

Unintentional Household Poisoning in Children

Akzidentelle Vergiftungen im Haushalt im Kindesalter

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Bibliography

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Abstract



Despite the major reduction in fatal paediatric poisonings that has been achieved in industrialised countries over the last few decades, unintentional paediatric poisoning remains a major public health issue worldwide. In this article, we aim to provide clinicians dealing with poisoned children an overview of the problem and specific guidance on the identification and management of significant poisoning. Substances most frequently ingested by children in the developed world include household chemicals, medication, and plants. Although the great majority of such poisonings have no or limited clinical effects, it puts substantial burden on health care systems. Importantly, a few poisons can kill after ingestion of very small amounts. Unintentional poisoning in developing countries can be much more serious, following ingestion of kerosene, caustic agents, herbal remedies, insecticides or herbicides. Management of symptomatic patients involves supportive care, if available the administration of antidotes, and the removal of the offending drug from the body. Recent position papers on gastric decontamination indicate that such interventions are only rarely necessary. To further reduce the number of deaths and disabilities in the industrialised world and to begin to have an effect in the developing world, much more work is required to both identify and implement prevention strategies to reduce the number of cases of paediatric poisoning.

Introduction



While most significant poisonings in adolescents and adults are intentional [1,2], poisoning in toddlers and infants is almost always unintentional, secondary to their explorative behaviour and

Zusammenfassung



Trotz der Verringerung der tödlichen Vergiftungen im Kindesalter in den letzten Jahrzehnten in den Industrieländern stellen akzidentelle Vergiftungsunfälle bei Kindern weiterhin ein schwerwiegendes Problem dar. Ziel dieser Arbeit ist es, einen Überblick über akzidentelle Vergiftungen im Kindesalter und deren Behandlung zu geben. Die am häufigsten ingestierten Substanzen in Industrieländern durch Kinder sind Haushaltsmittel, Medikamente und Pflanzen. Obwohl die meisten dieser Ingestionen zu keiner oder nur geringer klinischer Symptomatik führen, stellen sie durch Inanspruchnahme medizinischer Leistungen eine nicht unerhebliche Belastung für das Gesundheitssystem dar. Von Bedeutung ist zudem, dass einige wenige Substanzen auch in sehr geringen Mengen zu Todesfällen führen können. Akzidentelle Vergiftungen in Entwicklungsländern sind häufig durch Kerosin, ätzende Substanzen, traditionelle Heilmittel und Insektizide und Herbizide verursacht. Die Behandlung vergifteter Kinder ist meist supportiv; in Einzelfällen ist die Gabe eines Antidots, oder eine primäre oder sekundäre Giftentfernung notwendig. Nach Maßgabe der neuen Leitlinien zur primären Giftentfernung der europäischen und amerikanischen Fachgesellschaften ist diese allerdings nur noch in seltenen Fällen indiziert. Um die Anzahl der Vergiftungs- und Todesfälle durch Vergiftungen weiter zu reduzieren sind weitere Maßnahmen insbesondere auf dem Gebiet der Prävention erforderlich.

tendency to place objects in their mouth. On occasion, therapeutic error can occur at home. Although unintentional paediatric exposures to poisonous substances often present as an emergency, it is important to realise that approximately 97% of such cases in the developed world

have no or limited clinical effects [3], and the child has usually a good outcome with minimal intervention. On the contrary, in the developing world, severe injury due to unintentional poisoning is a frequent occurrence in children [4–13].

As a result of prevention programmes and measures, a significant reduction in fatal poisoning in young children has been achieved in North America and Europe. However, children continue to be exposed to toxic agents, including newly emerging substances and products. Since the foundation of the first Poison Control Centres (PCC) in the late 1940's and early 1950's in Europe and the United States, PCCs have played a pivotal role in the management of poisoned children.

In the last decades, several broadly accepted practices in treating poisoned patients have come in question. In 1997/1999 and 2004/2005, the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists (AACT/EAPCCT) published position papers on gut decontamination that have substantially changed the primary approach to the poisoned child [14–21].

The objective of this review is to provide clinicians dealing with poisoned children an overview of the problem of unintentional household poisoning including epidemiology, common patterns, and preventive measures as well as specific guidance on the identification and rationale management of significant poisoning.

Methods: Search strategy and selection criteria

▼ We did a comprehensive search on MEDLINE (January, 1966–May, 2006) to identify scientific reports relating to this topic. The search terms included the words “intoxication”, “poisoning”, “children”, “toddler”, “childhood”, “household”, “home”, “accidental”, “unintentional”, “developed countries”, “developing countries”, and “prevention”. We mainly selected publications from the past 15 years, but we did not exclude commonly referenced and highly regarded older publications. Appropriate sources from the reference lists of these articles were also considered. Relevant review articles and book chapters were also included. There was no restriction on language of publication.

Epidemiology of unintentional paediatric household poisoning

▼ Despite the reduction in fatal poisoning seen in young children in North America and Europe over the last few decades [22–25], toxic exposures and poisonings continue to be a worldwide health care problem of considerable concern. It is a particularly severe problem in the developing world where the great majority of deaths from poisoning – as many as 99% in some estimates – occur [26,27]. Although most deaths are due to intentional self-poisoning, unintentional paediatric poisoning is still responsible for a considerable number of deaths and injuries in these regions.

Although the proportion of exposures reported to PCCs is estimated to be as low as 26 percent (in the USA) [28], the Toxic Exposure Surveillance System (TESS) database of the American Association of Poison Control Centers (AAPCC) provides a valuable perspective on trends and patterns of exposure to poisons in children in developed countries. However, the accuracy of these data may be distorted by inherent biases including the

reporting process itself, and under- and overreporting of poisonous events [28,29]. The analysis of TESS data for trends may prove most useful as the inherent biases in TESS reporting are likely to be consistent over many years [30].

According to the TESS database, in 2004 more than 1 million exposures to poisons occurred in children less than 6 years of age (peak age one to three years) in the United States and most occurred in the home [24]. Although this age group was responsible for the majority of poisoning reports (51.3%), it was responsible for only a small minority of deaths (2.3%). A male predominance is found for poison exposure victims younger than 13 years [24].

Unintentional poisonings outnumber intentional poisonings in children by far. In most cases, ingestion is the route of exposure. The proportion of patients treated in health care facilities is strongly correlated to age. Around 10% of children under 6 years of age and 13.4% of children between 6 and 12 years of age are managed in health care facilities compared to 48.5% of teenagers and 36.7% of adults [24].

Products that are most accessible to children, such as cosmetics and personal care products, cleaning products, analgesics, and cough and cold medicine, are responsible for the majority of unintentional exposures and poisonings in the developed world (► **Table 1** and **2**). In the last decade a sharp increase in poisonous events has been noticed for dietary supplements, herbal preparations, and ethnic remedies [31,32]. As herbal medicine become more available in Western countries, unintentional intoxication with heavy metal (lead, mercury, and arsenic) has emerged as an issue of substantive concern [33,34]. Furthermore, a recent study has shown that many paediatric health care providers are not familiar with the risk profile of these substances [35].

The exposure frequency reflects product availability, accessibility to the child in the home, and packing, rather than their inherent toxicity [25]. Unintentional poisoning by medication is one of the leading specific causes of injury in children aged 18 to 35 months in the United States [36]. Substances associated with the greatest risk of death to children (based on hazard-factor analysis) are listed in ► **Table 3** and **4** [29,37]. A small group of pharmaceutical and non-pharmaceutical household products can cause life-threatening sequelae when ingested even in very small quantities (1–2 tablets or 1 to 2 teaspoons; ► **Table 4**) [38–44].

With some regional variation because of lifestyle and cultural differences between various countries and ethnic groups, the TESS data from North America is comparable to data from other industrialised countries as far as age distribution, substances ingested, unintentional mode of ingestion, and good prognosis are concerned [2,3,45–56].

In contrast to the available data in the developed world, figures on unintentional poisoning in children in the developing world are largely based on hospital admission data. Although the unintentional mode and age distribution are also seen for paediatric poisonings in the developing world, the type of substances ingested, and morbidity and mortality rates differ markedly [4–7]. In developing countries, kerosene and paraffin – largely used as a fuel and light source – are two of the most common poisons ingested by children; both potentially causing death [7–9]. Since agricultural pesticides have become a common household product in many rural areas of the developing world in the last decades, episodes of unintentional pesticide poisoning in children are now an important cause of morbidity and mortality [5,7,10]. The lack of facilities for safe storage and disposal ensures fre-

Table 1 Common non-pharmaceutical products involved in unintentional household poisoning in children*

Product	Characteristics	Symptoms	Treatment
Aftershave, alcohols, cologne, mouthwash, perfumes	Ethanol containing agents; perfumes contain up to 75% to 95%	CNS and respiratory depression, hypoglycaemia, acidosis	Clinical observation and hospital admission depending on the ingested amount; blood glucose measurement; Administer oral or intravenous glucose in hypoglycaemic children depending on severity; respiratory support as needed
Bleach	Household solutions contain approximately 3–10% sodium hypochlorite or less commonly 3% hydrogen peroxide; extremely unpalatable; unlikely to cause serious damage. Industrial bleach: up to 50% of sodium hypochlorite	Nausea, emesis, diarrhoea; oesophageal injury rarely occurs; hypernatraemia, hyperchloraemic acidosis. External contamination may result in eye or skin irritation	Administer fluids; hospital admission of children at risk of developing oesophageal injury (see <i>oesophageal burns</i>)
Button batteries	Toxicity occurs when button batteries remain in the oesophagus, the nose, the ear, or if they are leaky before ingestion. If they rapidly reach the stomach, toxicity is unlikely	Difficulty swallowing, vomiting, haematemesis. In case of ingestion of leaky battery, hypersalivation, drooling	X-ray to confirm ingestion. Battery lodged in the oesophagus should be quickly removed by endoscopy. Same applies to battery impacted in the nose or ear. Batteries in the stomach or the intestine should not be removed unless there are signs of perforation, obstruction, or if they were leaky
Detergents	3 chemical categories: non-ionic, anionic, cationic	Non-ionic, anionic (low toxicity): Respiratory symptoms secondary to foam aspiration rarely occur. Cationic: Corrosive lesions if concentrated solution is involved	Administer oral fluids; further treatment depending on the presence of respiratory symptoms and corrosive lesions (see <i>oesophageal burns</i>)
Dishwasher powders, liquids, tablets	Older or professional use products: Strongly alkaline; possible severe corrosive injury	Hypersalivation, drooling, vomiting, haematemesis, pain. Oesophageal injury may occur in the absence of oral burns	Remaining products must be washed off; administer oral fluids; supportive treatment (see <i>oesophageal burns</i>)
Disinfectants and antiseptics	May contain a number of toxic constituents (chlorhexidine, hexylresorcinol, hydrogen peroxide, ichthammol, iodine, phenol, potassium permanganate); usually they are found in very low quantities in diluted solutions	Irritation of the oral mucosa, and transient gastrointestinal upset, possibly corrosive effects, aspiration pneumonia. Systemic toxicity: Acidosis, CNS depression, hepatic/renal damage depending on substances involved	Administer fluids; Precise identification of involved substance is essential. In case of oesophageal injury (see <i>oesophageal burns</i>)
Essential oils	Volatile mixtures of esters, alcohols, and ketones; Some substances, eg camphor, are very toxic	Initial effects: Mucosal irritation, vomiting, epigastric pain; secondary hepatic and renal failure possible; sedation, seizures. Respiratory compromise if aspirated	Clinical observation; supportive treatment if indicated
Nail care/Nail varnish removers	Typically contain acetone or ethyl acetate, but other solvents may be used including methanol; artificial nail products containing methacrylic acid may cause severe caustic injury; artificial nail removers containing nitroethane may cause methemoglobinemia, and acetonitrile may cause cyanide poisoning	Irritation of mucus membranes, vomiting, CNS depression; ketosis, acidosis, hyperglycaemia possible	Clinical observation may be indicated; hospital admission needed in symptomatic children; Nitroethane and acetonitrile ingestions require referral to the ED; measurement of blood glucose; monitor respiratory and renal function; supportive care. In case of oesophageal injury (see <i>oesophageal burns</i>)
Nicotine	Toxic alkaloid found in a range of plants, most notably tobacco and smoking cessation products that contain nicotine (gums, transdermal patches, nasal sprays). Most frequently ingested in the form of cigarette or cigarette butt	Vomiting most common symptom. Confusion, convulsions, and dysrhythmias may occur only if large amounts are ingested	Usually no specific treatment is required; consider activated charcoal depending on ingested amount and age; supportive care in case of seizures and cardiovascular compromise.
Petroleum distillates(paraffin, kerosene, petrol, diesel, lubricating, engine oils)	Low systemic toxicity	Aliphatic hydrocarbons: Main hazard: Chemical pneumonitis. Many aromatic and halogenated hydrocarbons may cause CNS depression, seizures, and cardiac arrhythmias	Clinical observation; hospital admission in symptomatic children; administer fluids; chest X ray and supportive treatment if indicated. Extracorporeal membrane oxygenation (ECMO) could be used in severe cases of chemical pneumonitis

Rat and mouse poisons (domestic rodenticides)	Accurate identification of the constituents may be difficult; most substances are based on warfarin or long acting anticoagulant substances; alphachloralose is used rarely; carbamate pesticides are used in some regions	Bleeding, CNS depression with alphachloralose; cholinergic features with carbamates (see <i>OP pesticides</i>)	Determination of prothrombin time or INR at 12 and 36–48 h post ingestion if ingested substance exceeds 0.5 mg/kg of warfarin, or if 0.01 mg/kg of any other anticoagulant has been ingested. Consider administering oral charcoal. Administer vitamin K per os if prolongation of prothrombin time
Toilet cleaner blocks	Two types: Cistern or rim blocks; acid or detergent based; low systemic toxicity, local corrosive damage may occur	Gastrointestinal irritation/upset	Administer fluids. In case of oesophageal injury (see <i>oesophageal burns</i>)
Turpentine	Essential oil	Irritation of gastrointestinal mucosa, metabolic acidosis, hepatic/renal failure, altered level of consciousness. Respiratory compromise if aspirated <i>into the lungs</i>	Admit to hospital if symptomatic; supportive treatment
Laundry powder	Contains mixtures of enzymes, perfumes, softeners, and anionic and non-ionic detergents; low toxicity	Vomiting	No specific treatment required; administer oral fluids
White spirit/Turpentine substitutes	Relative low toxicity when ingested	Gastrointestinal irritation, CNS depression if ingested in large quantities. Main toxicity due to aspiration; Symptoms may develop after an interval of 24 hours	Assessment of respiratory system in all patients, children with signs of chemical pneumonitis: Chest X-ray; supportive treatment. ECMO could be used in severe cases of chemical pneumonitis.

Data presented in table 1 is based on selected review articles [71, 105, 119, 120], including the primary citations of these review articles. Selected issues of importance are also referenced [96–104, 121–127]

Table 2 Common pharmaceuticals involved in unintentional poisoning in children^{*}

Drug	Characteristics	Symptoms	Treatment ([*] the use of gastrointestinal decontamination techniques is not explicitly stated, but its use can be derived from the AACT/EAPCCT position papers)
Antibiotics	Serious toxicity from single ingestion unlikely except for chloramphenicol	Transient gastrointestinal disturbance	Usually no treatment is required
Salicylate (Aspirin)	Stimulation of respiration by a direct action on the respiratory centre. Uncoupling of oxidative phosphorylation in skeletal muscle. Acidosis enhances transfer of salicylate across the blood-brain barrier	Abdominal pain, nausea, vomiting, tinnitus, dizziness, decreased hearing, hyperventilation (respiratory alkalosis), and metabolic acidosis. Initial excitement or agitation may be followed by CNS depression and coma. Dehydration	Determination of plasma salicylate level 3–6–12 hours post-ingestion if ingested amount is > 150 mg/kg of aspirin or aspirin-equivalent until documented downward trend. Measurement of electrolytes, renal function, blood glucose, clotting, and acid-base balance. Vigorous correction of dehydration. Urinary alkalinization (urine pH \geq 7.5) first line treatment in children with moderately severe poisoning who do not yet meet the criteria for haemodialysis. Consider haemodialysis if serum salicylate concentration \geq 950 mg/l (7 mmol/l), or in children with unresponsive acidosis, seizures, coma, renal failure, or progressive deterioration
Cough and decongestant preparations	Frequently ingested unintentionally. Active ingredients include: Sympathomimetics, opioids, and expectorants. The ingestion of several active ingredients in a single preparation can cause a confusing clinical picture and potentiate adverse effects	Dependent on the active ingredient: Hypertension, reflex bradycardia, arrhythmias, convulsions, respiratory depression, coma	Hospital admission dependent on type and amount of ingested substance, and severity of symptoms. Treatment is supportive
β_2 agonists and sympathomimetics	Variable toxicities. Phenylephrine and ephedrine have narrow therapeutic index. Pseudoephedrine is less toxic. Oral toxicity is rare with β_2 agonists	Vasodilatation, tachycardia, Hypo/hypertension, arrhythmias, agitation, skeletal muscle tremor, metabolic acidosis, hyperglycaemia, hypokalaemia, mydriasis, convulsions	In most instances no aggressive treatment is warranted. In hypotensive children, administer intravenous fluids. Benzodiazepines can be given to control seizures, and to slow heart rate. Consider β blockers (propranolol, esmolol) in symptomatic tachycardic children (Caveat: asthmatic children). Phenolamine can be used if child is hypertensive. Supplement potassium if indicated.

Benzodiazepines	Low-moderate toxicity	Drowsiness, ataxia, hallucinations, confusion, and agitation. Respiratory depression, bradycardia, and hypotension possible	Clinical observation of asymptomatic children; Symptomatic children require hospital admission. Supportive treatment if necessary. Flumazenil, a competitive antagonist to benzodiazepines, is not generally indicated because of fear of multiple ingestion (although very rare in young children) including substances that decrease seizure threshold
Fluoride	Ingestion of more than 5–10 mg/kg causes toxicity	Tetany, convulsions, ventricular arrhythmias, coma from hypocalcaemia, hypomagnesaemia, and hyperkaleamia	Symptomatic children require hospital admission. Electrolytes, creatinine, and ECG should be monitored. In case of large ingestion, oral antacid containing calcium can be useful. Intravenous calcium or magnesium to correct hypocalcaemia or hypomagnesaemia
Non-steroidal anti-inflammatory drugs (NSAIDs)	Ibuprofen accounts for 65–81 % of childhood NSAID exposures, mefenamic acid for 10%, and diclofenac 6%. Generally of low toxicity, but mefenamic acid and phenylbutazone may cause significant toxicity	Gastrointestinal upset, headache, dizziness, tinnitus, and visual disturbance. Hypotension, tachycardia, and hypo-thermia rarely occur. In large overdose electrolyte disturbances, metabolic acidosis, CNS depression, convulsions (mefenamic acid), respiratory depression, renal/hepatic failure, and arrhythmias (phenylbutazone) may be seen	Symptomatic children require hospital admission. Oral fluids should be encouraged and dehydration corrected. Electrolytes, creatinine, and acid-base balance should be monitored. Diazepam is the treatment of choice for convulsions
Oral contraceptives	Very low toxicity	Transient gastrointestinal upset. Possible vaginal bleeding during the first few days following ingestion	No treatment required
Paracetamol (acetaminophen)	Toxic paracetamol concentrations associated with the unintentional ingestion in children are extremely rare. Toxicity may be increased in pre-term infants and newborns, pregnant women and foetus, fasting children with hyperpyrexia, children with anorexia nervosa, and those who take drugs that induce the cytochrome P450 system	Nausea, vomiting, abdominal pain, signs and symptoms of hepatic dysfunction	No treatment necessary if ingested dose is < 150 mg/kg in healthy, non-fasted children. If the dose ingested cannot be confirmed or is ≥ 150 mg/kg, measurement of blood paracetamol concentration at least four hours following ingestion is indicated. Recently a dose of 200 mg/kg has been used by some instead of 150 mg/kg in children less than 6 years of age. The need for treatment with intravenous infusion of acetylcysteine (150 mg/kg in 60 min, then 50 mg/kg in 4 h, followed by 100 mg/kg in 16 h) or oral (140 mg/kg loading dose followed by an additional 17 doses of 70 mg/kg every 4 h) can be derived from the standard Rumack-Matthew normogram. Assessment of electrolytes, creatinine, liver enzymes, and coagulation parameters is mandatory
Topical medicinal products	Most products are of low toxicity. Products with potentially toxic active ingredients include salicylates in wart and callus treatments, thioglycolate in depilatory creams, and methylsalicylate in liniments	Nausea, vomiting, and diarrhoea; oropharyngeal irritation and burning may occur; corrosive or systemic injury may be seen after ingestion of large amounts	In most instances no treatment is warranted, otherwise dependent on active ingredient
Vitamin preparations	Low toxicity in overdose; Caveat: May contain iron	None	No treatment required if iron supplementation is excluded

Data presented in table 2 is based on selected review articles and case reports [71, 77, 88, 120, 128–131], including the primary citations of these review articles

quent unintentional poisonings [57,58]. Other commonly ingested poisons include caustic soda and traditional medicines (eg, Indian teething powder containing mercury) [6, 11–13, 59, 69]. Traditional medicines appear to represent a particular threat to very young children (< 1 year of age) with a high rate of case fatality [13].

Prevention measures

▼ There has been a substantial reduction in the incidence of unintentional childhood poisonings over the past decades in the developed world [22], which is largely the result of interventions aiming to prevent exposure [61]. The Federal Caustic Poison Act in the year 1927 was the first specific regulatory measure in the United States to deal with household poisoning. The 1960 passage of the Federal Hazardous Labelling Act mandated proper labelling of products as a passive

Table 3 Pharmaceutical and non-pharmaceutical substances with a high potential for toxicity*

Substance	Characteristics	Symptoms	Treatment (* the use of gastrointestinal decontamination techniques is not explicitly stated, but its use can be derived from the AACT/EAPCCT position papers)
Antihistamines (H ₁ and H ₂ receptor antagonists)	H ₁ antagonists: Anti-cholinergic, anti-serotnergic, and anti-adrenergic properties. Cardiac toxicity mediated by myocardial sodium channel blockade or by potassium channel blockade (terfenadine or astemizole; both removed from the US market). H ₂ receptor antagonists rarely cause significant toxicity	CNS depression, nausea, emesis. Anti-cholinergic side effects in overdose (dry mouth, mydriasis, hallucinations, convulsions). Cardiac dysrhythmias with prolongation of QRS and the QT interval, ventricular tachyarrhythmias, Torsades de pointes. Rhabdomyolysis	Clinical observation; Symptomatic children require hospital admission. ECG monitoring; Administer intravenous fluids in hypotensive children, avoid epinephrine because of possible paradoxical hypotension. Tachyarrhythmias with QRS widening: An initial bolus of 1 ml/kg of 8.4% sodium bicarbonate. Further doses of sodium bicarbonate may be required to keep the arterial pH between 7.45 and 7.55, and QRS complex <0.1 s. Consider lidocaine in ventricular tachycardia (VT). Administration of magnesium sulphate in children with Torsades de pointes dysrhythmia (15–30 mg/kg). Defibrillation is mandatory in children with pulseless VT or ventricular fibrillation. Benzodiazepines are given if convulsions or agitation occur
β blockers	Competitively antagonise the binding of noradrenaline and adrenaline to β receptors	Bradycardia and hypotension, varying degrees of heart block, shock, and pulmonary oedema; tachycardia and hypertension can occur if a partial agonist with intrinsic sympathomimetic activity is ingested. CNS effects include lethargy, coma, hallucinations, and convulsions. Hypoglycaemia	Clinical observation of asymptomatic children. Symptomatic children require intensive monitoring. Hypotension may respond to intravenous fluids. In refractory hypotension, intravenous glucagon (50–150 μg/kg in 5% dextrose) is the drug of choice. Atropine, glucagon, isoproterenol or cardiac pacing may be required in bradycardic dysrhythmias. Prolonged external chest compressions in case of drug failure. Regular assessment of blood sugar and administration of glucose if necessary is essential
Calcium channel blockers (CCBs)	Dihydropyridines (eg, nifedipine): Most prominent effects on peripheral vascular smooth-muscle. Phenylalkylamine (Verapamil): Most prominent effects on myocardial smooth muscle. Benzothiazepine (Diltiazem): Characteristic effects are in between nifedipine and verapamil. Diarylaminopropylamine ether In toxic concentrations the effects between the different types of CCBs cannot be easily distinguished. Narrow therapeutic index	In moderate poisoning hypotension, reflex tachycardia (in nifedipine poisoning), facial flushing, nausea and emesis, and headache may occur. In severe poisoning, bradycardia, sino-atrial and AV-blockade, junctional escape rhythms, profound hypotension, profound negative inotropy, cardiogenic shock, asystole, ventricular fibrillation, CNS depression, generalised seizures, metabolic acidosis, hyperglycaemia may be seen.	Admission to hospital; monitoring of cardiovascular parameters. Assessment of serum electrolytes. In case of symptomatic bradycardia administer atropine (10–20 μg/kg). In children with hypotension aggressive volume resuscitation is required; consider (repetitive) intravenous calcium (0.3–0.6 ml/kg calcium gluconate 10%) over 5 min; epinephrine/norepinephrine, isoproterenol, or phosphodiesterase inhibitors (second-line) may be indicated. Consider: Glucagon (50–150 μg/kg in 5% dextrose), high-dose insulin/glucose. Consider cardiac pacing in case of refractory bradycardia and intra-aortic balloon counterpulsation in refractory hypotension. Caveat: Symptoms may be delayed and may re-occur after a symptom-free interval in sustained-release drugs
Cocaine	Inhibition of uptake of dopamine, noradrenaline, and 5-hydroxytryptamine (5-HT) from synapses. Psychomotor stimulant	Agitation, mydriasis, fever, diaphoresis, emesis, hallucinations, convulsions, hypertension, chest pain, myocardial ischaemia, tachycardic arrhythmias, and cerebral infarction. Hyperthermia, rhabdomyolysis	Hospital admission: Administer oxygen. Administer benzodiazepines in case of agitation, hallucinations, and convulsions. Hypertension and chest pain require treatment with diazepam, morphine, and nitrates, and anti-coagulants. If unresponsive, consider calcium channel blockers or phentolamine. Correction of acidosis as it exacerbates cardiac toxicity; ventricular arrhythmias may respond to sodium bicarbonate (in case of QRS widening) or lidocaine. Aggressive physical cooling if hyperthermic

Digoxin	High potential for severe toxicity in overdose, especially in children with underlying cardiac disease; narrow therapeutic index. Plants containing cardiac glycosides can give same clinical presentation	Nausea, vomiting, visual disturbances, hypotension, hyperkalaemia, and cardiac arrhythmias	Hospital admission: Monitoring of blood pressure, ECG, electrolytes, and creatinine. Determination of plasma digoxin concentrations ≥ 6 hours post-ingestion (blood level not always correlated with symptoms). Hyperkalaemia ($>5\text{--}5.5$ mmol/l) indicate severe toxicity. Bradyarrhythmias: Atropine or cardiac pacing for persistent symptomatic bradycardia. Tachyarrhythmias: Lidocaine, phenytoine. Digoxin-specific antibodies in life-threatening cardiac glycoside poisoning, or if serum potassium $>5\text{--}5.5$ mmol/l in setting of acute digoxin intoxication. Correct hypo/hyperkalaemia, and hypomagnesaemia
Ethylene glycol	Found in various types of antifreeze and windscreen wash. Rapid absorption from the stomach. Metabolic degradation by alcohol dehydrogenase (ADH) to a variety of toxic metabolites. Increased anion gap	After ingestion of ≥ 0.1 ml/kg: Nausea, emesis, abdominal pain, CNS depression, convulsions; ≥ 0.2 ml/kg: Metabolic/lactic acidosis, hypocalcaemia, renal failure, CNS depression, convulsions	Hospital admission: Assessment of plasma ethylene glycol as well as measurement of blood gases, serum electrolytes, and renal function. Antidotes in symptomatic children or those with a plasma ethylene glycol level >3.2 mmol/l (20 mg/dl): Ethanol (initial dosage 0.6–0.8 g/kg, followed by 0.1 g/kg/h). Fomepizole: Initial dosage: 15 mg/kg, followed by 4-times 10 mg/kg every 12 h. In case of renal failure, haemodialysis is required. Consider haemodialysis if level >8 mmol/l (50 mg/dl), or if resistant metabolic acidosis. Fomepizole and ethanol are dialysed and the dosage needs to be adjusted when dialysis is performed. Supportive care: Correction of acidosis with sodium bicarbonate, and glucose for hypoglycaemia
Isoniazid	Antituberculous drug causing deficiency of the inhibitory neurotransmitter γ -aminobutyric acid with a very high toxicity	Intractable, early-onset seizures resistant to most conventional anticonvulsants. Profound anion gap metabolic acidosis, hyperglycaemia, hypokalaemia, and ketonuria	Hospital admission: Symptomatic patients receive repeated administration of intravenous pyridoxine (vitamin B ₆): 1 gram pyridoxine per 1 gram isoniazid; if dose unknown 70 mg/kg to a maximum of 5 g). Use diazepam to treat seizures until pyridoxine becomes available. Aggressive supportive treatment
Iron	Highly toxic; may be contained in vitamin preparations; toxicity depends on the elemental iron content of the salt as the supplement	Early signs include vomiting, diarrhoea, abdominal pain, gastrointestinal haemorrhage; After apparent stabilisation (6–24 h post ingestion), mitochondrial toxicity may evolve resulting in shock, acidosis, coma, seizures, hepatic and renal failure. Late sequelae are seen rarely and include gastrointestinal scarring and stricture formation (gastric outlet obstruction)	If ingested dosage >40 mg/kg hospital admission is required. Abdominal X-ray examination; whole bowel-irrigation if undissolved iron tablets are visible; if tablets are confined to stomach: repeated gastric lavage or endoscopic removal. Determination of serum iron level 4–6 h post-ingestion, repetition at 8 h in case of sustained release preparations; if serum levels exceeds 500 $\mu\text{g/dl}$ (~ 90 $\mu\text{mol/l}$) regardless of symptoms, and at 350–500 $\mu\text{g/dl}$ (63–90 $\mu\text{mol/l}$) for symptomatic patients administer intravenous deferoxamine 15 mg/kg/h. Intensive supportive care
Isopropanol	Alcohol found in various household products (eg, nail polishes, hairsprays, antifreezes, car screen washes). Rapid absorption from the stomach and mucus membranes. Conversion to acetone by ADH. Excretion through the lungs and kidneys	Gastric irritation, CNS depression, and hypotension. Ketonemia and ketonuria.	Asymptomatic children: Short period of clinical observation and administration of fluids. Symptomatic patients require intensive support. Hypotension: Treatment with intravenous fluids and inotropes. Haemodialysis is rarely useful, but could be considered in patients with failure of supportive measures
Metformin	Inhibits gastrointestinal glucose uptake; increases its uptake into the muscles and fat tissue, and reduces hepatic gluconeogenesis	Profound lactic acidosis, but hypoglycaemia is unlikely	Clinical observation of asymptomatic patients; Monitoring of serum electrolytes, lactate, and bicarbonate. Oral or intravenous glucose administration if indicated. In severe lactic acidosis, consider haemodialysis
Methadone	Synthetic μ opioid receptor agonist commonly used in the treatment of chronic pain and as a maintenance substitute in heroin addicts	CNS depression, ataxia, miosis (pinpoint pupils), arterial hypotension, emesis, respiratory depression. Prolonged duration of toxicity.	Hospital admission; intensive care monitoring and treatment if indicated; consider administration of naloxone (100 $\mu\text{g/kg}$). May need to be repeated or given by infusion (2/3 of effective dose per hour). Caveat: The duration of effect of naloxone is much shorter (approximately 1 h) than that of methadone

Methanol	Constituent of antifreezes, windshield washes, and various household products. Rapidly absorbed from the gastrointestinal tract; Metabolisation by ADH. Increased anion gap	Irritation of mucus membranes; abdominal pain, nausea, emesis, retinal toxicity, neuritis of the optic nerve, metabolic acidosis, convulsions, and coma	Hospital admission: Measurement of blood gases, electrolytes, renal function and methanol level. Treatment is similar to ethylene glycol poisoning, both ethanol and fomepizole inhibiting its metabolism. Antidotes in symptomatic children or those with a plasma methanol level > 8 mmol/l (20 mg/dl). In addition, consider folic acid 1–2 mg/kg every 4–6 h. Consider haemodialysis if level > 15.6 mmol/l (50 mg/dl), or if resistant metabolic acidosis. Fomepizole and ethanol are dialysed and the dosage need to be adjusted when dialysis is performed. Supportive care: Correction of acidosis with sodium bicarbonate, and hypoglycaemia with glucose
Monoamine oxidase (MAO) inhibitor	Poisoning by MAO is uncommon in children secondary to a decline in their prescription	Sympathomimetic effects, excessive CNS stimulation, convulsions, hyperthermia, and rhabdomyolysis	Clinical observation of asymptomatic patients; Supportive care
Organophosphate (OP) and carbamate insecticides	Constituents of insecticides; acetylcholinesterase inhibition; stimulation of acetylcholine receptors throughout body. Common poison in the developing world	Muscarinic effects: Increased secretions from salivary, lacrimal, bronchial, and gastrointestinal glands, and increased peristaltic activity, bronchoconstriction, bradycardia, hypotension, miosis, loss of visual acuity; urinary/faecal incontinence. Nicotinic effects: Muscle stimulation followed by paralysis. Direct CNS effects: Coma, convulsions, respiratory and cardio-circulatory failure	Clinical observation of asymptomatic children; assessment of cholinesterase enzyme activity; supportive care in patients with mild symptoms; Atropine is given as an antidote (0.01–0.02 mg/kg; second-line medication: pralidoxime or obidoxime (reactivates inactivated acetylcholinesterase). Intensive supportive care including mechanical ventilation, inotropes depending on clinical condition. Extracorporeal detoxification does not give benefit
Selective serotonin reuptake inhibitors (SSRI)	SSRI usage has increased in recent years. Less toxic in overdose than tricyclic antidepressants	Emesis, agitation, tremor, nystagmus, drowsiness; convulsions, and dysrhythmias. Sinus tachycardia, bradycardia. QT prolongation are seen mainly with citalopram overdose. Serotonergic syndrome especially when coingested with TCA, MAO inhibitors or other SSRIs	Clinical observation of asymptomatic patients; Supportive treatment. In case of cardiac dysrhythmias, see <i>tricyclic antidepressants (TCA)</i>
Sulfonylureas for treatment of diabetes mellitus	Hypoglycaemia by depolarisation of pancreatic β cells and increase in insulin release	Hypoglycaemia, tremor, convulsions, coma	Clinical observation of asymptomatic patients. Symptomatic children: Intensive monitoring. Intravenous glucose infusion (often require central line). Subcutaneous injection of the somatostatin analogue, octreotide (50–100 μ g), in case of resistant hypoglycaemia; if unavailable, consider diazoxide (1.25 mg/kg)
Theophylline	High toxicity in overdose with an overall low frequency of ingestion in overdose. Increases cardiac conduction velocity, increases catecholamine liberation, reduces coronary blood flow, and decreases the ventricular fibrillation threshold	Vomiting, tachycardia, tachypnoea, tremors, agitation, and convulsions. Metabolic disturbances: Hyperglycaemia hypokalaemia, metabolic acidosis, respiratory alkalosis. Supraventricular and ventricular dysrhythmias	Hospital admission if ingested amount exceeds 10 mg/kg and if clinical effects are present. Blood gas analyses, measurement of serum electrolytes. Correction of hypokalaemia. Supportive care. Administration of benzodiazepines is the primary treatment of supraventricular tachycardia. In case of failure, consider CCBs (diltiazem, verapamil), or β blockers (esmolol, metoprolol, propranolol) in non-asthmatic children. Ventricular arrhythmias are best treated with lidocaine or β blockers. Administer benzodiazepines for convulsions. Haemoperfusion/haemodialysis can be indicated if level > 100 mg/l (550 μ mol/l) or status epilepticus

Tricyclic antidepressants (TCAs)	Blockade of noradrenaline and serotonine reuptake; Anticholinergic and antihistaminergic properties. In addition, TCA exert a quinidine like membrane stabilising effect which causes delayed conduction and myocardial depression. QRS widening >0.10–0.12s and TCA concentration are best indicators in predicting complications (seizures, ventricular arrhythmia, and death)	Anticholinergic symptoms, drowsiness, ataxia and extrapyramidal dyskinetic syndrome, CNS depression, agitation, convulsions. Cardiac arrhythmias occur frequently and are the most common cause of death; they include sinus tachycardia, QT or PR prolongation, and ventricular ectopics. Hypotension	Clinical observation of asymptomatic patients; ECG in all children (look for QRS widening). Compromising arrhythmias: An initial bolus of 1 ml/kg of 8.4% sodium bicarbonate. Further doses of sodium bicarbonate may be required to keep the arterial pH between 7.45 and 7.55. Arrhythmias unresponsive to sodium bicarbonate may be treated with lidocaine (1 mg/kg). Life threatening arrhythmias may respond to cardioversion. Prolonged external cardiac massage may be mandatory in patients with electromechanical dissociation. Administer intravenous fluids and vasopressors to correct hypotension. Glucagon can also be used to treat refractory hypotension
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Data presented in table 3 is based on selected review articles [71, 105, 120, 128, 130] including the primary citations of these review articles; selected issues of importance are also referenced [132–144]

*Information given in table 1–3 is provided for illustration purposes, and clinicians are directed to seek more detailed information about individual case management in a poisoning emergency by calling their local Poison Control Center. In each case, the judgement of the specialist in poison information might override any specific information provided in table 1–3

Table 4 Examples of substances causing life-threatening sequelae when ingested in very small quantities (1–2 tablets, 1–2 teaspoons) [38–44]

Intoxicants
Pharmaceutical
Calcium channel blockers
Chloroquine/Hydroxychloroquine
Clonidine
Clozapine/olanzapine
Flecainide
Imidazolines
Methylsalicylate
Loxapine
Opioids
Phenothiazines (thioridazine and chlorpromazine)
Quinine
Sulfonylureas
Theophylline
Tricyclic antidepressants (amitriptyline, imipramine and desipramine)
Non-pharmaceutical
Camphor
Ethylene glycol
Lindane
Methanol
Podophyllin
Selenious acid

preventive strategy in the United States. Other important passive interventions in the USA have included the federal regulation of product packaging by the Poison Prevention Packaging Act (PPPA) in 1970 which authorized the US Consumer Product Safety Commission to require the use of special child-resistant packaging for toxic substances used in or around the house [62]. The widespread introduction of child-resistant containers and blister packaging has been particularly effective in decreasing fatalities from the ingestion of prescription drugs by children [63,64]. Child-resistant packaging is defined by the PPPA to be packaging that is “difficult for children under age five years to open”, but “not difficult for normal adults to use properly” [62]. Product reformulations have also contributed to a reduction in the number of deaths. The removal of the toxin and its substitu-

tion by less toxic, but equally effective substances has been found to be effective for such products as household bleach, ethanol-containing mouthwashes, antiseptics and disinfectants. In January 1997, the US Food and Drug Administration (FDA) required that oral dosage forms containing more than 30 mg of elemental iron per dosage unit be packaged in strip or blister packs with strong warning labels. Recent data seem to indicate that these changes have resulted in a significant reduction in the number of paediatric deaths from iron ingestion [64]. However, confounding parameters like trends in the total sales of iron products, changes in consumer habits or prescribing practices have to be taken into account [65].

For prevention, new areas of concern include dietary supplements, herbal preparations, and ethnic remedies. Since most of these products are marketed as dietary supplements, in the United States they are regulated under the Dietary Supplement Health and Education Act, which does not require proof of safety or efficacy [66]. New regulations will have to be put in place to decrease the risk of these new threats to children in developed countries.

Active interventions have also been used with some success and include community-based poisoning prevention strategies (eg, stores moving toxic cleaning products to higher shelves) and community-wide efforts at educating consumers about poisoning (eg, offer instructions on the safe storage of household product, use in the home of warning labels and telephone stickers with the number of the local PCC on it) [67]. However, warning labels (eg, Mr Yuk, skull and cross bones) that are widely used in the USA to deter children are no longer recommended by the US National Committee for Injury Prevention and Control since they tend to attract children rather than deter them [68]. The addition of aversive bittering agents to some liquid chemicals, in another attempt to discourage their ingestion by toddlers, is a still unproven approach to poisoning prevention [69].

Health care providers seeing children poisoned at home are encouraged to seek a reason for the ingestion to reduce the risk of recurrence [70]. Attention should be given to family stressors, eg. ill health, including psychiatric disturbances, marital discontent and separation, spousal abuse, unemployment, or other financial burdens since social determinants influence who is at risk for exposure or poisoning [71–73]. In addition, language and cultural barriers must be taken into account [74]. If adequate

support is not provided to a dysfunctional family, a recurrence of poisoning is more likely [72]. Guidance should be given to the parents concerning proper storage of toxic products in their household and the use of child-resistant packages. It is also important that general practitioners and the pharmacists know which medicines are most commonly involved in serious paediatric poisoning (● **Table 3** and **4**), and to give precautionary advice to parents [75].

Data from recent studies, however, indicate that these prevention interventions are only partially effective [76, 77], and children continue to be exposed to household poisons because of improper storage [78]. Hence, additional preventive strategies need to be developed and evaluated. One strategy undertaken by the Consumer Product Safety Commission in the USA is to increase consumer acceptance of child-resistant packaging by encouraging the design of packaging that is both child-resistant and easy to use for all adults (ie, packaging that will rely more on cognitive abilities than strength) [79].

PCCs play a role in preventing injury and undue treatment from unintentional household poisonings. Since their development in the late 1940's and early 1950's, PCCs have improved access to both poisons information and more sophisticated interventions in industrialised countries [24, 37]. The identification of hazardous pharmaceuticals and non-pharmaceuticals by PCCs have contributed to the implementation of preventive measures [80]. A benefit-cost analysis of PCCs in the United States estimated that PCCs reduced the number of patients (of all ages) who were medically treated for poisoning by around 24% and the number of hospitalisations by 12% [81]. Their role in the developing world is not yet clear.

Due to the paucity of health care resources in the developing world, measures to prevent poisoning in children are especially important, and are a challenge. Interventions that are most effective in changing high risk behaviour are a combination of legislation, educational programmes, information to parents on home hazard reduction, and free supply of safety equipment. As an example, the STOP (Safety Towards Our People) project was launched by the South African Department of Health to tackle the enormous problem of unintentional kerosene ingestion. This campaign focused on prevention through education using print and TV media, training people to teach accident prevention, and free distribution of child-resistant safety closures to kerosene users [82]. Another interventional trial demonstrated that the use of child-resistant containers caused a 47% drop in unintentional paraffin poisoning in children in South Africa [83].

The most effective strategic approach concerning pesticide poisoning will probably include short-term goals like restricting the access to the most hazardous poisons/pesticides and medium- and long-term objectives focusing on the substitution of pesticides with safe and cost-effective alternatives, possibly guided by the establishment of a minimum pesticide list [84], and development of future agricultural practices where pesticide usage is reduced to a minimum [85]. Adequate storage of pesticides is of utmost importance [86].

Approach to the poisoned child

Diagnosis, substance identification, risk and toxicity assessment

Appropriate initial decision-making in a poisoned child requires accurate identification of the substance (name, manufacturer,

Table 5 Examples of substances with late onset of symptoms

Intoxicants
Pharmaceutical
Diphenoxylate and atropine
Drugs taken concomitantly with anticholinergic agents
Enterosoluble medications
Hypoglycemic agents
Iron
Medications that increase the QT interval
Monoamine oxidase (MAO) inhibitor
Paracetamol/acetaminophen
Sustained release medication
Thyroid hormones (rarely give significant symptoms)
Non-pharmaceutical
Acetonitrile
Hydrofluoric acid (dermal exposure)
Ethylene glycol (especially if co-ingested with alcohol)
Methanol (especially if co-ingested with alcohol)

ingredients, quantities, concentrations, production date), the amount ingested (dosage per kilogram body weight), and the time interval since ingestion. It is important to make specific inquiries into the drugs prescribed to each family member, both currently and in the past, and the accessibility of household products [87]. In case of unexplained clinical symptoms, it is essential to consider co-ingestion of other substances, product contamination, a manufacturing or labelling error or product tampering. There are a number of drugs and household products that are commonly involved in toxic accidents in children (● **Table 1–4**).

A direct relationship between the amount consumed and the risk of adverse clinical effects exists for many toxic substances. However, often it is difficult to assess the exact dosage taken by a child, eg when the ingestion is unwitnessed or when a large amount of a liquid toxin has been in part ingested and in part spilled [88]. Since multiple patients are involved in up to 5% of poisonings [24], it is important to consider the involvement of other children and to assume that each individual has consumed the maximum amount (a “worst-case scenario”).

The route of exposure is important; besides the most common route of oral toxic exposure, parenteral, inhalation, ocular, or dermal contamination may occur. The time interval since ingestion provides important insight as to the risk for deterioration for many pharmaceuticals and non-pharmaceuticals. Intoxication is unlikely to develop if no clinical or toxic effects have occurred for those substances typically associated with rapid onset of poisoning; however, foreseeing clinical effects for poisons with delayed onset is difficult (● **Table 5**). Information is available for a variety of poisons on the time between ingestion and onset of symptoms and signs [89]. The time interval since ingestion is also important for determining whether gastric emptying techniques, activated charcoal, or specific antidotes should be employed [14–21].

In general, the toxic effects of a particular poison are comparable between children and adults. However, variations in biological processes related to absorption, distribution, metabolism and elimination (eg, immature enzyme function, larger liver weight/body weight ratio, immature renal function) have to be taken into consideration as well as differences in anatomy and physi-

Table 6 Examples of recognisable toxic syndromes (toxidromes) [87, 145]

Poison syndrome	Symptoms and signs	Possible toxins
Sympathomimetic syndrome	Hyperpyrexia, flushing, tachycardia, hypertension, mild mydriasis, sweating, tremor, autonomic storm, rhabdomyolysis, myocardial infarction, subarachnoid haemorrhage	Cough and decongestant preparations, amphetamines, cocaine, ecstasy
Anticholinergic activity	Disorientation, tremor, coma. Dry red, hot skin, dry mucus membranes, urinary retention, persistent tachycardia, marked mydriasis, fever	Tricyclic antidepressants, antiparkinsonian drugs, antihistamines, atropine and nightshade (<i>Datura stramonium</i> and <i>Solanum dulcamara</i>), antispasmodics, phenothiazines, mushroom poisoning (<i>Amanita</i> species)
Cholinergic syndrome (including increased parasympathetic nervous system activity)	Miosis, diarrhoea, urinary incontinence, sweating, excessive salivation, muscle weakness, fasciculation, paralysis	Organophosphate and carbamate insecticides, drugs for myasthenia gravis (eg pyridostigmine), physostigmine
Opiate syndrome	Coma, miosis, respiratory depression, hypotension, hyporeflexia	Opioids, clonidine, imidazolines in overdose
Neuroleptic malignant syndrome	Short episode of agitation and disorientation, stupor, tremor, akinetic rigidity, dystonia or chorea, hyporeflexia, increased muscular tone. Hyperpyrexia, tachypnoea, tachycardia, unstable blood pressure, rhabdomyolysis, disseminated intravascular coagulation	Phenothiazines, butyrophenones, atypical antipsychotics
Serotonergic syndrome	Altered mental status/cognitive and behavioural changes (confusion, disorientation, coma) Hyperpyrexia, Neuromuscular dysfunction (<i>hyperreflexia</i> , myoclonus, rhabdomyolysis), Renal failure, disseminated intravascular coagulation	Monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, lithium, lysergic acid diethylamide, dextromethorphan, meperidine, amphetamine congeners (eg, methylenedioxymethamphetamine), mirtazipine
Extrapyramidal dystonic syndrome	Dyskinesia, torticollis, opisthotonus, trismus	Neuroleptics, metoclopramide, dimenhydrinate

ology in children (eg, body composition: lower lipid content, greater water content, larger brain weight/body weight ratio, greater blood flow to CNS) [90]. Although many physical signs occur in poisoned children, a detailed physical examination may be helpful in identifying the toxic substance since various poisons produce distinct patterns of vital signs and clinically obvious end-organ symptoms, termed a toxidrome. • **Table 6** depicts examples of distinct toxidromes and their possible aetiology.

Often, it is difficult to decide if a child with suspected poisoning requires admission to a hospital. If possible, both the nature and the quantity of the intoxicant consumed by the child must be taken into consideration. As a rule, substances of moderate to severe toxicity cause signs and symptoms in most children within 2 to 4 hours post ingestion. However, various substances will result in toxic sequelae beyond this time frame. Delayed manifestations result from the formation of toxic metabolites or from delayed onset (• **Table 5**) [71]. In most cases, referral to a health care facility is not required for unintentional paediatric exposures to household products. The circumstances surrounding an exposure may have an important impact on the management of the affected child [91]. Important factors that must be taken into account include past medical history (including prior ingestions and injuries), family circumstances, housing, the provision of follow-up, and the ready availability of emergency care in case of sudden clinical deterioration [73].

A discrepancy between the history of ingestion given by the parents and the child's developmental stage raises the possibility of Munchausen syndrome by proxy as a severe form of child abuse [92].

The division of substances into three principal categories, i.e. no or low toxicity, intermediate toxicity, and high toxicity should guide the physician's approach and management to the intoxicated child. • **Table 1–4** provide data on common and very toxic

substances involved in paediatric poisoning, and the necessity for therapeutic interventions. It is advisable to contact a local PCC in case of unintentional paediatric intoxications, since they may be able to differentiate between substances unlikely to cause significant effects (non-toxic or minor effects) and significant toxic accidents in children. This will result in a more rationale approach to the child with unintentional poisoning – i.e., reducing undue treatment and prompt initiation of adequate therapies if indicated – which in turn will reduce health care expenditures and improve outcome [80, 81, 93].

General supportive care

Since approximately 97% of all unintentional paediatric exposures to poisonous substances in the developed world produce no or minor toxic effects, most cases do not require specific interventions. Treatment should focus on assessment of airway, breathing, and circulation, and then provision of supportive care as necessary.

Pulmonary and respiratory system

Signs and symptoms of increased respiratory effort may result from airway obstruction, direct pulmonary damage, pulmonary oedema, or toxin-induced metabolic acidosis. The most common factor contributing to death from poisoning is loss of airway-protective reflexes. Depression of the respiratory system may be caused by numerous agents (• **Table 1–3**). In general, pulse oximetry is indicated for any child with altered mental status or exposure to poisons that cause compromise of blood oxygen-carrying capacity. In order to quantify concentrations of carboxyhaemoglobin, methaemoglobin, and sulphaemoglobin haemoglobin co-oximetry may be indicated. In children with suspected chemical pneumonitis or aspiration pneumonia and respiratory distress, a chest radiograph may be warranted. The

need for oxygen and respiratory support depends on the clinical condition of the poisoned child with pulmonary compromise. The use of extracorporeal membrane oxygenation is very rarely needed.

Cardiovascular system

Numerous intoxicants are known to cause cardiovascular instability (● **Table 1–3**). The need for non-invasive and invasive haemodynamic monitoring largely depends on the clinical condition of the intoxicated child, which in turn relates to the amount and type of the substance ingested. Vigorous fluid resuscitation may be required due to profound volume depletion and hypovolaemic shock secondary to diuresis, vomiting, and diarrhoea. Administration of vasopressors may be needed in patients with hypotension unresponsive to adequate fluid replacement. An electrocardiogram is indicated for a child potentially poisoned with a substance capable of inducing cardiac dysrhythmia and any unresponsive patient [94]. A variety of common pharmaceutical and non pharmaceutical agents have a dysrhythmogenic propensity, especially if overdosed. However, the presence of any dysrhythmia in a poisoned child is not uniformly indicative of direct cardiac drug toxicity. The initial most important step in treatment is to provide adequate resuscitation and supportive therapy. Correction of underlying hypoxia or hypercarbia and disturbances of electrolytes or acid-base balance should be performed since they may serve as promoter of dysrhythmogenesis. Only if supportive measures fail to treat dysrhythmias and cardiovascular depression occurs should specific anti-dysrhythmic therapy be initiated.

Central nervous system (CNS)

Many pharmaceuticals and non-pharmaceuticals are capable of depressing or stimulating the CNS (● **Table 1–3**). CNS depression is common in severe intoxications and may cause airway compromise, respiratory failure, or aspiration. On the other hand, drug-induced stimulation can cause agitation or seizures in children. Other neurological symptoms related to childhood poisonings include disorientation, emotional disturbance, autonomic dysfunction, gait disorders, and dystonic movement disorders [95]. The neurologic manifestations in children may be abrupt, transient, or fluctuate with alternating excitation and depression [71]. Securing the patency of airways is crucial in patients with CNS depression. Any patient with altered mental status or the potential to develop hypoglycaemia from poisoning must have a bedside glucose assessment. Benzodiazepines are first line drugs in the treatment of convulsions.

Oesophageal burns

The diagnostic and therapeutic approach to the child with caustic ingestion is still under debate [96–102]. While the overall outcome for most children is good in the developed world, caustic ingestions remain a significant source of morbidity and mortality in developing countries [11].

In European countries in the early 1990's, superficial oesophageal burns occurred in approximately 20% of caustic ingestions, deeper burns in 5%, and stricture formation in 1–3% [103]. The presence or absence of early symptoms and signs does not reliably predict the severity or frequency of oesophageal injury in children; [104] however, persistent hypersalivation and dysphagia beyond 12–24 hours post ingestion are associated with oesophageal scar formation [103]. Respiratory distress is indicative of involvement of the larynx [105]. In case of accidental

involvement of the eyes, eye irrigation using Morgan's lenses until the eye pH is back to normal may be mandatory. The knowledge of the chemical structure of the corrosive agent (e.g. acid, base, or quaternary ammonium compound), and the amount ingested and its concentration is important for individual risk assessment.

The immediate oral administration of fluids may be considered in children with caustic ingestions, although no clear benefit has been demonstrated; however, attempts at neutralisation of the corrosives, or gastric decontamination are discouraged [105]. The need for early endoscopy (within 12–24h post ingestion) remains an issue of controversy. The indication for endoscopy should be made on clinical grounds – ie, in children with a strongly suspected ingestion, especially that of a strong alkali, oral burns, and symptoms – while bearing in mind that most children will have no or only minor ill effects after an ingestion. Despite the ongoing controversy and increasing evidence that steroid treatment does not improve long term outcome [96], steroids are still used by many clinicians in patients with severe non perforating mucosal damage (second-degree burns that are extensive or circumferential) [107, 108]. The role of antibiotics in oesophageal burns is still under debate, but antibiotics are generally indicated/given if perforation occurs and are often used together with steroids for severe mucosal injury.

Toxicology testing

Although comprehensive toxicology testing in children with suspected ingestion of an unknown agent may be useful in rare instances (eg, suspected child abuse as forensic evidence) [108], the routine use of such testing in children is costly and does not alter the medical management of most poisoned children [94]. Since the results of toxicological testing may have important medico-legal and social consequences, samples (urine, blood) are obtained early and stored for future use if indicated. When a specimen will likely be involved in a future medico-legal matter, chain-of-custody procedures may be warranted and the assistance of qualified laboratory staff should be sought. However, chain-of-custody documentation is not necessary for clinical toxicology purposes [109]. For a limited number of poisons the use of precise quantitative assays to assess drug levels is the most useful type of assay since the initiation of antidote administration, haemodialysis, haemoperfusion, or chelation therapy is often dependent on the data provided by such assays. Examples include paracetamol/acetaminophen, salicylates, theophylline, iron, lithium, methanol, ethylene glycol, and lead.

Gastrointestinal decontamination



Gastric lavage, Ipecac syrup, Single dose activated charcoal, multiple doses of activated charcoal, Whole bowel irrigation

Since preventing the absorption of toxic substances has been a core principle in clinical toxicology, gastrointestinal decontamination procedures have been widely promoted in clinical practice and remained the standard of care for several decades. The recent focus on evidence-based clinical approaches has challenged this dogma because of paucity of outcome data [110, 111]. It is now considered that gastrointestinal decontamination techniques should be used in only a selected number of cases and only once the child has been resuscitated and stabilised.

Based on experimental and clinical studies in adults, gastric lavage may be beneficial to the child who presents with a recent ingestion of a very toxic substance [15]. For gastric lavage to be performed properly, the child should be placed in a left lateral Trendelenburg position in order to minimise the propulsion of the gastric contents into the duodenum and reduce the risk of aspiration. However, gastric lavage carries risks and over the last years has been gradually replaced in hospitals by activated charcoal (see below).

Ipecac syrup has been used for decades to promote vomiting in the setting of early acute oral poisoning, often at home. In contrary to gastric lavage, ipecac can easily be administered by parents or caregivers. However, ipecac has been relegated to a less prominent role in gastrointestinal decontamination. It is now almost never used in hospitals and there is debate about whether it should be recommended for treatment in the home. It may be indicated in children who have ingested a potentially toxic amount of a poison if there will be a delay of greater than 1 h before the child will arrive at an emergency medical facility and if ipecac syrup can be administered within 60 min of the ingestion [16,20]. Also, one should take into consideration that the use of ipecac syrup may delay more specific and effective treatment that might be provided at a hospital (eg, activated charcoal, oral antidotes). In accordance with the position paper by the EAPCCT/AACT, the American Academy of Pediatrics – a long-standing advocate of the use of ipecac – issued a guideline in 2003 that ipecac should no longer be used routinely in poisoned children at home [112].

Single dose activated charcoal has emerged as the mainstay of gastrointestinal decontamination in poisoned patients over the last few decades [113]. Activated charcoal may be considered if a child has ingested a potentially toxic amount of a poison – up to one hour after ingestion – which is known to be adsorbed by charcoal [17]. Although volunteer studies in adults have not demonstrated substantial decreased drug absorption after 60 minutes, potential benefit after one hour cannot be excluded especially for substances with a high potential for toxicity (► **Table 1–4**). The oral dosage regimen recommended is 1.0 g/kg body weight or the dosage can be related to the estimated amount of toxin (10:1 ratio).

The main contraindications to the use of the above techniques include loss of airway protective reflexes, ingestion of a corrosive such as a strong acid or alkali, or ingestion of hydrocarbon with high aspiration potential.

The rationale for multiple doses of activated charcoal (MDAC) is based on enhancing both preabsorptive and postabsorptive elimination. The use of MDAC should be considered only if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, or theophylline [18]. Because of the propensity of laxatives to cause fluid and electrolyte derangement, in particular in young children, cathartics should not be co-administered to this age cohort [19]. After the initial administration of 1 gram/kg body weight of activated charcoal, it should be given at a rate of 0.25 g/kg/h. Its administration should be continued until the child's condition and laboratory parameters, including plasma drug concentrations are improving. There are three absolute contraindications to this procedure: an unprotected airway, intestinal obstruction, and a gastrointestinal tract not anatomically intact; relative contraindications include decreased peristalsis such as occurs following overdoses of drugs with opioid or anticholinergic properties.

Whole bowel irrigation (WBI) with polyethylene glycol balanced electrolyte solution has greatest utility for potentially toxic ingestions of sustained-release or enteric-coated drugs in patients presenting more than two hours after ingestion [21]. Furthermore, WBI can also be considered for patients who have ingested substantial amounts of iron because of the high morbidity and mortality of this poisoning and a lack of other options for gastrointestinal decontamination. Its usefulness is limited because it is a labour intensive procedure rarely adequately completed in the busy emergency department or intensive care unit.

WBI is best administered through a nasogastric tube. A recommended dosing schedule for WBI is: children 9 months to 6 years: 0.5 l/h, children 6–12 years: 1 l/h, and adolescents and adults: 1.5–2 l/h. It is recommended that WBI should be continued until the rectal effluent is clear. However, treatment may be extended based on corroborative evidence of continued presence of toxins in the gastrointestinal tract. Contraindications to WBI include bowel perforation, bowel obstruction, clinically significant gastrointestinal haemorrhage, ileus, unprotected or compromised airway, haemodynamic instability, and intractable vomiting.

The majority of studies showing benefit of these gastric decontamination techniques have been of experimental human overdoses in which sub-toxic amounts of poison are used. There are few data suggesting any benefit from human ingestions of toxic quantities of poison.

Enhanced elimination

▼ Urinary alkalization and extracorporeal elimination techniques

Urinary alkalization (urine with a pH ≥ 7.5) enhances the excretion of weakly acidic drugs by increasing the proportion of ionised drug in the tubule, thus preventing its reabsorption. The evidence for clinical utility of urine alkalization is limited to a few substances that undergo significantly enhanced excretion. It should be considered as first line treatment for children with moderately severe salicylate poisoning who do not meet the criteria for haemodialysis [114]. It may also be considered with high urine flow for severe chlorophenoxy herbicide poisonings [114]. For phenobarbital poisoning, urinary alkalization is less effective than MDAC, but could be considered if the later is contraindicated [115]. On the contrary, urinary acidification for poisoning with weakly alkaline drugs (amphetamine, strychnine, quinine, quinidine, and phencyclidine), on the contrary, is no longer recommended.

Extracorporeal elimination techniques (dialysis, haemoperfusion, and haemofiltration) are rarely employed in the management of children with unintentional poisoning. They may be indicated in severely poisoned children when conventional intensive supportive care fails, when the normal route of toxin elimination is impeded, and when the amount of toxin absorbed or its high concentration in serum will likely result in substantive injury [115]. While numerous case reports have been published in the medical literature, the efficacy of such techniques is very difficult to assess in prospective randomised clinical trials. It is generally accepted that extracorporeal elimination techniques are of benefit if endogenous clearance is increased by 30% or more [115]. The effectiveness of dialysis is dependent on the toxin having a high water solubility, a low volume of distri-

bution (<1–2l/kg), low molecular weight (<500Da), and low plasma protein binding. Commonly dialysed substances include lithium, salicylates, methanol, and ethylene glycol. Other substances that are exceptionally dialysed include aminoglycosides, bromates, diethylene glycol, ethanol, isopropyl alcohol, metformin, methotrexate, procainamide, and thallium. Haemoperfusion involves the passage of blood through a cartridge containing a very large surface area of sorbent, either activated charcoal or carbon. Such toxins must have a high affinity for the adsorbent and a fast rate of equilibrium from peripheral tissues to the blood. In contrast to haemodialysis, haemoperfusion is not limited by plasma protein binding [116]. A substance for which haemoperfusion is used is theophylline. Other substances for which haemoperfusion is used include atenolol, carbamazepine, disopyramide, meprobamate, phenobarbital, phenytoin, paraquat, valproic acid and sotalol. Haemofiltration has the potential to remove compounds with a high molecular weight (>500–10–40Da; heparin, insulin, vancomycin myoglobin) [117].

Antidotal therapy

The use of antidotes is the mainstay of therapy in only a few poisonings (examples are listed in **Table 1–3**). The benefit of an antidote is based on its mechanism of action: some displace poisons from their site of action (eg, compete at a receptor binding sites), while others prevent the production of toxic metabolites (eg, blocking of enzymes), or by restoring function (eg, restoration of enzyme activity, detoxification of toxic metabolites). Several antidotes enhance the excretion of a detoxification complex [71]. The introduction of fomepizole as an antidote for ethylene glycol and methanol poisoning in 1998 constitutes a recent success in medical toxicology [118].

Conclusions and implications for the future

Unintentional childhood poisoning is a well-recognised and somewhat preventable problem that affects large numbers of children worldwide. Unintentional intoxication has a significant impact on the child, the families, and on the utilisation of health-care resources. In the developed world, advances have been made in the prevention and treatment of unintentional poisoning in children, thereby significantly cutting down on the number of deaths.

In the future, the effectiveness of packaging requirements for non-pharmaceutical substances commonly used in households that are also covered by child-resistant packaging requirements should be assessed. It will be important to introduce new regulatory measures covering emerging substances like dietary supplements, herbal preparations, and traditional remedies. Social disparity issues must be addressed and included in prevention programmes since the incidence of poisoning in children is related to social and economic status. In developing countries, the implementation of preventive and educational programmes will be of pivotal importance in order to reduce the number of severe intoxications, hospital admissions, and fatalities in children.

In the future clinical toxicology should be directed towards the further development of clinical and basic science research, the establishing of regional poison treatment centres, and the train-

ing of physicians committed to clinical toxicology. It will be important to disseminate current knowledge on clinical toxicology in the medical community, and to provide up-to-date continuing medical education for the primary care physician. PCCs will play a decisive role in the growing field of toxic- and pharmacovigilance by generating data on future trends in (childhood) poisoning. In order to provide more sophisticated data on the epidemiology of unintentional paediatric poisoning, it will be crucial to remove barriers to reporting to PCCs, to harmonise the terminology and the reporting of poison incidents, to distinguish potential exposures from real intoxications, and to integrate PCC databases with those already in existence. Closer co-operation and data exchange between PCCs throughout the world can be anticipated as health care providers will be confronted with a plethora of toxic substances from foreign countries secondary to substance trafficking, migration and increased individual mobility.

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