic	?	?	?	Corrosion, dyspnea, stridor, hepatic toxicity
Prajmaline	518.6	60%	?	?	5–7 hr	10%	Yes	CV, respiratory, and CNS toxicity
Prazepam	324.8	97%	?	Lipophilic	1–2 hr	Little	?	CNS depression
Prazosin	382.4	90%	0.5	?	2.5 hr	3.50%	?	Sudden hypotension
Primidone	218.3	<20%	0.64–0.86	Hydrophilic	12–22 hr	15%–25%	?	CNS and respiratory depression, suppress skeletal smooth and myocardium

Continued

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON[a]	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Procainamide[310]	235.3	15%	1.7–2.2	Hydrophilic	3 hr	50%–60%	?	Lethargy, confusion, hypotension, ventricular arrhythmias, SLE-like syndrome
Propafenone[311–313]	341.5	95%	2.5–4	?	4 hr	<1%	?	CV, neurologic and GI symptoms
Propoxyphene	339.5	73%–80%	10–20	Lipophilic	4 hr	<10%	Indirect	CNS depression, respiratory depression
Propranolol	259.3	93%	3.5	Lipophilic	2–3 hr	Mostly	?	CV toxicity, respiratory and CNS symptoms+I221
Protriptyline	263.4	92%	Large	Lipophilic	55–92 hr	2%	?	Cardiotoxicity, coma, seizures, hyperthermia, urinary retention, ARDS
Pyrethrum	?	?	?	Lipophilic	?	?	?	Contact dermatitis, anaphylactic reactions, GI symptom, CNS excitation
Pyrithyldione	167.2	?	?	Hydrophilic	10~20 hr	3%	?	Drowsiness, mydriasis, GI disturbances, hepatic injury, respiratory depression
Q								
Quinidine	360.5	60%–95%	2–3.5	?	6–8 hr	15%–40%	Indirect	Tinnitus, dizziness, GI disturbances, CV and CNS effects, hypotension
Quinine[314,315]	324.4	69%–92%	1.8–2.2	Lipophilic	9–15 hr	25%	?	Hypersensitivity, gastric distress, hemolysis, cinchonism, amblyopia
R								
Repaglinide	452.6	>98%	31	Lipophilic	1 hr	0.10%	?	Hypoglycemia, respiratory, GI, musculosketetal symptoms
Reserpine	608.7	40%–95%	Very Large	Lipophilic	4–5 hr	8%	?	CNS and CV toxicity
Rosiglitazone	357.4	99.8%	17.6	Lipophilic	3–4 hr	0	?	Upper respiratory tract infection, headache, back pain, sinusitis, diarrhea
S								
Salbutamol[316,317]	239.3	?	?	?	2.7–5 hr	?	?	Fine tremor of skeletal muscle, hypotension, tachycardia
Salicylates[318–321]	180.15	50%–80%	0.2–0.5	Lipophilic	2–30 hr	3%–30%	Yes	Respiratory and acid-base disturbances, GI, hepatic and CNS toxicity, hyperthermia
Secobarbital	238.3	30%–70%	1.6–1.9	Lipophilic	22–30 hr	5%	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Sertraline[322,323]	306.2	98%	?	Lipophilic	26 hr	Little	?	Somnolence, tremor, dizziness, ejaculation failure, mouth dry, GI symptoms
Sodium azide[324,325]	66	?	?	Hydrophilic	2.5 hr	?	?	CV, pulmonary, hematologic and neurologic effects, electrolyte disturbance
Sodium chloride[326]	58.5	0%	0.6	Hydrophilic	?	?	Yes	CNS and GI toxicity, hyperthermia, metabolic acidosis
Sodium nitroprusside	298	?	?	?	3–11 min	20%–50%	?	Vasodilatation, hypotension, circulatory collapse
Sotalol	272.4	0%	1.6–2.4	Hydrophilic	15–17 hr	>80%	?	CV toxicity, respiratory and CNS symptoms
Sparfloxacin	392.4	45%	3.1–4.7	Lipophilic	20 hr	50%	?	Photosensitivity, GI symptoms, insomnia, QT interval prolongation
Strychnine[327–330]	334.2	Low	13	Lipophilic	10–16 hr	5%–20%	Indirect	Muscle spasms, respiratory and cardiac failure, hyperthermia, lactic acidosis

TABLE 101.1A

Poison Index List of Pharmacokinetics and Toxicity—cont'd

	PHARMACOKINETICS						TOXICITY	
DRUG OR POISON*	MW	PPB	VD	SB	$T_{1/2}$	EU	NEPHROTOXICITY	TOXICITY IN OTHER SYSTEMS
Sulfuric acid	98	?	?	Hydrophilic	?	?	Yes	High causticity, acidosis, hemolysis, DIC, hepatotoxicity
T								
Temazepam	300.7	97%	1	Lipophilic	6–16 hr	2%	?	CNS depression
Terbutaline[331,332]	225.3	?	?	?	3–4 hr	?	?	Fine tremor of skeletal muscle, headache, tachycardia
Tetrachloroethylene[333]	165.9	?	8.1	Lipophilic	6–8 day	>80%	Yes	CNS, GI and CV symptoms, coagulopathy, hepatotoxicity
Tetrazepam	288.8	30~70%	3.3	Lipophilic	10–20 hr	Little	?	CNS depression
Thallium[334–337]	205.4	?	11	Hydrophilic	10–30 day	3%	?	GI, neurologic, and CV symptoms, hair loss, alopecia areata, Mee's lines
Theophylline[338–342]	180.2	50%	0.5	Hydrophilic	7–9 hr	10%	?	CNS, GI and CV symptoms, metabolic and acid-base disturbance
Thiamylal	276.3	>70%	Large	Lipophilic	?	?	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Thiopental	241.3	72%–86%	1.4–1.7	Lipophilic	5–17 hr	Little	?	CNS and respiratory depression, suppress skeletal smooth and myocardium
Tocainide	192.3	50%	1.5–3.2	?	7–15 hr	40%	?	CNS, cardiovascular, and GI toxicity
Tolazamide	311.4	?	?	?	7 hr	85%	?	Hypoglycemia, GI, dermatologic symptoms
Tolbutamide[343]	270.3	96%	?	?	4.5–6.5 hr	?	?	Hypoglycemia, dizziness, asthenia, headache, nausea
Toluene[344]	92.1	?	?	Lipophilic	21 hr	?	?	Eyes, lungs, skin, and GI mucosa effects
Tranylcypromine	133.2	?	?	Hydrophilic	1.9–3.5 hr	2%	Indirect	CNS, CV and hepatic toxicity
Trazodone[345,346]	371.9	90%	0.8–1.3	?	1 hr	Little	?	Drowsiness, vomiting, priapism, respiratory arrest, seizure
Triazolam	343.2	80%–90%	1.0–1.5	Lipophilic	3 hr	2%	?	CNS depression
Trichloroacetic acid[347]	147.4	?	?	Hydrophilic	Longer	?	Yes	See chloral hydrate
Trichloroethylene[348–351]	131.4	High	10	Lipophilic	0.5 hr	Little	?	CNS, cardiac, respiratory, GI, and hepatic toxicity
Troglitazone	441.5	>99%	10.5–26.5	Lipophilic	16–34 hr	<3%	?	Hepatic injury, GI symptom, asthenia, back pain, dizziness
Trovafloxacin	416.4	76%	Large	?	9.1–12.2 hr	6%	?	Convulsions, decreased activity, diarrhea, sleepiness, tremor
V								
Valproic acid[352–356]	144.2	90%	0.1–0.5	Lipophilic	1 hr	2%–3%	Indirect	GI, hepatic, CNS, hematologic and CV toxicity
Vancomycin[357–360]	1449.2	55%	0.5–1	?	5.5 hr	Mostly	Yes	Hypotension, cyanosis, ototoxicity, neurotoxicity, hematologic toxicity
Verapamil[361–364]	454.6	90%	4–6	Lipophilic	2–7 hr	Little	?	CV and CNS toxicity
Viloxazine	237.3	80%–90%	?	?	3 hr	Little	?	GI and CNS symptoms
Vincristine[365,366]	824.9	75%	Large	?	7 min	15%	?	CNS toxicity
Vinyl chloride[367]	62.5	?	?	Lipophilic	?	?	?	CNS, cardiac and respiratory toxicity

*Data from Seyffart G: Poison Index: The Treatment of Acute Intoxication. Lengerich, North Rhine–Westphalia, Germany, Pabst Science Publishers, 1997.

ARDS, Adult respiratory distress syndrome; *CNS,* central nervous system; *CV,* cardiovascular; *DIC,* disseminated intravascular coagulation; *EU,* excreted in urine as the parent drug; *GI,* gastrointestinal; *MW,* molecular weight (Daltons); *PPB,* plasma protein binding; *SB,* solubility; $T_{1/2}$, plasma half-life; *VD,* apparent volume of distribution (L/kg).

? No experience or controversial

TABLE 101.1B

Poison Index List of Treatment

	TREATMENT										
DRUG OR POISON*	GD	IAC	FD	SA	HD	CRRT	HP_A	HP_R	PD	PE	Supportive treatment or Antidote
A											
Acebutolol[87,88]	‡‡,<6 hr	‡‡	(+)	No	+		(+)	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Acarbose	(++)	?	O	No	(+)		?	?	O	?	Symptomatic treatment, Closely monitor blood glucose
Acetazolamide[89,90]	?	?	?	No	+		(++)	?	O	?	Symptomatic treatment
Acetic acid[91,92]	+	?	+	No	‡‡		O	O	?	‡	Analgesics, treatment of asphyxia and metabolic acidosis
Acetohexamide	(++)	?	?	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Acetonitrile[93,94]	?	?	?	YES	(++)		‡	?	?	?	**Antidotes**: Disulfiram
Acetaminophen	?	?	?	Yes	1D	3D (if HD is not available)	?	?	?	?	**Antidotes:** N-acetylcysteine (NAC)
Aconitine[95,96]	‡‡	‡‡	+	No	?		‡	?	?	?	Immediate cardiac monitoring and oxygen administration
Acyclovir[97]	(++)	?	(+)	No	‡‡		(++)	?	+	O	
Ajmaline[98]	++	++	O	No	(+)		(++)	(+++)	?	?	Continuous ECG monitoring, control arrhythmias, sodium substitution
Allobarbital	‡‡,<8 hr	‡	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Alprazolam[99]	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Alprenolol	‡‡,<3 hr	(++)	O	No	+		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Aluminum	(++)	?	O	Yes	+		+	?	?	?	DFO: iv. 5 mg/kg once a week until a serum Al increment <75ug/l
Amanita phalloides[100–102]	‡‡,<15 hr	‡‡	‡‡‡	No	+		++	+++	?	‡‡	Fluid, elctrolyte and glucose substitution, corticosteroids, liver protection or transplatation
Aminocaproic acid	(++)	?	?	No	(+)		?	?	?	?	Symptomatic treatment
Amiodarone[103]	‡‡	‡‡	O	No	O		(+)	(+)	?	?	
Amitriptyline[104,105]	‡‡‡	‡‡‡	O	?	O		‡‡	+	O	‡	Sodium bicarbonate infusion, monitoring of CV, CNS and respiratory function
Amlodipine[106,107]	‡‡,<3 hr	‡‡	+	?	O		O	O	?	?	See verapamil
Amobarbital	‡‡,<8 hr	‡	O	No	‡‡		‡‡‡	‡‡‡	O	?	Stabilization of circulatory and respiratory function, good nursing
Amoxapine	‡‡‡	‡‡‡	O	?	O		(+)	(+)	O	?	Sodium bicarbonate infusion, monitoring of CV, CNS and respiratory function
Amphetamines[108,109]	‡‡‡	‡	‡	No	O		O	O	O	?	Cooling measures, benzodiazepines
Aniline[110]	‡‡	O	‡	O	++		?	?	?	?	Monitoring blood gas, oxygen therapy
Aprobarbital	‡‡,<8 hr	‡	O	No	‡‡		‡‡‡	‡‡‡	O	?	Stabilization of circulatory and respiratory function, good nursing
Arsenic[111,112]	‡‡	‡	++	Yes	+		‡	?	O	?	Four chelating agents: BAL, D-penicillamine, DMSA, DMPS; Exchange transfusion
Arsine	O	?	‡	?	+		?	?	+	?	Alkalinizing urine, monitoring of cardiac function, electrolyte and blood gas

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Aspirin	ǂ,<8 hr	ǂ	ǂǂǂ	No	ǂǂǂ		ǂǂ	ǂǂ	ǂ	?	Correction of acidosis, electrolyte imbalance, dehydration, hypoprothrombinemia
Astemizole[113]	ǂǂ	ǂǂ	O	No	O		O	O	?	?	EKG monitoring is mandatory
Atenolol[114,115]	(+++)	(++)	++	No	++		++	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Atropine[116,117]	ǂǂ	ǂǂ	ǂǂ	Yes	O		?	?	?	?	Physostigmine is the antidote:0.02~0.06 mg/kg i.v. >5 min; treatment of hyperthermia
Azalea	(++)	(++)	(+)	No	?		?	?	?	?	No experience, see aconitine
B											
Baclofen[118]	ǂ	ǂ	ǂǂ	No	O		?	?	O	?	Early supportive measures. Continuous monitoring of EKG, respiration and temperature
Barbital	ǂǂ,<8 hr	2D	ǂ	No	1D	3D (if HD is not available)	1D (if HD is not available)	1D (if HD is not available)	O	?	Stabilization of circulatory and respiratory function, good nursing
Barium[119,120]	ǂǂ	?	ǂ	No	ǂ		?	?	?	?	Calcium administration, cardiac monitoring, control of respiration; magnesium sulfate?
Benzydamine[121]	ǂǂ,<1 hr	?	(+)	No	?		O	(+)	?	?	Treatment of convulsions: Chlorpromazine and chlordiazepoxide
Bismuth[122]	ǂǂ,<10 hr	ǂǂ	+++	Yes	++		?	?	ǂ	?	Antidotes: BAL, DMSA, DMPS, D-penicillamine and its *N*-acetyl derivative
Boric acid[123]	ǂǂ	O	ǂ	No	ǂǂǂ		O	O	ǂǂǂ	?	Supportive and symptomatic treatment
Bromates[124,125]	ǂǂ	?	O	No	ǂǂ		?	?	ǂǂ	?	Intravenous administration of sodium thiosulfate
Bromazepam[126]	(+++)	(++)	O	Yes	?		ǂǂ	?	?	?	
Bromides	ǂǂ	O	ǂ	No	ǂǂǂ		O	O	?	?	Supportive and symptomatic treatment
Bromisoval	ǂǂ	ǂǂ	O	No	ǂǂǂ		ǂǂǂ	ǂǂǂ	ǂǂ	?	Prevention od DIC, artificial respiratory utilizing, administration of digitalis glycosides
Brotizolam	ǂǂ,<3 hr	ǂ	O	Yes	?		?	?	?	?	
Buflomedil[127,128]	ǂ	ǂ	(+)	No	O		?	?	?	?	Supportive and symptomatic treatment
Buprenorphine[129]	?	?	(+)	No	O		?	?	?	?	See morphine
Butabarbital	ǂǂ,<8 hr	ǂ	O	No	ǂǂ		ǂǂǂ	ǂǂǂ	O	?	Stabilization of circulatory and respiratory function, good nursing
Butalbital	ǂǂ,<8 hr	ǂ	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
C											
Cadmium	ǂǂ,<3 hr	?	O	No	O		O	O	O	?	Supportive and symptomatic treatment
Caffeine[130,131]	ǂǂ,<4 hr	ǂǂ	O	No	ǂ		(++)	ǂǂ	?	?	See theophylline
Camphor[132]	ǂǂ,<2 hr	O	O	No	O		O	O	?	?	Supportive and symptomatic treatment
Carbamates[133,134]	++	++	O	Yes	++		++	++	?	?	Antidote: atropine, See organochlorines
Carbamazepine[135–138]	ǂǂǂ, <10 hr	1D	ǂ	No	1D	3D (if HD is not available)	1D (if HD is not available)	1D (if HD is not available)	ǂ	ǂ	Monitoring of respiratory and cardiac function
Carbon monoxide	O	O	O	No	O		O	O	O	?	HBOT: hyperbaric oxygen therapy
Carbon tetrachloride	ǂǂ	?	O	Yes	(+)		(++)	?	?	?	Antidote: acetylcysteine. Treatment of hypercoagulation and hyperventilation

Continued

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	GD	IAC	FD	SA	HD	CRRT	HP_A	HP_R	PD	PE	Supportive treatment or Antidote
Carbromal	‡	‡	O	No	‡‡		‡‡	‡‡	‡	?	Prevention od DIC, artificial respiratory utilizing, administration of digitalis glycosides
Carisoprodol[139]	(++)	(++)	(++)	No	?		?	?	?	?	See meprpbamate
Carvedilol[140]	(++)	?	O	No	+		?	?	(+)	?	Symptomatic treatment
Chloral hydrate[141,142]	‡	?	O	No	‡‡		‡	(+++)	?	?	Supportive and symptomatic treatment
Chlorambucil	(+)	?	O	No	O		?	?	?	?	Supportive and symptomatic treatment
Chloramphenicol	‡,<1 hr	‡	O	No	O		++	++	O	?	Supportive and symptomatic treatment
Chlorates[143]	‡	?	O	?	‡‡		?	?	‡‡	?	Antidotes: sodium thiosulfate, methylene blue, ascorbic acid?
Chlordiazepoxide[144]	(++)	(++)	O	Yes	?		?	?	?	?	See benzodiazepines
Chlorine and chloramine	?	?	?	No	?		?	?	?	?	Supportive and symptomatic treatment
Chlormezanone	(++)	?	O	No	?		?	?	?	?	Supportive and symptomatic treatment
Chlorophenoxy compounds	‡	‡	O	No	?		(+)	?	?	?	Supportive and symptomatic treatment
Chloroquine[145–148]	‡	‡	O	No	O		++	++	O	?	Diazepam and epinephrine combined with mechanical ventilation, symptomatic treatment
Chlorpheniramine[149,150]	(++)	?	?	No	(++)		?	?	(++)	?	Symptomatic treatment
Chlorpromazine	‡	‡	O	No	O		+	?	O	?	Treatment of respiratory depression and cardia abnormalities, sympotomatic treatment
Chlorpropamide[151,152]	(++)	?	(++)	No	(++)		‡	?	‡	?	Treatment of hypoglycemia
Chlorprothixene	‡	‡	O	No	O		++	?	O	?	Treatment of dysrhythmias
Cinoxacin	(++)	?	(++)	No	(++)		?	?	(++)	?	Symptomatic treatment
Ciprofloxacin[153–156]	(++)	‡	(+)	No	(+)		?	?	(+)	?	Symptomatic treatment
Citalopram[157–159]	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
Clobazam	‡,<3 hr	†	O	Yes	?		?	?	?	?	
Clomipramine[160,161]	(++)	O	O	?	O		(+)	(+)	O	?	See amitriptyline
Clonazepam	(+++)	(++)	?	Yes	?		?	?	?	?	
Clonidine[162–165]	‡	‡	O	Yes	+		†	?	?	?	Antidotes: naloxone and tolazoline. Supportive and symptomatic treatment
Clorazepate	(+++)	(++)	?	Yes	?		?	?	?	?	
Clotiazepam	‡,<3 hr	†	O	Yes	?		?	?	?	?	
Cocaine[166–168]	O	O	O	No	+		+	?	?	?	Supportive and symptomatic treatment
Codeine	‡	‡	‡	Yes	O		(+)	?	?	?	Antidote: naloxone. Establish adequacy of respiratory function and circulation
Colchicine[169–172]	‡‡, <12 hr	‡‡	O	No	O		O	O	O	?	All intensive care measures are required, supportive and symptomatic treatment
Cresol	‡	‡	‡	No	+++		?	?	?	?	See phenol
Cyanide/Hydrogen cyanide[173–177]	‡	‡	O	Yes	++		†	?	?	?	Antidotes: thiosulfate, sodium nitrite, amyl nitrte, aminophenols, hydroxocobalamin,dicobalt-EDTA
Cyclobarbital	‡,<8 hr	†	O	No	‡‡		(+++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Cyclobenzaprine[178]	(++)	?	O	?	O		(+)	?	?	?	See amitriptyline
Cyclopentobarbital	‡,<8 hr	†	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Cycloserine D	‡	?	(++)	No	‡		?	?	‡	?	
Dapsone[179,180]	‡,<6 hr	‡	++	Yes	O		++	?	?	?	Antidute: methylene blue. Supportive and symptomatic treatment
Desipramine	(++)	?	O	?	O		(+)	(+)	?	?	See amitriptyline

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Dextromoramide	(++)	?	(++)	?	?		?	?	?	?	See morphine
Diacetylmorphine	‡‡	‡‡	O	Yes	O		+	?	?	?	Antidote: naloxone. Establish adequacy of respiratory function and circulation, withdrawal and dependence
Diazepam[181]	‡‡,<3 hr	‡‡	O	Yes	O		O	O	O	?	Antidotes: flumazenil and physostigmine
Diazoxide[182]	(+)	?	(++)	No	+		?	?	+	?	Treatment of hyperglycemia, hypotension, prolonged surveillance more than 7days
Dibenzepin[183]	(++)	(++)	(++)	?	O		(+)	(+)	O	?	See amitriptyline
Dichloroethane[184,185]	(++)	(++)	O	Yes	?		‡	?	?	?	See carbon tetrachloride
Dicyclomine	?	?	?	No	?		?	?	?	?	Supportive and symptomatic treatment, physostigmine maybe be tried
Dieffenbachia[186]	?	?	?	?	?		?	?	?	?	Supportive and symptomatic treatment
Diethylene glycol[187,188]	‡‡	‡‡	‡	Yes	‡‡		?	?	?	?	Antidote: fomepizole. See ethylene glycol, symptomatic treatment
Digitalis[189–192]	‡‡,<2 hr	‡‡	O	Yes	O		+	+	?	‡	Antidote: Fab fragments. Supportive and symptomatic treatment
Digoxin[193,194]	‡‡,<3 hr	‡‡	O	Yes	O	O	O	O	O	‡	Antidote: Fab fragments. Supportive and symptomatic treatment
Dihydrocodeine[195,196]	(++)	(++)	(+)	Yes	?		?	?	?	?	See codeine
Diltiazem[197,198]	‡‡,<3 hr	O	O	?	O		O	O	?	‡	See verapamil
Dimenhydrinate[199]	‡‡	‡‡	O	No	?		?	?	?	?	Symptomatic treatment. See diphenhydramine
Dinitro phenol	‡‡	‡‡	‡‡	No	++		?	?	?	?	See phenol
Dinitro-o-cresol	‡‡	‡‡	‡‡	No	+++		?	?	?	?	See phenol
Diphenhydramine	‡‡	?	O	Yes	O		+++	+++	?	?	Antidoye: physostigmine? Symptomatic treatment
Disopyramide[200]	‡‡	‡‡	‡	No	++		‡‡	‡‡‡	?	O	Arterial cardiac monitoring, evaluation of respiratory function, treatment of arrhythmias
Dothiepin[201,202]	‡	‡‡	(+)	?	O		(+)	(+)	O	?	See amitriptyline
Doxepin[203]	(++)	(+)	O	?	‡		(+)	‡‡	O	?	See amitriptyline
Doxorubicin	?	?	O	?	O		O	O	O	?	Symptomatic treatment
Doxylamine[204]	(+)	?	(++)	?	?		?	?	?	?	Surpportive treatment
E											
Encainide	(++)	?	(++)	?	+		?	?	?	?	Sodium substitution. See flecainide and quinidine
Enoxacin	(++)	?	(+)	No	(+)		?	?	(+)	?	Symptomatic treatment
Ergotamines[205]	‡‡	‡‡	O	?	?		?	?	?	?	Intravenous administration of vasodilators. Surpportive treatment
Erythromycin	(++)	?	O	No	(+)		?	?	(+)	?	Symptomatic treatment
Escitalopram[206]	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
Esmolol	?	?	(+++)	No	(++)		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Ethchlorvynol	‡‡‡	‡‡‡	O	No	++		‡‡	‡‡‡	+	?	Physical assessment, treatment of severe respiratory depression
Ethinamate	(++)	(++)	O	No	‡‡		?	?	?	?	See barbiutrates
Ethyl alcohol	‡‡,<90 min	?	O	Yes	‡‡‡		‡	O	‡‡‡	?	Antidotes: naloxone and physostigmine. Surpportive treatment
Ethylene glycol[207,208]	‡‡,<12 hr	‡‡	‡	Yes	‡‡‡		(+)	?	‡‡	‡	Antidote: 4-methylpyrazole. Treatment of respiratory insufficiency, acidosis; ethanol administration

Continued

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
F											
Fenfluramine[209]	‡	‡	?	No	O		?	?	O	?	Careful cardiac monitoring. Symptomatic treatment
Fentanyl[210,211]	?	?	‡	Yes	O		?	?	?	?	Antidote: naloxone. Management of respiratory depression
Flecainide[212–214]	‡‡	‡‡	‡	?	+		++	?	?	?	Sodium substitution. Symptomatic treatment.
Flunitrazepam[215]	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Fluorine and Fluorides[216]	‡‡,<45 min	O	O	Yes	++		?	?	?	?	Antidote: calcium. Surpportive treatment
Fluoxetine[217,218]	‡‡,<8 hr	‡‡	O	No	O		O	O	O	?	
Fluoxetine[219]	(++)	?	‡‡	No	(++)		?	?	(+)	?	Symptomatic treatment
Flurazepam[220]	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Fluvoxamine	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
Formic acid	+	?	?	No	‡‡‡		O	O	?	?	Analgesics, treatment of asphyxia and metabolic acidosis
G											
Gatifloxacin	(++)	?	(++)	No	(+)		?	?	(+)	?	Symptomatic treatment
Gemifloxicin	(++)	?	(+)	No	(++)		?	?	(+)	?	Symptomatic treatment
Germanium[221,222]	?	?	?	?	?		?	?	?	?	
Gliclazide[223]	(++)	?	?	No	(+)		?	?	(+)	?	Symptomatic treatment, Closely monitor blood glucose
Glimepiride	(++)	‡‡	(++)	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Glipizide	(++)	?	O	No	(++)		?	?	(++)	?	IV dextrose, use of octreotide as an antidote, restoring acid-base balance
Glutethimide	‡‡	‡‡	O	No	(+)		‡‡‡	‡‡‡	(+)	?	Treatment of respiratory depression and celebral edema
Grepafloxacin	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
H											
Halazepam	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Haloperidol	‡‡,<8 hr	‡‡	O	No	O		‡	‡	?	?	Treatment of respiratory depression, hypertension and arrhythmias
Heptabarbital	‡‡,<8 hr	‡	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Hexachlorophene	‡‡	‡‡	‡‡	No	O		(+)	?	O	?	See phenol
Hexobarbital	‡‡,<8 hr	‡	O	No	(++)		(+)	(+)	O	?	Stabilization of circulatory and respiratory function, good nursing
Hydralazine	‡‡,<1 hr	‡‡	O	No	?		?	?	?	?	Surport of CV symptoms
Hydrochloric acid	+	?	?	No	?		?	?	?	?	Analgesics, treatment of asphyxia and metabolic acidosis
Hydrocodone	?	?	?	Yes	?		?	?	?	?	Antidote: levallorphan. See morphine
Hydromorphone	?	?	O	Yes	?		?	?	?	?	Antidote: naloxone. See morphine
I											
Imipramine[224–226]	?	?	?	?	?		?	?	?	?	See amitriptyline
Iron[227–231]	‡	O	?	Yes	O		+	?	?	?	Chelator: DFO (desferrioxamine)
Isocarboxazid[232]	‡‡	‡‡	O	?	?		?	?	?	?	Closely monitoring for at least 24 hr. Symptomatic treatment
Isoniazid[233–235]	‡‡,<2 hr	‡‡	‡‡‡	Yes	+++		(+)	?	++	?	Antidote: pyridoxine (vitamine B6)
Isoprenaline	(+)	?	?	No	?		?	?	?	?	Supportive and symptomatic treatment
Isopropyl alcohol[236,237]	‡‡,<30 min	O	O	No	‡‡‡		‡	O	‡‡	?	Treatment of hypotension, warming, measure for respiratory assistance
L											
Lactic acid	+	?	?	No	‡‡‡		O	O	‡‡	?	Analgesics, treatment of asphyxia and metabolic acidosis
Lead[238–241]	‡‡	‡‡	‡‡	Yes	O		O	O	O	?	Chelator: Ca-Na-EDTA, BAL(dimercaprol), D-penicillamine, DMSA

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Levofloxacin	(++)	?	(++)	No	(+)		?	?	O	?	Symptomatic treatment
Lidocaine[242,243]	‡‡	‡‡	‡‡	No	?		?	‡‡	?	?	Symptomatic treatment
Lithium	‡,<8 hr	O	‡	No	1D	1D (if HD is not available)	O	?	‡	?	Symptomatic treatment
Lofepramine	(++)	?	?	?	O		(+)	(+)	?	?	See amitriptyline
Lomefloxacin	(++)	?	(++)	No	(+)		?	?	(+)	?	Symptomatic treatment
Lorazepam	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Lorcainide[244]	(++)	?	O	No	?		?	?	?	?	Symptomatic treatment. See flecainide and quinidine
Lormetazepam	‡‡,<6 hr	‡	O	Yes	?		?	?	?	?	
M											
Mannitol	O	O	O	No	‡‡		?	?	‡	?	Support treatment
Maprotiline	‡‡	‡‡	O	No	O		+	+	O	?	Support treatment
Medazepam	(+++)	(++)	?	Yes	?		?	?	?	?	
Mephobarbital	‡‡,<8 hr	‡	‡	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Meprobamate	‡‡,<4 hr	‡‡	++	No	‡‡		‡‡‡	‡‡‡	++	?	Treatment of hypotension, respiratory failure, convulsion
Mercury[245–248]	‡	‡	++	Yes	+		‡	?	+	‡	Antidotes: BAL, DMSA, DMPS, D-penicillamine and its N-acetyl derivative
Metformin[249–253]	(++)	?	‡‡	No	1D	2D (if HD is not available)	?	?	(+++)	O	Symptomatic treatment, Closely monitor blood glucose
Methadone[254–256]	‡	‡	O	Yes	O		O	O	O	?	Antidote: noloxone. Stabilization of vital function
Methaqualone	‡‡,<4 hr	‡‡	O	No	+		+++	+++	+	?	Support treatment
Methohexital	‡‡,<8 hr	‡	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Methotrexate[257–264]	‡	‡	‡	Yes	‡		‡‡	‡‡	O	‡‡‡	Antidote: folinic acid
Methotrimeprazine	(+++)	?	O	No	O		?	?	O	?	
Methsuximide	(+)	?	O	No	+		++	?	+	?	
Methyl alcohol[265]	‡‡‡,<8 hr	‡‡	O	Yes	1D	1D (if HD is not available)	‡	O	‡	?	Antidote: pyrazole and 4-methylpyrazole. Ethanol substitution, adequate ventilation
Methyldopa	‡‡	‡‡	(++)	No	+++		?	?	++	?	Symptomatic treatment
Methylphenobarbital	‡‡,<8 hr	‡	‡	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Methyprylon	‡‡,<4 hr	‡‡	O	No	+		+	?	+	?	Surpportive treatment
Metoprolol[266,267]	‡‡,<3 hr	‡‡	++	No	+		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Mexiletine[268,269]	(++)	‡‡	?	No	?		?	?	?	?	See lidocaine
Mianserin	‡‡,<2 hr	?	O	No	O		(+)	(+)	?	?	Symptomatic treatment
Midazolam[270]	‡‡,<3 hr	‡	O	Yes	+++		?	?	?	?	
Minoxidil[271,272]	?	?	?	?	?		?	?	?	?	
Monochloroacetic acid[273,274]	O	O	?	?	?		?	?	?	?	Symptomatic treatment
Morphine	‡‡	‡‡	O	Yes	O		+	?	O	?	Antidote: naloxone. Establish adquacy of respiratory function and circulation
Moxifloxacin[275]	(++)	‡‡	?	No	(++)		?	?	(+)	?	Symptomatic treatment
N											
Nadolol	‡‡,<8 hr	‡‡	O	No	+		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Nalidixic acid	(++)	?	(++)	No	(++)		?	?	(++)	?	Symptomatic treatment
Nateglinide[276]	(++)	?	O	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Nifedipine[277,278]	‡‡,<3 hr	‡	O	?	O		‡	?	?	?	See verapamil
Nitrazepam	‡‡,<6 hr	‡	O	Yes	?		?	?	?	?	

Continued

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Nitric acid	+	?	?	No	?		O	O	?	?	Analgesics,treatment of asphyxia and metabolic acidosis
Nitrites and nitrates	‡‡	O	‡	Yes	?		?	?	?	?	Antidote: methylene blue. Supportive treatment
Norfloxacin[279]	(++)	?	(+)	No	O		?	?	O	?	Symptomatic treatment
Nortriptyline	‡‡‡	‡‡‡	O	?	O		(+)	(+)	O	?	See amitriptyline
NSAIDs	‡	‡	O	No	O		‡‡	‡‡	O	?	Supportive treatment
O											
Ofloxacin	(++)	?	(++)	No	(+)		?	?	(+)	?	Symptomatic treatment
Oleander/Oleandrin[280–285]	‡‡,**<2 hr**	‡‡	O	Yes	O		+	+	?	?	See digitalis
Orciprenaline	(+)	?	?	No	?		?	?	?	?	Supportive and symptomatic treatment
Organochlorines	‡‡	‡‡	O	No	?		++	++	?	?	Respiratory support, treatment of seizures and arrhythmias
Organophosphates[286,287]	‡‡	‡‡	‡	Yes	+		‡‡	‡‡	?	‡	Antidote: atropine. Treatment of respiratory problems, blood gas and cardiac monitoring
Orphenadrine[288]	‡,**<1 hr**	?	O	Yes	+++		?	?	?	?	Antidote: physostigmine. Symptomatic treatment
Oxaflozane[289]	?	?	?	?	?		?	?	?	?	
Oxalic acid	‡	?	‡	No	‡‡‡		O	O	‡‡‡	?	Prevention of hypocalcemia tetany
Oxazepam	(+++)	(++)	?	Yes	?		?	?	?	?	
Oxprenolol	‡‡,**<3 hr**	‡‡	O	No	+		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Oxycodone	(++)	(++)	O	?	?		?	?	?	?	See morphine
P											
Paracetamol[290–292]	O	‡‡	O	No	‡‡		?	?	‡	+++	Intensive supportive treatment
Paraphenylenediamine[293,294]	?	?	?	No	?		?	?	?	?	Symptomatic treatment
Paraquat[295–297]	‡‡	‡	O	No	‡		‡‡	+	O	++	anti-oxidants drugs, cytotoxic drug use, prevention of lung fibrosis
Pargyline	‡‡	‡‡	O	?	?		?	?	?	?	Closely monitoring for at least 25 hr. Symptomatic treatment
Paroxetine	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
Pefloxacin[298]	(++)	?	?	No	(+)		?	?	‡	?	Symptomatic treatment
Pentachlorophenol[299,300]	‡‡	‡‡	(++)	No	?		?	?	?	‡	Symptomatic treatment
Pentobarbital[301]	‡‡,**<8 hr**	‡	O	No	‡‡		‡‡‡	‡‡‡	O	?	Stabilization of circulatory and respiratory function, good nursing
Phencyclidine	‡‡	‡‡	‡	No	O		?	?	O	?	Symptomatic treatment
Phenelzine	‡‡	‡‡	O	?	?		?	?	?	?	Closely monitoring for at least 26 hr. Symptomatic treatment
Phenobarbital	‡‡,**<8 hr**	‡	‡	No	‡‡		‡‡‡	‡‡‡	O	?	Stabilization of circulatory and respiratory function, good nursing
Phenol and derivatives[302]	‡‡	‡‡	‡‡	No	O		‡‡	?	O	?	Symptomatic treatment
Phenylbutazone[303]	‡	‡	O	No	+		‡‡	‡‡	?	‡	Supportive treatment
Phenytoin[304–306]	‡	‡	O	No	**1D**		1D (if HD is not available)	1D (if HD is not available)	O	O	Symptomatic treatment
Philodendron	?	?	?	?	?		?	?	?	?	Supportive and symptomatic treatment
Phosphoric acid	+	?	?	No	‡‡‡		(+)	(+)	?	?	Analgesics, treatment of asphyxia and metabolic acidosis
Phosphorus	‡‡	‡‡	O	No	O		O	O	O	?	Symptomatic treatment
Pindolol	‡‡,**<3 hr**	‡‡	(++)	No	?		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Pioglitazone	(++)	?	O	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Platinum[307]	(++)	(++)	?	No	O		?	?	?	?	Symptomatic treatment

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Potassium permanganate[308,309]	(+)	?	O	No	++		O	O	?	?	Symptomatic treatment
Prajmaline	?	?	‡	No	?		?	‡	?	?	
Prazepam	‡,<6 hr	†	O	Yes	?		?	?	?	?	
Prazosin	?	?	?	?	?		?	?	?	?	
Primidone	‡,<8 hr	†	†	No	++		†††	†††	O	?	Stabilization of circulatory and respiratory function, good nursing
Procainamide[310]	‡,<4 hr	‡	‡	No	†		†	+++	O	?	Treatment of dysrhythmias
Propafenone[311–313]	?	?	O	No	+		?	++	?	?	See quinidine
Propoxyphene	‡,<5 hr	‡	O	Yes	O		O	O	O	?	Antidote: naloxone. Surportive treatment
Propranolol	‡,<3 hr	‡	(++)	No	+		+	+	?	?	Intensive supportive care, management of arrhythmias and hypotension
Protriptyline	†††	†††	O	?	O		(+)	(+)	O	?	See amitriptyline
Pyrethrum	?	?	?	No	?		?	?	?	?	Surportive treatment
Pyrithyldione	‡,<4 hr	‡	O	No	+		+	?	+	?	See methyprylon
Q											
Quinidine	‡,<5 hr	‡	†	No	+		+	(+)	+	?	Symptomatic treatment
Quinine[314,315]	‡,<6 hr	†	O	No	+		+	?	+	?	Symptomatic treatment
R											
Repaglinide	(++)	?	O	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Reserpine	†	†	(+)	No	O		O	O	O	?	Maintenance of blood pressure
Rosiglitazone	(++)	?	O	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
S											
Salbutamol[316,317]	†	†	?	No	?		?	?	?	?	Supportive and symptomatic treatment
Salicylates[318–321]	‡,<8 hr	‡	‡	No	1D	3D	1D	1D	1D	?	Urine alkalinization, correction of acidosis, electrolyte imbalance, dehydration
Secobarbital	‡,<8 hr	†	O	No	‡		†††	?	O	?	Stabilization of circulatory and respiratory function, good nursing
Sertraline[322,323]	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
Sodium azide[324,325]	‡	?	?	No	?		?	?	?	?	Symptomatic treatment
Sodium chloride[326]	‡	O	‡	No	†††		O	O	†††	?	Dilution therapy. Symptomatic treatment
Sodium nitroprusside	‡	‡	O	Yes	++		?	?	?	?	See cyanide
Sotalol	‡,<6 hr	‡	‡	No	++		?	?	?	?	Intensive supportive care, management of arrhythmias and hypotension
Sparfloxacin	(++)	?	(++)	No	(++)		?	?	(+)	?	Symptomatic treatment
Strychnine[327–330]	†,<2 hr	†	O	No	O		O	O	O	?	Support of respiration, prevention of convulsions, treatment of hyperthermia
Sulfuric acid	+	?	?	No	?		?	?	?	?	Analgesics, treatment of asphyxia and metabolic acidosis
T											
Temazepam	‡,<6 hr	†	O	Yes	?		?	?	?	?	
Terbutaline[231,232]	(+)	?	?	No	?		?	?	?	?	Supportive and symptomatic treatment
Tetrachloroethylene[333]	†	?	O	No	O		?	?	O	?	Carbon dioxide-induced hyperventilation, avoid catacholamines
Tetrazepam	‡,<3 hr	†	O	Yes	?		?	?	?	?	
Thallium[334–337]	†	†	†	Yes	1D	1D (if HD is not available)	1D (if HD is not available)	1D (if HD is not available)	O	†	Chelate: prussian blue
Theophylline[338–342]	†	1D	O	No	1C	3D	1C (if HD is not available)	1C (if HD is not available)	O	†	Monitoring of vital functions. Symptomatic treatment.
Thiamylal	‡,<8 hr	†	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing

Continued

TABLE 101.1B

Poison Index List of Treatment—cont'd

	TREATMENT										
DRUG OR POISON*	**GD**	**IAC**	**FD**	**SA**	**HD**	**CRRT**	**HP_A**	**HP_R**	**PD**	**PE**	**Supportive treatment or Antidote**
Thiopental	‡‡,<8 hr	‡	O	No	(++)		(++)	(++)	O	?	Stabilization of circulatory and respiratory function, good nursing
Tocainide	‡‡	‡‡	‡‡	No	(+)		?	?	?	?	See lidocaine
Tolazamide	(++)	?	(++)	No	(++)		?	?	(+)	?	Symptomatic treatment, Closely monitor blood glucose
Tolbutamide[343]	(++)	‡‡	?	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Toluene[344]	‡	?	‡	No	‡		?	?	?	?	Removal from the area of exposure, irrigate eyes, avoid catecholamines
Tranylcypromine	‡‡	‡‡	O	?	++		?	?	?	?	Closely monitoring for at least 27 hr. Symptomatic treatment
Trazodone[345,346]	?	?	?	No	?		?	?	?	?	Symptomatic and surportive treatment
Triazolam	‡‡,<3 hr	‡	O	Yes	?		?	?	?	?	
Trichloroacetic acid[347]	+	?	‡	No	‡‡‡		?	?	?	?	Analgesics,treatment of asphyxia and metabolic acidosis
Trichloroethylene[348–351]	++,<2 hr	O	O	No	O		O	O	O	?	Atificial ventilation, avoid catecholamines
Troglitazone	(++)	?	O	No	(++)		?	?	(++)	?	Symptomatic treatment, Closely monitor blood glucose
Trovafloxacin	(++)	?	O	No	(++)		?	?	(+)	?	Symptomatic treatment
V											
Valproic acid[352–356]	‡	‡	O	No	‡‡‡		‡‡	‡‡	?	?	Symptomatic treatment
Vancomycin[357–360]	‡	‡	O	No	‡		‡	(+)	O	‡	
Verapamil[361–364]	‡‡,<3 hr	‡	+	?	O		‡	O	?	‡	Antidotes: calcium, 4-aminopyridine, glucagon? Supportive and symptomatic treatment
Viloxazine	‡‡‡	‡‡‡	O	?	O		+	+	O	?	See amitriptyline
Vincristine[365,366]	?	?	O	No	?		?	?	?	‡	Monitoring of vital functions. Symptomatic treatment
Vinyl chloride[367]	+	?	‡	No	?		?	?	?	?	Removal from the area of exposure, irrigate eyes, avoid catecholamines

*Data from Seyffart G: Poison Index: The Treatment of Acute Intoxication. Lengerich, North Rhine–Westphalia, Germany, Pabst Science Publishers, 1997.

Abbreviation:
MW = Molecular Weight (Daltons),
PPB = Plasma Protein Binding
VD = Apparent Volume of Distribution (l/kg)
SB = Solubility
$T_{1/2}$ = Plasma Half-life
EU = Excreted in Urine as the parent drug
GD = Gastrointestinal Decontamination after poisoning by ingestion
IAC = Instillation of Activated Charcoal after poisoning by ingestion
FD = Forced Diuresis
SA = Special Antidote
HD = Hemodialysis
HP_A = Hemoperfusion using activated charcoal
HP_R = Hemoperfusion using exchange resin Amberlite XAD-4
PD = Peritoneal Dialysis
PE = Plasma Exchange
O = Not recommended or removal negligible for various reasons
‡,‡‡,‡‡‡ = Good and effective removal, method indicated
+,++,+++ = Removal appreciable, but clinical effect minimal, not uniform or controversial
(+),(++),(+++) = No experience but appreciable removal can theoretically be expected
Level 1 = Strong recommendation, " We recommend … "
Level 2 = Weak recommendation, " We suggest … "
Level 3 = Neutral recommendation, " It would be reasonable … "
Grade A = High level of evidence
Grade B = Moderate level of evidence
Grade C = Low level of evidence
Grade D = Very low level of evidence
? = No experience or in controversial
CNS = Central Nervous System
CV = Cardiovascular
GI = Gastrointestinal
DIC = Disseminated Intravascular Coagulation
ARDS = Adult Respiratory Distress Syndrome

TABLE 101.1C

Poison Index List of Indication for Extracorporeal Treatment (From EXTRIP Workgroup)

DRUG OR POISON*	INDICATION
Acetaminophen	N-acetylcysteine (NAC) is the mainstay of treatment. Extracorporeal treatment is reserved for rare situations when the efficacy of NAC has not been definitively demonstrated. [1D]
Barbital	coma, shocked, or activated charcoal treatment don't work [1D]
Carbamazepine	seizures refractory to treatment or life threatening dysrhythmias [1D]
Lithium	concentration of Lithium is over 4.0 mEq/L when the kidney function is impaired consciousness, seizures, life-threatening dysrhythmias, irrespective of the concentration of Lithium.[1D
Metformin	Lactate concentration > 20 mmol/L [1D] Blood pH is less than or equal to 7.0 [1D]
Methyl alcohol	Severe methanol poisoning features (coma,seizure et al) Serum methanol concentration>700 mg even under fomepizole therapy [1D]
Phenytoin	prolonged coma is present or expected. [1D], prolonged incapacitating ataxia [3D]
Salicylates	>7.2 mmol/L [100 mg/dL] [1D];
Thallium	history or clinical features, Tl concentration is >1.0 mg/L [2D]
Theophylline	concentration>100 mg/L[1C]

*Level 1 = Strong recommendation, " We recommend … "
Level 2 = Weak recommendation, " We suggest … "
Level 3 = Neutral recommendation, " It would be reasonable … "
Grade A = High level of evidence
Grade B = Moderate level of evidence
Grade C = Low level of evidence
Grade D = Very low level of evidence

Key Points

1. The management of the poisoned patient requires appropriate decontamination, antidote administration, and elimination enhancement. The decision should be based on drug toxicity and properties and should balance the potential benefit against the risk of administration.
2. Activated charcoal remain an important consideration in the treatment of severe poisoning, even if there is a dispute in clinical benefit. Some modalities have little or no impact on patient outcome and should be abandoned.
3. Extracorporeal treatments play a crucial role in the treatment. Hemodialysis (HD) is the most commonly used therapy for poisoning. Hemofiltration and hemodiafiltration have theoretic similar or greater clearance capacities than HD; however, their clinical use in poisoning is restricted by their limited availability. Hemoperfusion, therapeutic plasma exchange, and continuous renal replacement therapy may have a role in selected cases, whereas further studies are required for albumin dialysis.
4. The position paper and system review by the American Academy of Clinical Toxicology, the European Association of Poison Centres and Clinical Toxicologists, and the Extracorporeal Treatment in Poisoning study group may provide valuable evidence-based clinical recommendations.
5. Reflecting the necessarily urgent nature of the clinical response to poisoning, treatment often is based on clinical experience; well-designed, evidence-based studies are needed.

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A complete reference list can be found online at ExpertConsult.com.

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