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The History, Importance, and Challenges of Pediatric Toxicology (A Review Article)

Anahita Alizadeh [1], * Nafiseh Pourbadakhshan [2]

[1] Department of Clinical Toxicology, MTRC (Medical Toxicology Research Center), Mashhad University of Medical Sciences, Mashhad, Iran.

[2] Clinical Research Development Unit of Akbar Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

Pediatric clinical toxicology represents a dynamic and evolving field that merges pediatric medicine, pharmacology, and emergency care. Globally, pediatric poisonings remain among the top drivers of emergency department visits, hospital admissions, and avoidable morbidity. This discipline addresses diagnostic, therapeutic, and preventive strategies for poisonings in children, reflecting the unique physiological and pharmacokinetic profiles that differentiate them from adults. The present review consolidates the historical milestones, clinical advancements, educational strategies, and credible resources. It also addresses the challenges and obstacles to the advancement of this field, the specific complexities in this scientific branch, and offers suggestions for paying more attention to the knowledge of pediatric toxicology and helping to advance this branch of science.

Key Words: Clinical toxicology, History, Knowledge, Morbidity, Pediatric.

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Corresponding Author:

Nafiseh Pourbadakhshan; Clinical Research Development Unit of Akbar Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email : pourbadakhshann@mums.ac.ir

1- INTRODUCTION

Poisonings are one of the leading preventable causes of illness and death among children worldwide. Exposures span a broad spectrum from toddlers' accidental ingestion of household chemicals, medications, and illicit substances to adolescents' intentional overdoses or occupational chemical exposures (1). Globally, pediatric poisonings remain among the top drivers of emergency department visits, hospital admissions, and avoidable morbidity (2). Scenarios range from the ingestion of household cleaners in young children to deliberate exposures in teenagers (3,4). Of the more than 2 million human poisoning cases reported annually to the American Association of Poison Control Centers (AAPCC) National Poison Data System, roughly half involve children (5).

Pediatric toxicology presents distinct challenges. The World Health Organization's 2025 report estimates 1.2 million unintentional poisonings each year in children under five, with 40% attributed to household medications. Figures that underscore both the physiological vulnerability of young patients and persistent gaps in foundational and clinical expertise (6,7). Despite rapid advances in technology, the proliferation of new chemicals and pharmaceuticals, and the expanding digital landscape that increases risk exposure for youth, pediatric toxicology remains relatively underemphasized (8). Concurrently, worsening social stressors and rising rates of substance misuse and suicide attempts among children and adolescents demand focused attention to the field's evolving challenges (9).

Children's inherent susceptibility reflects behavioral and biological factors, including exploratory tendencies, greater exposure per unit body weight, and rapidly changing physiology. Key pediatric–adult differences, such as metabolic enzyme activity, organ perfusion patterns, and total body water, directly influence toxicokinetic and toxicodynamic (10). Accordingly, pediatric toxicology requires specialized diagnostic pathways, age-adjusted antidote dosing, and tailored treatments that often diverge from adult protocols. Optimal care hinges on swift recognition, principle-based supportive management, and prompt access to expert consultation (10).

Clinical presentations in children are frequently nonspecific, including altered mental status, hypotension, metabolic acidosis, dysglycemia, or seizure (11). These signs can mimic metabolic, infectious, neurologic, or diabetic ketoacidosis etiologies. Therefore, pediatricians thoroughly trained in both general pediatrics and toxicology, including pediatric dosing, fluid therapy, and differential diagnosis, are essential to accurately identify and manage poisoning among competing diagnoses (10, 12).

This article was prepared as a narrative review of the history, importance, clinical management, educational challenges, and available resources in pediatric toxicology. Relevant literature was identified through searches of major biomedical databases such as PubMed/MEDLINE, Scopus, and Web of Science, supplemented by additional sources from reference lists of key articles, textbooks, and recognized organizations including the World Health Organization and poison control networks. Search terms included combinations of "pediatric toxicology," "childhood poisoning," "poison control centers," "clinical management," "pediatric pharmacokinetics," "education," and "prevention." Priority was given to peer-reviewed studies, clinical guidelines, and authoritative reference sources. Because this was a narrative review, no formal meta-analysis was performed.

2-1. Historical Evolution of Pediatric Toxicology

The development of toxicology has been a long and winding road. In ancient times, poisons were used mysteriously by magicians and kings for purposes of terror or entertainment, but from the 18th century, with the pioneering work of people such as Felice Fontana (who published his classic work on European snake venom in 1781) and Matteo Orfila (the father of modern toxicology with his Traite de poisson in 1814), the field gradually moved from mythology to an empirical science based on careful observation. In the 20th century, following World War II, poison control centers emerged, and in 1974, medical toxicology was recognized as a distinct specialty. This development culminated in the founding of the American College of Medical Toxicology (ACMT) in 1994 and the establishment of fellowship programs under the ACGME (13,14). Recognition of poisoning as a distinct medical emergency began to coalesce in the mid-20th century, shifting from purely symptomatic management to proactive identification and specialized treatment protocols (13,15). Despite all the differences between pediatric and adult poisonings, pediatric clinical toxicology has not yet been defined as an independent subspecialty in many countries.

2-2. Physiological and Pharmacokinetic Characteristics in Pediatrics

Understanding how children handle xenobiotics differently from adults is central to pediatric toxicology, as age-dependent physiology reshapes the onset, intensity, and duration of toxic effects (16-18). In absorption, neonates and young infants exhibit enhanced gastrointestinal uptake of many agents due to higher gastric pH, which reduces the ionization of weak acids, and a relatively larger intestinal mucosal surface area. Dermal absorption is likewise amplified by a higher surface–area–to–weight ratio and a thinner stratum corneum (19). In distribution, infants' greater total body water expands the volume of distribution for hydrophilic compounds, while limited adipose stores reduce the sequestration of lipophilic drugs. Combined with immature plasma protein binding, especially reduced albumin affinity. These features increase the free, pharmacologically active fraction (15-18). Metabolism reflects hepatic maturation: Phase I oxidative capacity via CYP isoforms (e.g., CYP2D6, CYP3A4) often lags for months to years, prolonging xenobiotic half-lives and heightening toxicity risk from therapeutic accumulation or overdose; Phase II conjugation pathways mature heterogeneously, with delayed glucuronidation predisposing to buildup of toxic metabolites for substrates such as acetaminophen and morphine (17,20). Developmental enzymes involved in human metabolism were classified into three categories: 1) those that are expressed during all or part of the embryonic period, but are silenced or expressed at low levels in the 1–2 years after birth; 2) those that are expressed at relatively constant levels during fetal development, but increase somewhat after birth; and 3) those whose onset of expression can occur in the third trimester, but a significant increase is observed in the first 1–2 years after birth (20-21).

Excretion is constrained in early life because glomerular filtration and tubular function are reduced, with GFR typically reaching adult levels only by 6–12 months. Consequently, renally cleared toxins and metabolites demand age-adjusted dosing and monitoring. Collectively, these physiological distinctions justify specialized pediatric toxicology protocols, which are grounded in age-specific pharmacokinetic modeling (22).

Today, given the advancement of science and technology, the creation of new chemicals and drugs, the evolutionary process of humans, and especially the differences between children and

adolescents, and the risk of various poisonings for children and adolescents, it is necessary to pay attention to and promote the field of pediatric toxicology from multiple aspects. Some of these aspects are listed below.

2-3. Global Burden and Epidemiology of Pediatric Poisoning

Poisoning in children is a persistent and uneven global threat, with patterns of exposure shifting alongside economic development yet consistently impacting survival in early childhood. As summarized by the World Health Organization and allied surveillance networks, poisoning remains a leading cause of unintentional death among children under five, and national reporting systems document millions of pediatric exposures each year, a substantial proportion of which progress to moderate or severe illness requiring advanced critical care. Across settings, the epidemiology diverges: in high income countries, pharmaceuticals dominate acetaminophen, opioids, benzodiazepines, stimulants, iron supplements, and concentrated household products such as laundry detergent pods driven by toddler exploratory ingestion, adolescent access to recreational or prescription drugs, and polypharmacy in caregivers; typical sequelae include acute liver failure, central nervous system depression, and metabolic derangements In low and middle income countries, pesticides (notably organophosphates and carbamates), hydrocarbons like kerosene and gasoline, traditional remedies, and button batteries are more common, with risks amplified by unclear labeling, language barriers, unsafe storage (e.g., fuels in beverage containers), and limited access to poison centers and advanced care—often culminating in respiratory failure, seizures, corrosive injury, and diffuse neurotoxicity. Strengthened poison control infrastructure 24/7 hotlines, interoperable international data sharing, and digitized toxicology registries such as the NPDS, has measurably reduced mortality by enabling rapid triage, precise exposure identification, and timely, protocol driven management; moreover, advanced analytics of these datasets guide targeted public health responses to emerging threats, including synthetic cannabinoids and nicotine rich e liquids (23-26).

2-4. Origins and Evolution of Poison Control Centers

Poison control centers (PCCs) transformed clinical toxicology by unifying expertise, data, and decision support into an accessible public service. The modern era began in 1953 with the first centralized PCC in Chicago, Illinois—an initiative often attributed to pioneering clinicians who recognized the need for rapid, coordinated guidance. From the outset, centers standardized responses by offering a single point of expert consultation, systematized exposure data collection for surveillance, and real-time triage advice, which reduced unnecessary emergency visits and expedited care when escalation was warranted. As poison control centers expanded across the United States, the AAPCC emerged to harmonize quality and data standards, laying the groundwork for national interoperability and benchmarking.

Technological integration accelerated this evolution. Beginning in the 1970s, proprietary toxicology databases, such as POISINDEX, aggregated product compositions and evidence-based treatment protocols, enabling consultants to deliver product-specific recommendations rapidly and consistently. Parallel developments across Western Europe—particularly in the United Kingdom, France, and Sweden saw the establishment of specialized toxicology units within academic medical centers and regional trauma networks, often spanning both adult and pediatric care to ensure

continuity and depth of expertise. These institutional frameworks amplified capacity for complex case management, training, and research.

Crucially, the surveillance insights generated by PCC networks fueled preventive public health action. Robust datasets underpinned regulations mandating child-resistant packaging for medicines and household chemicals, reforms in prescription refill packaging, and mass media campaigns addressing high-risk ingestions such as iron tablets and petroleum distillates (Together, these measures measurably reduced pediatric exposures and severity. By linking 24/7 clinical consultations, curated knowledge bases, and population-level surveillance, PCCs helped shift pediatric toxicology from anecdote-driven practice to an evidence-based discipline with standardized protocols and continuous quality improvement (27-32).

2-5. Modern Clinical Management in Pediatric Toxicology

Modern pediatric toxicology management relies on a structured, rapid sequence that prioritizes stabilization before any decontamination or antidotal therapy, applying an age-appropriate ABC approach (Airway, Breathing, Circulation) tailored to the suspected toxin and clinical context. Initial actions focus on immediate hemodynamic, respiratory, and neurologic assessment—addressing hypoxia, hypotension, hypoglycemia, seizures, and temperature abnormalities without delay. Core supportive steps include supplemental oxygen, securing reliable intravenous or intraosseous access (often two lines when feasible, particularly with corrosive or cytotoxic exposures), continuous cardiac and pulse oximetry monitoring, frequent neurologic checks, bedside glucose testing, and serial blood gases as indicated (33–36).

Decontamination is considered only when it will not compromise stabilization and when timing and toxin characteristics favor benefit: single-dose activated charcoal at 1 g/kg (max 25–50 g) within about one hour for charcoal-adsorbable agents, avoiding use in patients with depressed mental status, seizures, or caustic ingestion unless the airway is protected. Gastric lavage and whole-bowel irrigation are seldom required. They are reserved for massive, life-threatening ingestions that are poorly adsorbed by charcoal, such as iron, lithium, or specific sustained-release formulations, ideally after consultation with toxicology (33–36). Antidotes are deployed in a protocol-driven, toxin-specific manner: N-acetylcysteine for acetaminophen toxicity (with weight-based IV regimens guided by serum levels and timing on the Rumack–Matthew nomogram); hydroxocobalamin as the preferred pediatric therapy for cyanide poisoning; carefully titrated naloxone for opioid toxicity, especially cautious in neonates to mitigate withdrawal; and fomepizole or, where appropriate resources dictate, ethanol for methanol or ethylene glycol poisoning (34–36). When indicated, elimination can be enhanced to shorten toxin exposure: urinary alkalinization for salicylates with a target serum bicarbonate of roughly 25–30 meq/L while monitoring potassium and volume status, and extracorporeal therapies (hemodialysis or hemoperfusion) for select poisons with favorable dialyzability profiles, such as lithium, methanol, and severe salicylate toxicity unresponsive to conservative measures (33–36). Throughout, rapid recognition, meticulous supportive care, consultation with poison control or a medical toxicologist, and iterative reassessment remain the cornerstones of optimizing outcomes (33-37).

2-6. Educational Challenges and Advancement Needs in Pediatric Toxicology Training

Medical toxicology fellowships, requiring a 2-year program post-residency in specialties like pediatrics and managed through the National Residency Matching Program's Emergency Medicine Match, remain accessible yet underutilized by pediatricians—despite 75% of the 28 U.S. programs (as of 2021) accepting their applications, only 36% have trained one in the past 5 years, with applicants citing persistent barriers (9,37). Pediatric clinical toxicology receives pedagogical neglect in medical schools, appearing merely as brief segments in general pharmacology or emergency medicine rather than standalone courses, while deficiencies persist in up-to-date CME, refresher training on emerging toxins and trends, and simulation for high-acuity events like caustic burns or salicylate-induced multi-system failure, leaving general practitioners and pediatricians ill-equipped for complex cases (9,38). Key curricular gaps include absent dedicated modules integrating chemistry, physiology, and management; scarce, geographically limited hands-on CME for novel substances; and underused high-fidelity simulations. Strategic remedies encompass simulation-based modules for rapid diagnosis, toxin-related seizures, and antidote use; mandatory interdisciplinary CME workshops uniting pediatricians, emergency physicians, intensivists, toxicologists, and pharmacists; vetted bedside checklists for the top 10 pediatric ingestions; and expanded, funded Pediatric Clinical Toxicology fellowships to build expertise pipelines, despite limited resources, these steps promise competence across the pediatric workforce.

2-7. Strategic Remedies for Educational Enhancement

To bridge gaps in pediatric toxicology training and ensure competence across the workforce, key strategies include implementing standardized, scenario-based simulation modules targeting critical decision points like rapid differential diagnosis in altered children, toxin-associated seizure management, and stress-induced antidote administration; establishing required interdisciplinary CME workshops mandating participation from pediatricians, emergency physicians, critical care intensivists, clinical toxicologists, and pharmacists to foster shared protocol understanding; developing, vetting, and disseminating concise pocket-sized algorithms (physical and digital) for the 10 most common pediatric ingestions, enabling bedside access even before poison control center consultation; and aggressively promoting and funding accredited Pediatric Clinical Toxicology fellowships at major academic centers to build a pipeline of board-certified experts for research and teaching—ultimately providing complete, specialized toxicology training for pediatricians. Although resources remain limited, these measures, offer pathways for familiarization and advancement. Also, training pediatricians in pediatric clinical toxicology and establishing a subspecialty in pediatric clinical toxicology can be very useful in this field.

2-8. Global Resources in Pediatric Toxicology

Reliable, rapidly accessible, validated reference systems are the bedrock of effective toxicological management in any setting.

1. Poisindex (Lexicomp/Elsevier): Remains the gold standard for detailed information on commercial products, including specific ingredients, exposure pathways, management strategies, and anticipated toxicological syndromes. Its integration into major Electronic Health Records (EHRs) streamlines data capture (39, 40).

***2. TOXNET (NIH/NLM*)**: Although largely transitioned into other databases (like PubChem and other NLM resources), the historical repository of toxicology and environmental hazard data remains a crucial academic reference point (41).

***3. World Health Organization (1) (WHO) Poisoning Guidelines*:** Provides the framework for national strategies, especially crucial for LMICs lacking proprietary database access, offering standardized treatment recommendations for globally prevalent poisons (e.g., organophosphates)

Core Textbooks and Handbooks:

1- Essential foundational texts include Clinical Toxicology of Commercial Products (Dart et al.).
2- Handbook of Pediatric Toxicology (Nelson et al.), which provides a deep scientific context.
3- Pediatric Toxicology. Erickson TB et al. 2005.
4- Poisoning in children, Singh UK et al 2013, 4th ed.
5- EAPCCT (European Association of Poisons Centers and Clinical Toxicologists) Portal: A vital source for contemporary European consensus statements, clinical toxicology research, and best practice guidelines developed through multinational collaborative studies.

Proposal

a. Establishing an international online core to provide daily information on the symptoms and treatments of all types of poisoning in children, so that all member countries can receive information and provide advice on poisoning in children at all times of the day and night. It should also have regional and local branches that provide users with sufficient information on specific poisonings and bites in each region.

b. Establishing a subspecialty in pediatric toxicology in medical schools, especially in developing countries. It is also essential for the field of pediatric toxicology to receive financial support from governments.

c. Launching one or more magazines on the topic of pediatric and adolescent toxicology.

d. To unify global preventive efforts, reduce disparities in care, and raise sustained public and professional awareness, we formally propose the establishment of an International Day with the title of Pediatric Poisoning Prevention Day (PPPD).

The date of this day can be chosen with the help and advice of the World Health Organization.

This annual observance would serve as a coordinated, worldwide advocacy platform:

- ***Public Awareness Campaign:*** Focusing on high-impact, culturally relevant messaging regarding safe medication storage (e.g., "Lock It Up, Put It Away"), the dangers of household chemicals, and immediate access numbers for local emergency services or PCCs.

- ***Designing computer games*** to teach the principles of poisoning prevention in schools, kindergartens, and child care centers

- ***Developing an action plan*** and investigating and monitoring poisoning in children and adolescents for each geographical area, especially in developing and selected countries

- ***Professional Empowerment:*** Organizing synchronized global CME sessions, research webinars focusing on emerging toxins, and joint simulation exercises led by participating national toxicology societies.

- ***Infrastructure Advocacy:*** Championing investment in robust 24/7 toxicology hotlines, digital data-sharing platforms, and the recruitment and training of toxicology specialists, especially in underserved regions.

3- CONCLUSION

Pediatric toxicology faces urgent global challenges due to children's unique physiological vulnerabilities (heightened dermal absorption, immature metabolism) and expanding exposure to household toxins, pharmaceuticals, and illicit substances. While poison control centers and evidence-based antidotes have reduced mortality, significant disparities persist. Modern clinical strategies—targeted decontamination, precision antidotes, and enhanced elimination techniques—require wider global adaptation. Crucially, medical education must bridge training gaps through the use of simulations, interdisciplinary collaboration, and specialized fellowships. These measures aim to unify prevention efforts, promote safe-storage education, and reduce the WHO-reported 1.2 million annual unintentional pediatric poisonings through infrastructure investment and public advocacy.

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The authors have no competing interests to disclose.

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