

The Toxicology Investigators Consortium Case Registry—the 2013 Experience

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of the Toxicology Investigators Consortium

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Abstract The Toxicology Investigators Consortium (Toxic) Case Registry was established in 2010 by the American College of Medical Toxicology. The Registry includes all medical toxicology consultations performed at participating sites. This report summarizes the Registry data for 2013. A query of the Toxic Registry was carried out for the dates of January 1 through December 31, 2013. Specific data reviewed for analysis included demographics (age, gender), source of consultation, reasons for consultation, agents involved in toxicological exposures, signs, symptoms and clinical findings, and treatment. A total of 8,598 cases were entered into the Registry in 2013. Females accounted for 49.2 % of cases, males for 47.7 %, and gender was not reported in 3.1 %. The majority of patients (63.4 %) were adults between the ages of 19 and 65 years. There were 93 fatalities (1.1 %). Most referrals for medical toxicology consultation originated from the emergency department (59.7 %) or inpatient services (16.7 %). Exposures to pharmaceutical products (intentional and unintentional) made up 50.0 % of cases. Illicit drug abuse (8.0 %) and adverse drug reactions (ADRs) (4.8 %) were the next most frequent reasons

for consultation. Similar to past years, nonopioid analgesics, sedative-hypnotics, and opioids were the most commonly encountered agents. Symptoms or clinical findings were documented in 71.1 % of patients. Of all cases, 54.6 % required some form of medical treatment (antidotes, antivenom, chelation, specific types of supportive care). This report serves as a comprehensive survey of medical toxicology practice within participating institutions. Prior trends continued to apply this year and indicate analgesic (opioid and nonopioid), sedative-hypnotic/muscle relaxant agents, illicit drug use, and ADRs continue to be major toxicological problems. Cases requiring medical toxicology consultation in 2013 predominantly involved pharmaceuticals and illicit drugs. Reasons for these drug exposures were diverse and included intentional overdose, unintentional exposure, withdrawal syndromes, and ADRs. Nonopioid analgesics, sedative-hypnotic agents, and opioids remained the most frequently encountered agent classes. While over half of cases required some form of medical treatment, fatalities were uncommon.

Data contained in this manuscript has not been previously presented in any form.

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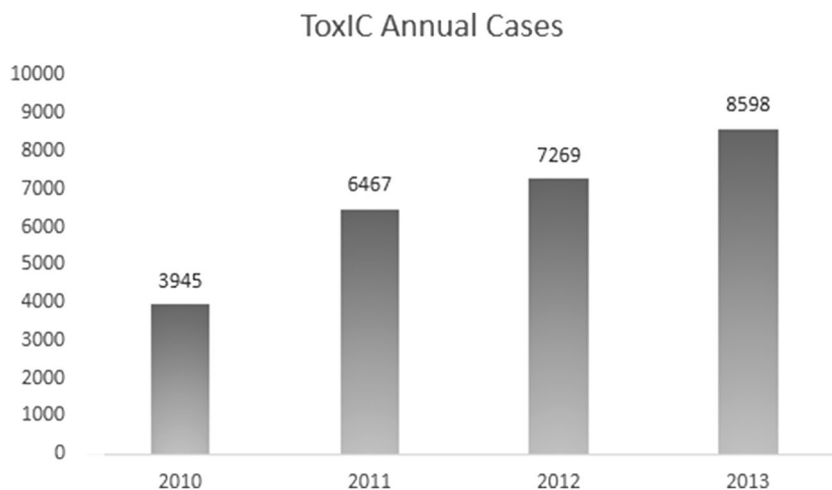
Introduction

In 2010, the Toxicology Investigators Consortium (Toxic) of the American College of Medical Toxicology (ACMT) created a registry intended to provide a tool for clinical toxicology research and toxico-surveillance [1]. Unlike other poisoning databases, the Toxic Registry prospectively collects information on patients seen in consultation by medical toxicologists as hospital inpatients or in outpatient clinics. These toxicologists enter the patient data directly into the Registry. Since its inception in 2010 with four initial participating institutions, the Toxic Registry has expanded to include investigators at

Table 1 Participating institutions

Arizona	Minnesota	Pennsylvania
Phoenix	St. Paul	Harrisburg
Banner Good Samaritan Medical Center	Regions Hospital	Harrisburg Hospital
Phoenix Children's Hospital		Philadelphia
	Missouri	Einstein Medical Center
California	Kansas City	Hahnemann University Hospital
Fresno	Children's Mercy Hospital & Clinics	St. Christopher's Hospital for Children
UCSF Fresno Medical Center	St. Louis	Mercy Fitzgerald Hospital
Los Angeles	Barnes Jewish Hospital	Mercy Philadelphia Hospital
USC Verdugo Hills Hospital		Einstein Medical Center Montgomery
San Francisco	Nebraska	Einstein Medical Center Elkins Park
San Francisco General Hospital	Omaha	Pittsburgh
	University of Nebraska Medical Center	UPMC Presbyterian/Shadyside
Colorado		UPMC Children's Hospital of Pittsburgh
Denver	New Jersey	UPMC Magee Women's Hospital
Denver Health Medical Center	Morristown	
University of Colorado Hospital	Morristown Medical Center	Texas
Porter and Littleton Adventist Hospital	New Brunswick	Dallas
Children's Hospital Colorado	Robert Wood Johnson University Hospital	Parkland Memorial Hospital
Swedish Medical Center	Newark	Children's Medical Center of Dallas
	University Hospital	UT Southwestern Medical Center
Connecticut	Newark Beth Israel Medical Center	Houston
Hartford		Ben Taub General Hospital
Hartford Hospital	New York	Texas Children's Hospital
CT Children's Medical Center	Manhasset	San Antonio
	North Shore University Hospital	San Antonio Military Medical Center
Indiana	New Hyde Park	
Indianapolis	Long Island Jewish Medical Center	Utah
IU Health Methodist Hospital	New York	Salt Lake City
Wishard Memorial Hospital	Mount Sinai Hospital	Primary Children's Hospital
Riley Hospital for Children	Staten Island University Hospital	University Hospital
IU Health University Hospital	Bellevue Hospital Center	
	NYU Langone Medical Center	Virginia
Illinois	Elmhurst Medical Center	Charlottesville
Chicago	Rochester	University of Virginia Health Systems
John H. Stroger, Jr. Hospital of Cook County	Strong Memorial Hospital	Richmond
Evanston	Huther Doyle	VCU Medical Center
North Shore University Health System	Highland Hospital	
		Wisconsin
Massachusetts	North Carolina	Milwaukee
Boston	Charlotte	Froedtert Hospital
Beth Israel Deaconess Medical Center	Carolinas Medical Center	Children's Hospital of Wisconsin
Boston Children's Hospital		
Worcester	Ohio	Australia
UMass Memorial Medical Center	Cincinnati	Blacktown, New South Wales
	Cincinnati Children's Hospital Medical Center	Blacktown and Mt. Druitt Hospital
Michigan	Oregon	
Grand Rapids	Portland	Israel
Spectrum Health Hospitals	Oregon Health & Science University Hospital	Haifa
	Doernbecher Children's Hospital	Rambam Health Care Campus

Fig. 1 Annual ToxIC cases



38 sites who see patients at 69 separate facilities. The object of this report is to summarize the Registry’s 2013 data.

Patients entered from January 1, 2013 through December 31, 2013 are described in this report. This is the fourth annual report for the Registry [2–4].

Several sub-registries were developed after the inception of ToxIC. Three were added in 2013 focusing on North American snake bites, prescription drug misuse, and a clinical poisoning severity score. These, in addition to the existing ones on caustic ingestions and lipid resuscitation therapy, bring the total number of sub-registries to five. During 2013, six abstracts based on Registry data were presented at three national and international meetings.

Methods

Participating investigators agree to enter data on all of their medical toxicology consultations into the Registry. Cases are

entered on a password-protected, online data collection form. The site is maintained by the ACMT and is overseen by the ToxIC Registry Steering Committee. The Registry is Health Insurance Portability and Accountability Act compliant and does not collect any identifying patient information. Participation in the Registry is compliant with local Institutional Review Board policies and procedures as well as the Western Institutional Review Board.

Collected data include presenting signs, symptoms, clinical course, treatments, patient demographics, location, and the reason for toxicological exposure. The term consultation is used in this report to describe any encounter with the medical toxicologist, including admission to a toxicology inpatient service and consultation on other inpatient units, emergency department, and outpatient clinic visits. The online collection form is formatted to ensure that the data remain organized and easily searchable. There are also areas for free-text entry where providers may describe the case in more detail or offer supplementary information that is not available as a preexisting check box. As part of the Registry’s mission of providing a real-time toxico-surveillance tool, a component of the standard data form is a sentinel detection field that signals novel or unusual cases.

Table 2 Demographics of Registry cases

	<i>N</i> (%)
Male	4,100 (47.7)
Female	4,234 (49.2)
Pregnant	56 (0.6)
Gender unspecified	264 (3.1)
Age (years)	
<2	324 (3.8)
2–6	435 (5.1)
7–12	183 (2.1)
13–18	1,283 (14.9)
19–65	5,455 (63.4)
66–89	453 (5.3)
>89	33 (0.4)
Unspecified	432 (5.0)

Table 3 Referral sources

	<i>N</i> (%)
Emergency department (ED)	5,133 (59.7)
Admitting service (inpatient)	1,433 (16.7)
Outside hospital transfer	629 (7.3)
Request from other hospital service (non-ED)	413 (4.8)
Primary care or outpatient physician	384 (4.5)
Unspecified	264 (3.1)
Self-referral	241 (2.8)
Employer, workers’ compensation, etc.	55 (0.6)
Poison control center	46 (0.5)

For this report, a search of the database was performed to identify encounters recorded from January 1, 2013 through December 31, 2013. Additional details collected in the sub-registries will be published separately.

In tables describing agent classes, unless otherwise indicated, substances with fewer than five occurrences were not listed as separate items. Exceptions to this practice include the agent comprising a significant fraction of the class or if there was only one agent in the table. Percentages noted in tables of specific agents represent the proportion of those agents within its agent class.

Results

The individual institutions participating in the ToxIC Registry are listed in Table 1. In 2013, a total of 8,598 cases, representing an increase of 18.3 % over 2012 (Fig. 1), were entered.

Table 4 Reasons for medical toxicology consultation

	<i>N</i> (%)
Intentional exposure—pharmaceutical	3,445 (40.1)
Unintentional exposure—pharmaceutical	851 (9.9)
Drug abuse—illicit drug	692 (8.0)
Adverse drug reaction (ADR, undesirable effect of therapeutic drug use)	412 (4.8)
Unintentional exposure—nonpharmaceutical	410 (4.8)
Not documented	361 (4.2)
Intentional exposure—nonpharmaceutical	351 (4.1)
Unidentified agent	272 (3.2)
Drug abuse—prescription drug	266 (3.1)
Organ system dysfunction	256 (3.0)
Withdrawal—ethanol	186 (2.2)
Interpretation of toxicology lab data	154 (1.8)
Alcohol (ethanol) abuse	148 (1.7)
Envenomation—snake	147 (1.7)
Environmental evaluation	143 (1.7)
Withdrawal—opioid	117 (1.4)
Adverse drug event (ADE, medication error resulting in harm)	107 (1.2)
Occupational evaluation	91 (1.1)
Withdrawal—sedative/hypnotic	52 (0.6)
Drug abuse—OTC drug	50 (0.6)
Envenomation—spider	43 (0.5)
Envenomation—scorpion	16 (0.2)
Withdrawal—other	13 (0.2)
Envenomation—other	6 (0.1)
Marine/fish poisoning	6 (0.1)
Withdrawal—cocaine/amphetamine	3 (0.1)

Demographics

Females comprised 4,234 (49.2 %) cases, compared to 4,100 (47.7 %) males. Gender was not reported in 3.1 % of cases.

Table 5 Agent classes involved in consultation

	<i>N</i> (%)
Analgesic (nonopioid)	1,490 (13.2)
Sedative-hypnotic/muscle relaxant	1,383 (12.26)
Opioid	1,250 (11.1)
Antidepressant	1,056 (9.4)
Ethanol	737 (6.5)
Sympathomimetic	702 (6.2)
Cardiovascular	687 (6.1)
Antipsychotic	626 (5.6)
Anticholinergic/antihistamine	617 (5.5)
Anticonvulsant	408 (3.6)
Psychoactive	302 (2.7)
Envenomation	188 (1.7)
Diabetic medications	181 (1.6)
Lithium	166 (1.5)
Metals	154 (1.4)
Cough and cold products	134 (1.2)
Gases/irritants/vapors/dusts	126 (1.1)
Herbal products/dietary supplements	119 (1.1)
Antimicrobial	113 (1.0)
Household product	113 (1.0)
Toxic alcohol	95 (0.8)
Caustic	88 (0.8)
Unknown agent	88 (0.8)
Hydrocarbon	84 (0.8)
Plants and fungi	71 (0.6)
Anticoagulant	58 (0.5)
Gastrointestinal agents	34 (0.3)
Endocrine	34 (0.3)
Other pharmaceutical product	30 (0.3)
Insecticide	27 (0.2)
Chemotherapeutic/immunological	23 (0.2)
Parkinson's disease agents	19 (0.2)
Rodenticide	15 (0.1)
Other nonpharmaceutical product	14 (0.1)
Herbicides	11 (0.1)
Anesthetics	11 (0.1)
Pulmonary	7 (0.1)
WMD/riot agent/radiological	3 (0.0)
Ingested foreign object	3 (0.0)
Fungicide	1 (0.0)

Percentages are out of the total number of reported agents (11,279). Of registry cases, 27.9 % reported exposure to multiple agents

WMD weapons of mass destruction

Table 6 Clinical signs and symptoms

	<i>N</i> (%)
Toxidrome	
Sedative-hypnotic	589 (6.9)
Anticholinergic	401 (4.7)
Opioid	259 (3.0)
Sympathomimetic	167 (1.9)
Serotonin syndrome	151 (1.8)
Sympatholytic	26 (0.3)
Overlap syndromes (chronic fatigue, multiple chemical sensitivity, etc.)	13 (0.2)
Neuroleptic malignant syndrome	11 (0.1)
Cholinergic	6 (0.1)
Major vital sign abnormalities	
Tachycardia (HR>140)	848 (9.9)
Hypotension (systolic BP<80 mmHg)	508 (5.9)
Bradycardia (HR<50)	286 (3.3)
Hypertension (systolic BP>200 mmHg or diastolic BP>120 mmHg)	180 (2.1)
Bradypnea (RR<10)	151 (1.8)
Hyperthermia (temp>105 °F)	28 (0.3)
Cardiovascular	
Prolonged QTc (≥500 ms)	289 (3.3)
Prolonged QRS (≥120 ms)	165 (1.9)
Ventricular dysrhythmia	71 (0.8)
Atrioventricular block (>1st degree)	44 (0.5)
Pulmonary	
Respiratory depression	483 (5.6)
Aspiration pneumonia	151 (1.8)
Acute lung injury/ARDS	63 (0.7)
Asthma/reactive airway disease	39 (0.5)
Neurological	
Coma/CNS depression	2,233 (26.0)
Delirium	795 (9.2)
Agitation	795 (9.2)
Hyperreflexia/myoclonus/tremor	533 (6.2)
Seizures	337 (3.9)
Hallucinations	218 (2.5)
Dystonia/rigidity/extrapyramidal symptoms	109 (1.3)
Weakness/paralysis	78 (0.9)
Numbness/paresthesia	62 (0.7)
Peripheral neuropathy (objective)	15 (0.2)
Metabolic	
Metabolic acidosis (pH<7.2)	350 (4.1)
Elevated anion gap (>20)	254 (3.0)
Hypoglycemia (glucose<50 mg/dL)	146 (1.7)
Elevated osmole gap (>20)	42 (0.5)
Gastrointestinal/hepatic	
Hepatotoxicity (AST≥1,000 IU/L)	312 (3.6)
Gastrointestinal bleeding	58 (0.7)
Pancreatitis	35 (0.4)

Table 6 (continued)

	<i>N</i> (%)
Corrosive injury	25 (0.3)
Hematological	
Coagulopathy (PT>15 s)	205 (2.4)
Thrombocytopenia (platelets<100 K/ μ L)	74 (0.9)
Leukocytosis (WBC>20 K/ μ L)	74 (0.9)
Hemolysis (Hgb<10 g/dL)	20 (0.2)
Pancytopenia	12 (0.1)
Methemoglobinemia (MetHgb≥2 %)	9 (0.1)
Renal/musculoskeletal	
Acute kidney injury (creatinine>2.0 mg/dL)	312 (3.6)
Rhabdomyolysis (CPK>1,000 IU/L)	245 (2.8)
Dermatological	
Rash	101 (1.2)
Blisters/bullae	32 (0.7)
Necrosis	21 (0.2)
Angioedema	12 (0.1)

CPK creatine phosphokinase, Hgb hemoglobin, WBC white blood cells, PT prothrombin time, AST aspartate aminotransferase, CNS central nervous system, ARDS acute respiratory distress syndrome, RR respiratory rate, BP blood pressure, HR heart rate

Fifty-six (1.3 %) were pregnant, 0.6 % of all cases. Adults between the ages of 19 and 65 accounted for a majority (63.4 %) of reported cases. Adolescents (13 to 18 years) were the next most frequent, making up 14.9 %. Additional demographic data are summarized in Table 2.

Source of Referrals and Primary Reason for Encounter

Hospital emergency departments were the most frequent source of referral, accounting for 5,133 (59.7 %) of Registry cases (Table 3). Inpatient services and patients transferred directly from other facilities were the next most common source of consultation. There were 384 outpatient referrals, accounting for 4.5 %. As seen in Table 4, exposures to pharmaceuticals, both intentional and unintentional, were the reason for referral in half of all cases. Drug abuse, encompassing illicit, prescription, and over-the-counter agents, was the next most frequent. Collectively, drug abuse was responsible for 11.7 % of cases. Adverse drug reactions (ADRs), defined in the Registry as undesirable effects of therapeutic drug use, were the reason for 4.8 %.

Agent Classes

A total of 11,279 individual agents were listed in case entries. The distribution of these agents among the 40 different substance classes predefined in the Registry is shown in Table 5. Exposure to more than one agent was reported in 27.9 % of

Table 7 Fatalities

Case	Age/ gender	Agents involved	Symptoms and clinical findings	Treatment
1	43 M	Acetaminophen, hydrocodone, carisoprodol	HT, CNS, HPT, CPT, AKI	NAC, NaHCO ₃
2	61 M	Metformin	HT, ALI, RD, CNS, HGY, MA, PNC, CPT	Continuous renal replacement
3	66 M	Metformin	MA, AG	Carnitine, hemodialysis
4	65 F	None listed	AG, CPT	
5	86 M	Citalopram, quetiapine, dextromethorphan	TC, AP, DLM, EPS, RFX	Antipsychotics, benzodiazepines
6	74 F	Acetaminophen	MA, AKI	None listed
7	85 M	Acetaminophen	HT, TC, RAD, HPT, PLT	NAC, albuterol, intubation
8	36 M	Kratom, lamotrigine, paroxetine, quetiapine	HTN, VD, QRS, RD, CNS, SZ, RBM	Atropine, lipid resuscitation, naloxone, NaHCO ₃ , neuromuscular blocker, opioids, vasopressors, CPR, intubation, IV fluids
9	23 M	None listed	HT, TC, BP, VD, RD, MA, AG, HPT, AKI, RBD	Atropine, naloxone, NaHCO ₃ , vasopressors, gastric lavage, charcoal, continuous renal replacement, CPR, intubation, IV fluids
10	19 F	Sympathomimetic unspecified	HT, TC, HYT, VD, AGT, SZ, MA	Calcium, lipid resuscitation, NaHCO ₃ , antiarrhythmics, benzodiazepines, neuromuscular blockers, vasopressors, CPR, intubation, IV fluids
11	29 M	Methamphetamine	HT, TC, VD, AGT, CNS, DLM, HYS, CPT, RBD	Factor replacement, lipid resuscitation, methylene blue, vasopressors, continuous renal replacement, CPR, intubation, transfusion
12	47 M	Cocaine, heroin, methadone	TC, HYT, AGT, HCN, AG, PNC, AKI	Benzodiazepines, neuromuscular blockers, opioids, intubation, IV fluids
13	49 F	Methamphetamine	HT, RD, CNS, MA, HPT, CPT, AKI, RBD	None listed
14	38 M	Heroin	BP, ALI, CNS, MA, AG, HPT, CPT, PLT, WBC, AKI, RBD	NAC, naloxone, NaHCO ₃ , neuromuscular blockers, vasopressors, CPR, intubations, IV fluids
15	65 M	Diphenhydramine	RD, AGT, CNS, DLM, EPS, RFX	Flumazenil, benzodiazepines, opioids, intubation
16	26 M	Oxycodone	HT, TC, CNS, MA, HPT	NAC, intubation, IV fluids
17	40 M	Methadone	HT, BC, MA	Vasopressors, CPR, intubation, IV fluids
18	86 M	Hydrochloric acid	MA, AG, CRV, NEC	None listed
19	43 F	Heroin, carisoprodol	HT, TC, CNS, MA, AG	Lipid resuscitation, naloxone, vasopressors, CPR, intubation, IV fluids
20	17 F	Methanol	HT, TC, RD, CNS, SZ, MA, AG	Fomepizole, continuous renal replacement, ECMO
21	17 F	Cannabinoid-synthetic	None listed	Vasopressors, CPR, intubation, IV fluids
22	56 M	Alkyl nitrite	HT, CNS, MA	Methylene blue, vasopressors, cardioversion, intubation, IV fluids
23	61 M	Cyanide	BC, BP, VD, RD, CNS	CPR, intubation
24	19 M	Cyanide	HT, TC, QRD, RD, CNS, MA, AG	Hydroxocobalamin, NaHCO ₃ , vasopressors, intubation, IV fluids
25	15 M	LSD	HT, BC, VD, RD, CNS, SZ, MA	NaHCO ₃ , vasopressors, CPR, intubation
26	21 M	Metformin	HT, TC, CNS, MA, AG	Fomepizole, NaHCO ₃ , hemodialysis, intubation
27	(>89) F	Atenolol	BC, AVB, AKI	Atropine, glucagon,
28	31 F	Aripiprazole, acetaminophen, prazosin, cyclobenzaprine	HT, CNS, MA, AG, HPT	NAC
29	69 M	Amlodipine, acetaminophen, oxycodone	HT, TC, AP, RD, CNS, HGY, MA, AG, HPT, PNC, CPT, PLT, WBC, AKI, RBD	NAC, anticonvulsants, benzodiazepines, glucose, vasopressors, hemodialysis, intubation, IV fluids
30	17 M	Aspirin	TC, VD, RD, AGT, CNS, MA, CPT	NaHCO ₃ , antiarrhythmics, anticonvulsants, benzodiazepines, neuromuscular blockers, vasopressors, urinary alkalization, cardioversion, CPR, intubation, IV fluids

Table 7 (continued)

Case	Age/ gender	Agents involved	Symptoms and clinical findings	Treatment
31	55 M	Verapamil, diltiazem	HT, BC, VD, QRS, QTc, AVB, AP, CNS, MA, HYS, CPT, PLT, WBC, AKI	Calcium, insulin-euglycemic therapy, methylene blue, NaHCO ₃ , benzodiazepines, neuromuscular blockers, vasopressors, charcoal, continuous renal replacement, CPR, intubation, IV fluids, pacemaker, transfusion
32	22 M	Methamphetamine	TC, QTc, AGT, DLM	None listed
33	(Unknown) F	Acetaminophen	ALI, MA, AG, HPT, AKI	NAC
34	(Unknown) F*	Acetaminophen	HT, HGY, MA, AG, HPT, GIB, PNC, CPT, AKI	NAC, glucose, steroids, vasopressors, hemodialysis, continuous renal replacement, CPR, intubation, IV fluids
35	(Unknown) F	Oxycodone	HT, BP, QRS, AP, RD, CNS, MA, AG, HPT, CPT, AKI	NAC, naloxone, benzodiazepines, neuromuscular blockers, vasopressors, CPR, intubation, IV fluids
36	45 M	Lisinopril, amlodipine	HT, ALI, HGY	Insulin-euglycemic therapy, lipid resuscitation, glucose, vasopressors, intubation, IV fluids
37	27 F	Acetaminophen	HPT	NAC
38	52 F	Acetaminophen, lorazepam	HT, CNS, MA, AG, HPT, PLT, PCT, AKI	NAC, vasopressors, hemodialysis, intubation, IV fluids
39	57 F	Acetaminophen	HT, TC, AP, CNS, HGY, RSH, BB	NAC, albuterol, glucose, vasopressors, intubation, IV fluids
40	61 F	Unknown agent	HT, BC, VD, CNS	Vasopressors, CPR, intubation
41	70 M	Hydrocodone	HT, HGY, MA, AKI	NAC, vasopressors, CPR, intubation
42	58 F	Acetaminophen, hydrocodone, morphine	BP, CNS, HPT, CPT	NAC, naloxone, vasopressors
43	65 F	Amlodipine, losartan, lorazepam	HT, CNS	Calcium, glucagon, insulin-euglycemic therapy, lipid resuscitation, vasopressors, intubation, IV fluids
44	46 M	Ethylene glycol	CNS, MA, AG, OG, WBC, AKI, RBM	Fomepizole, vasopressors
45	48 F	Diltiazem	HT, BC, AP, ALI, CNS, MA, AKI	Atropine, calcium, flumazenil, insulin-euglycemic therapy, lipid resuscitation, albuterol, benzodiazepines, neuromuscular blockers, vasopressors, glucose, CPR, intubation, IV fluids, pacemaker
46	29 F	Quetiapine, desvenlafaxine, escitalopram, bupropion	HT, QRS, CNS, MA, AG, AKI	Lipid resuscitation, vasopressors, CPR, intubation, IV fluids
47	25 F	Pseudoephedrine	TC, CNS	Benzodiazepines
48	70 M	Amlodipine, metformin	HT, CNS, MA, AKI	Calcium, insulin-euglycemic therapy, vasopressors, IV fluids
49	33 F	Acetaminophen, ibuprofen, diphenhydramine	RD, AG, HPT, CPT, AKI	Flumazenil, NAC, physostigmine, benzodiazepines, hemodialysis, intubation, IV fluids
50	59 F	Acetaminophen	HT, TC, VD, CNS, RFX, HGY, MA, AG, HPT, GIB, CPT, PLT, AKI	Factor replacement, NAC, naloxone, NaHCO ₃ , benzodiazepines, glucose, vasopressors, continuous renal replacement, intubation, IV fluids
51	52 M	Lorazepam	AP, ALI, RD, CNS, RFX	None listed
52	37 F	Hydrocodone, acetaminophen	VD, CNS, HPT, GIB, AKI, RBM	NAC, benzodiazepines, neuromuscular blockers, vasopressors
53	22 F	Diphenhydramine, hydroxyzine, quetiapine, citalopram, sertraline	HT, BC, QRS, RD, CNS, MA, RBM	None listed
54	49 M	Acetaminophen, ethanol	CNS, MA, AG, HPT, CPT, AKI	NaHCO ₃ , vasopressors, continuous renal replacement, intubation, IV fluids
55	50 F	Verapamil, metoprolol	HT, BC, VD, AVB, RD, CNS, MA, CPT, AKI	Calcium, insulin-euglycemic therapy, lipid resuscitation, methylene blue, NaHCO ₃ , benzodiazepines, neuromuscular blockers, vasopressors, CPR, intubation, IV fluids, pacemaker

Table 7 (continued)

Case	Age/ gender	Agents involved	Symptoms and clinical findings	Treatment
56	56 F	None listed	None listed	None listed
57	69 F	Cyanide	HT, TC, RD, CNS, MA, BB	Hydroxocobalamin, vasopressors, intubation, IV fluids
58	46 M	None listed	HT, TC, BC, ALI, RD, CNS, HGY, MA, AG, HPT, GIB, HYS, CPT, PLT	NAC, vasopressors, hemodialysis, continuous renal replacement, cardioversion, CPR, intubation, IV fluids
59	57 F	None listed	VD, CN, SZ, MA, AG, HPT, PCT, AKI, RBM	None listed
60	45 F	None listed	HT, CNS DLM, RFX, WKN, HGY, MA, HPT	None listed
61	61 M	Metformin	HT, CNS, DLM, HGY, MA, AG, CPT, WBC, AKI	NaHCO ₃ , steroids, vasopressors, continuous renal replacement, intubation, transfusion
62	56 M	None listed	MA, HPT	NAC
63	54 M	Opioid unspecified	HT, AP, CNS, MA, HPT, CPT, AKI, RBM, BB	Insulin-euglycemic therapy, NAC, naloxone, benzodiazepines, opioids, vasopressors, intubation, IV fluids
64	74 M	Rivaroxaban	HT, HPT, AKI	NAC, vasopressors, intubation, IV fluids
65	52 F	Ethanol	HT, CNS	CPR, intubation, IV fluids
66	47 F	Carisoprodol	CNS, RFX	Benzodiazepines
67	66 M	Fentanyl	CNS	Naloxone
68	35 F	None listed	HTN, RD, CNS, MA, CPT, AKI	Hemodialysis, CPR, intubation, IV fluids, transfusion
69	43 M	Gabapentin, ethanol	SZ	Vasopressors, CPR, intubation, IV fluids
70	33 M	NaHCO ₃	HT, RD, SZ, AKI	Vasodilators, vasopressors, intubation, IV fluids
71	28 M	Heroin	BC, BP, VD, QTc, AP, ALI, CNS, MA, AG, CPT, AKI, RBM	Atropine, naloxone, NaHCO ₃ , vasopressors, CPR, intubation,
72	50 M	Methylene chloride	HT, BC, BP, RD, CNS, MA, AG, RBM	Vasopressors, intubation, IV fluids
73	65 F	Acetaminophen, hydrocodone	CNS, AG, HPT, CPT	NAC, intubation, IV fluids
74	17 F	Ethanol	RD, CNS	IV fluids
75	46 M	Aspirin	TC, AGT, MA, AG, GIB, AKI	NaHCO ₃
76	83 F	Digoxin, amlodipine	WKN	Digoxin Fab
77	76 M	Digoxin	VD, AVB	Digoxin Fab
78	(>89) M	Digoxin	BC, AVB	Digoxin Fab
79	(Unknown) M	None listed	HGY	Glucose
80	16 F	None listed	HT, TC, BC, RD, CNS, SZ, MA, AG, HPT, CPT, WBC, AKI	NaHCO ₃ , vasopressors, continuous renal replacement, CPR, ECMO, intubation, IV fluids
81	6 M	None listed	TC, ALI, CNS, HPT	None listed
82	(Unknown) M	None listed	BC	None listed
83	39 F	Unknown agent	HT, VD, QTc, AP, MA, AKI	NaHCO ₃ , vasopressors
84	49 F	Metoprolol	HT, NC, BP, ALI, RD, CNS, MA, GIB, CPT	Calcium, insulin-euglycemic therapy, lipid resuscitation, NaHCO ₃ , neuromuscular blockers, vasopressors, CPR, intubation, IV fluids, pacemaker, transfusion
85	58 F	Acetaminophen	HT, TC, QRS, AGT, CNS, HGY, MA, AG, HPT, PNC, CPT, PLT	NAC, glucose, vasopressors, continuous renal replacement, intubation, IV fluids, transfusion
86	39 F	None listed	AGT, CNS, HGY, MA, AG, OG, PLT, WBC, AKI	Fomepizole, NAC
87	18 M	None listed	None listed	None listed
88	69 F	Acetaminophen	HT, AP, CNS, MA, AG, RBM	Lipid resuscitation
89	59 M	Ethanol	HT, TC, RD, MA, AG, HPT, GIB, PNC, HYS, AKI	Antiarrhythmics, benzodiazepines, hemodialysis, intubation

Table 7 (continued)

Case	Age/ gender	Agents involved	Symptoms and clinical findings	Treatment
90	26 F	None listed	HT, BC, BP, CNS	Naloxone, vasopressors, cardioversion, CPR, intubation
91	55 M	Acetaminophen, ethanol	HT, CNS, HGY, MA, AG, OG, HPT, CPT, AKI	Fomepizole, NAC, thiamine, vasopressors, continuous renal replacement, CPR, intubation, IV fluids
92	34 F	None listed	None listed	None listed
93	61 M	None listed	RD	None listed

TC tachycardia, *HT* hypotension, *BC* bradycardia, *HTN* hypertension, *BP* bradypnea, *HYT* hyperthermia, *QTc* QTc prolongation, *QRS* QRS prolongation, *VD* ventricular dysrhythmia, *AVB* AV block, *RD* respiratory depression, *AP* aspiration pneumonia, *ALI* acute lung injury/ARDS, *RAD* asthma/reactive airway disease *CNS* coma/CNS depression, *DLM* delirium, *AGT* agitation, *RFX* hyperreflexia/tremor, *SZ* seizures, *HCN* hallucinations, *EPS* dystonia, *WKN* weakness/paralysis, *PST* paresthesia, *NP* neuropathy, *MA* metabolic acidosis, *AG* anion gap, *HGY* hypoglycemia, *OG* osmole gap, *HPT* hepatotoxicity, *GIB* GI bleeding, *PNC* pancreatitis, *CRV* corrosive injury, *CPT* coagulopathy, *PLT* thrombocytopenia, *WBC* leukocytosis, *HYS* hemolysis, *PCT* pancytopenia, *MET* methemoglobinemia, *AKI* acute kidney injury, *RBM* rhabdomyolysis, *RSH* rash, *BB* blisters/bullae, *NEC* dermal necrosis, *AE* angioedema

cases. Nonopioid analgesics, sedative-hypnotic agents including muscle relaxants, and opioids were the most common categories comprising over a third of all reported agents. Overall, exposures to pharmaceutical products including prescription and nonprescription drugs were reported in 80.9 % of cases.

Signs and Symptoms

At least one clinical sign or symptom was reported in 6,116 (71.1 %) cases. These are summarized and organized by clinical syndrome or organ system in Table 6. Neurological signs or symptoms were described most frequently, with coma or CNS depression found in 26 % of all cases. This finding is consistent with the sedative-hypnotic toxidrome being most common among the syndromes. Agitation and delirium were also common, with each being reported in 9.2 % of cases. Among vital sign abnormalities, significant tachycardia (defined in the Registry as a heart rate of greater than 140 beats per minute) was the most frequent, described in 9.9 % of cases. All other categories of symptoms or findings were documented in less than 7 % of cases.

Fatalities

There were 93 (1.1 %) fatalities (Table 7) with 47.3 % being female. Their average age was 46.5 years. Nonopioid analgesics were the agent class most frequently associated with fatalities. At least one analgesic drug was implicated in 22.6 % of the fatalities. Opioids were the second most frequently implicated, comprising 17.2 % of the deaths. Cardiovascular drugs comprised the third most common class in fatal cases (15.1 %).

Individual Agent Classes

Tables 8 through 40 summarize the frequency of specific drugs enumerated by class.

Treatment

Specific treatments were provided to 4,695 (54.6 %) patients. At least one antidote was given to 2,334 (27.1 %) patients and 356 (4.1 %) received more than one, resulting in 2,825 instances of separate antidote administration (Table 41). *N*-acetylcysteine accounted for nearly a third (30.5 %) of all antidote administrations. Opioid antagonists (naloxone or nalmefene) and sodium bicarbonate were the next most frequent collectively comprising another 32.2 % of total antidote use. Antivenoms and chelators were used in 1.4 and 0.3 % of cases, respectively (Tables 42 and 43). Almost all antivenom treatments (91.8 %) involved polyvalent anti-Crotalidae Fab fragments. Over half of chelation treatments (53.6 %) utilized DMSA, with an additional 21.4 % of cases involving deferoxamine.

Supportive care with pharmacologic agents was provided in 1,681 (19.6 %) cases (Tables 44 and 45). A total of 2,089 treatments were documented, and 336 (3.9 %) patients received more than one type of treatment. Benzodiazepine administration accounted for over half (56.0 %) of

Table 8 Analgesics (nonopioid)

	<i>N</i> (%)
Acetaminophen	995 (66.8)
Aspirin	222 (14.9)
Ibuprofen	198 (13.3)
Naproxen	29 (1.9)
Salicylamide	14 (0.9)
Analgesic unspecified	8 (0.5)
Miscellaneous ^a	24 (1.6)

^a Includes diclofenac, meloxicam, phenazopyridine, methylsalicylate, metamizole, indomethacin, ketorolac, phenylbutazone, etodolac, nabumetone, and piroxicam

Table 9 Sedative-hypnotics/muscle relaxants

	N (%)
Benzodiazepines	802 (58.0)
Clonazepam	254 (18.3)
Alprazolam	242 (17.5)
Lorazepam	146 (10.6)
Diazepam	76 (5.5)
Benzodiazepine unspecified	47 (3.4)
Temazepam	17 (1.2)
Midazolam	5 (0.4)
Miscellaneous ^a	15 (1.1)
Muscle relaxants	271 (19.6)
Cyclobenzaprine	97 (7.0)
Carisoprodol	82 (5.9)
Baclofen	63 (4.6)
Tizanidine	20 (1.4)
Methocarbamol	6 (0.4)
Miscellaneous ^b	3 (0.2)
Barbiturates	51 (3.7)
Butalbital	33 (2.4)
Phenobarbital	12 (0.9)
Miscellaneous ^c	6 (0.4)
Nonbenzodiazepine GABA agonists (“Z-drugs”)	121 (8.7)
Zolpidem	112 (8.1)
Eszopiclone	7 (0.5)
Miscellaneous ^d	2 (0.1)
Other sedatives	138 (10.0)
Gabapentin	88 (6.3)
Buspirone	21 (1.5)
Pregabalin	15 (1.1)
Miscellaneous ^e	8 (0.5)
Sedative-hypnotic unspecified	6 (0.4)

^a Includes chlordiazepoxide, oxazepam, flurazepam, nitrazepam, chlorazepate, triazolam, and brotizolam

^b Includes chlorzoxazone, and metaxalone

^c Includes butabarbital, pentobarbital, and barbiturate unspecified

^d Includes zaleplon, and zopiclone

^e Includes phenibut, ramelteon, meprobamate, propofol, and chloral hydrate

pharmacologic supportive measures. Nonpharmacologic forms of supportive care were given in 1,527 (17.8 %) cases, with 350 (4.1 %) patients receiving more than one type of treatment. Intravenous fluid resuscitation (62.0 %) and intubation (31.6 %) together accounted for the majority of treatments.

Decontamination and enhanced elimination techniques were used in a small number of cases (Tables 46 and 47). Only 388 (4.5 %) patients received some form of decontamination, with 28 (0.3 %) receiving more than one type. Oral activated

Table 10 Opioids

	N (%)
Heroin	322 (25.7)
Oxycodone	269 (21.5)
Metadone	169 (13.5)
Hydrocodone	132 (10.6)
Tramadol	85 (6.8)
Buprenorphine	70 (5.6)
Morphine	67 (5.4)
Fentanyl	39 (3.1)
Hydromorphone	35 (2.8)
Codeine	30 (2.4)
Opioid unspecified	8 (0.6)
Oxymorphone	5 (0.4)
Tapentadol	5 (0.4)
Miscellaneous ^a	14 (1.1)

^a Includes loperamide, meperidine, naloxone, naltrexone, propoxyphene, diphenoxylate, and opium

Table 11 Antidepressants

	N (%)
Selective serotonin reuptake inhibitors (SSRIs)	387 (36.6)
Citalopram	143 (13.5)
Sertraline	101 (9.6)
Fluoxetine	71 (6.7)
Escitalopram	48 (4.5)
Paroxetine	24 (2.3)
Tricyclic antidepressants (TCAs)	161 (15.2)
Amitriptyline	115 (10.9)
Doxepin	24 (2.3)
Nortriptyline	13 (1.2)
Miscellaneous [†]	9 (0.9)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	107 (10.1)
Venlafaxine	67 (6.3)
Duloxetine	24 (2.3)
Desvenlafaxine	9 (0.9)
Fluvoxamine	7 (0.7)
Other antidepressants	401 (38.0)
Bupropion	198 (18.6)
Trazodone	142 (13.4)
Mirtazapine	41 (3.9)
Vilazodone	6 (0.6)
Antidepressant unspecified	5 (0.5)
Miscellaneous ^b	9 (0.9)

[†] Includes imipramine, desipramine, and clomipramine

^b Includes agomelatine, dosulepin, sibutramine, tranlycypromine, and phenelzine

Table 12 Sympathomimetics

	N (%)
Cocaine	313 (44.6)
Methamphetamine	115 (16.4)
Amphetamine	61 (8.7)
Methylphenidate	47 (6.7)
Methylenedioxy- <i>N</i> -methamphetamine	32 (4.6)
Dextroamphetamine	30 (4.3)
Sympathomimetic unspecified	23 (3.3)
Mephedrone	16 (2.3)
Dexmethylphenidate	12 (1.7)
Atomoxetine	10 (1.4)
Pseudoephedrine	8 (1.1)
Phenylephrine	7 (1.0)
25I-NBOMe	5 (0.7)
Miscellaneous ^a	23 (3.3)

^a Includes lisdexamfetamine, cathinone, phentermine, tetrahydrozoline, α -pyrrolidinopentiophenone (α -PVP), epinephrine, 2C-T-7, ephedrine, phendimetrazine, phenylpropanolamine, propylhexedrine, and methylone

charcoal made up the majority (79.4 %) of decontamination therapies. Enhanced elimination therapies were provided to 219 (2.5 %) patients with 22 (0.3 %) receiving more than one type. Hemodialysis and continuous renal replacement accounted for 62 % of enhanced elimination entries. The remaining included urinary alkalinization and multiple-dose activated charcoal. There was one instance of exchange transfusion.

Adverse Drug Reactions

ADRs were the reason for medical toxicology consultation in 580 (4.8 %) of the Registry cases. A total of 177 drugs were implicated at least once. Table 48 lists the 15 most frequently encountered drugs associated with ADRs (≥ 10 occurrences), along with their percentage of the total number of ADR cases. More than one drug was involved in 129 (22 %) of these cases.

Limitations

Reporting bias is a potential limitation of any database dependent on spontaneous reporting. However, all participating sites agree, as a condition of participation, that all of their cases will be entered into the Registry thus minimizing such bias. Incomplete data entry is a limitation. As seen in Tables 2, 3, and 4, some case data were missing. This is an area of ongoing quality improvement for the Registry. When such data are missing, it is typically less than 5 % of the total cases for any given field, making it unlikely to significantly impact the results and trends. However, this problem was most notable in the fatal cases (Table 7), where a specific exposure was not documented

Table 13 Cardiovascular agents

	N (%)
Beta blockers	185 (26.9)
Metoprolol	69 (10.0)
Propranolol	41 (6.0)
Atenolol	37 (5.4)
Carvedilol	13 (1.9)
Labetalol	13 (1.9)
Nebivolol	6 (0.9)
Miscellaneous ^a	6 (0.9)
Calcium channel antagonists	116 (16.9)
Amlodipine	61 (8.9)
Diltiazem	24 (3.5)
Verapamil	19 (2.8)
Nifedipine	10 (1.5)
Miscellaneous ^b	2 (0.3)
ACE inhibitors	64 (9.3)
Lisinopril	53 (7.7)
Enalapril	6 (0.9)
Miscellaneous ^c	6 (0.9)
Angiotensin receptor blockers	10 (1.5)
Losartan	6 (0.9)
Miscellaneous ^d	4 (0.6)
Cardiac glycosides	53 (7.7)
Digoxin	52 (7.6)
Digitoxin	1 (0.1)
Sympatholytics	154 (22.4)
Clonidine	129 (18.8)
Guanfacine	21 (3.1)
Xylazine	4 (0.6)
Diuretics	32 (4.7)
Hydrochlorothiazide	10 (1.5)
Furosemide	9 (1.3)
Miscellaneous ^e	13 (1.9)
Other antihypertensives and vasodilators	44 (6.4)
Prazosin	13 (1.9)
Cilostazol	11 (1.6)
Miscellaneous ^f	20 (2.9)
Antidysrhythmics	11 (1.6)
Amiodarone	5 (0.7)
Miscellaneous ^g	6 (0.9)
Other cardiovascular agents	12 (1.7)
Atorvastatin	5 (0.7)
Miscellaneous ^h	7 (1.0)

^a Includes nadolol, bisoprolol, and pindolol

^b Includes aranidipine and felodipine

^c Includes benazepril, perindopril, quinapril

^d Includes valsartan, and candesartan

^e Includes acetazolamide, spironolactone, pamabrom, chlorthalidone, and torsemide

^f Includes alkyl nitrite, isosorbide, antihypertensive unspecified, doxazosin, nitroglycerin, terazosin, amyl nitrite, hydralazine, and tamsulosin

^g Includes propafenone, flecainide, and mexiletine

^h Includes cardiovascular agent unspecified, lovastatin, pravastatin, and ranolazine

Table 14 Antipsychotics

	N (%)
Quetiapine	304 (48.5)
Risperidone	94 (15.0)
Olanzapine	60 (9.6)
Aripiprazole	54 (8.6)
Haloperidol	42 (6.7)
Ziprasidone	18 (2.9)
Clozapine	13 (2.1)
Chlorpromazine	11 (1.8)
Miscellaneous ^a	30 (4.8)

^a Includes lurasidone, paliperidone, perphenazine, asenapine, fluphenazine, loxapine, droperidol, iloperidone, prochlorperazine, zuclopenthixol, and antipsychotic unspecified

Table 15 Anticholinergics and antihistamines

	N (%)
Diphenhydramine	334 (54.1)
Hydroxyzine	72 (11.7)
Promethazine	36 (5.8)
Benztropine	34 (5.5)
Chlorpheniramine	32 (5.2)
Doxylamine	20 (3.2)
Antihistamine unspecified	16 (2.6)
Loratidine	13 (2.1)
Dicyclomine	11 (1.8)
Meclizine	10 (1.6)
Cyproheptadine	7 (1.1)
Hyoscyamine	6 (1.0)
Pyrilamine	6 (1.0)
Cetirizine	5 (0.8)
Scopolamine	5 (0.8)
Miscellaneous [†]	11 (1.8)

^a Includes anticholinergic unspecified, dimenhydrinate, oxybutynin, atropine, brompheniramine, chlorcyclizine, and trihexyphenidyl

Table 16 Anticonvulsants and mood stabilizers

	N (%)
Valproic acid	132 (32.4)
Lamotrigine	82 (20.1)
Phenytoin	62 (15.2)
Carbamazepine	59 (14.5)
Topiramate	26 (6.4)
Oxcarbazepine	22 (5.4)
Levetiracetam	12 (2.9)
Lacosamide	5 (1.2)
Miscellaneous ^a	8 (2.0)
Lithium ^b	166 (100.0)

^a Includes primidone, zonisamide, clobazam, and ethosuximide

^b Lithium is considered a separate category

Table 17 Psychoactives

	N (%)
Marijuana	123 (40.7)
Phencyclidine	62 (20.5)
Cannabinoid—synthetic	52 (17.2)
Gamma hydroxybutyrate (GHB)	15 (5.0)
Lysergic acid diethylamide (LSD)	15 (5.0)
Cannabinoid—nonsynthetic	11 (3.6)
Nicotine	7 (2.3)
Ketamine	5 (1.7)
Miscellaneous ^a	12 (4.0)

^a Includes donepezil, disulfiram, hallucinogen unspecified, dimethyltryptamine (DMT), gamma butyrolactone, ibogaine, mescaline, and rotundine

Table 18 Envenomations and marine poisonings

	N (%)
<i>Crotalus</i> spp.	66 (35.1)
<i>Agkistrodon</i> spp.	39 (20.7)
<i>Loxosceles</i> spp.	24 (12.8)
Unspecified snake	12 (6.4)
<i>Dendroaspis</i> spp.	9 (4.8)
<i>Centruroides</i> spp.	8 (4.3)
<i>Latrodectus</i> spp.	8 (4.3)
Unspecified envenomation	5 (2.7)
Miscellaneous ^a	17 (9.0)

^a Includes unspecified scorpion, unspecified spider, *Vipera palestinae*, jellyfish, ciguatera poisoning, unspecified insect, hymenoptera, scombroid poisoning, *Sistrurus* spp., and sting-ray envenomation

Table 19 Diabetic medications

	N (%)
Metformin	55 (30.4)
Insulin	44 (24.3)
Glipizide	31 (17.1)
Glyburide	28 (15.5)
Glimepiride	11 (6.1)
Miscellaneous ^a	12 (6.6)

^a Includes sitagliptin, sulfonylurea unspecified, pioglitazone, and linagliptin

Table 20 Metals

	N (%)
Lead	35 (22.7)
Cobalt	25 (16.2)
Mercury	25 (16.2)
Chromium	21 (13.6)
Iron	19 (12.3)
Arsenic	9 (5.8)
Copper	6 (3.9)
Miscellaneous ^a	13 (8.4)

^a Includes manganese, aluminum, cadmium, cesium, molybdenum, nickel, selenium, tin, and titanium

Table 21 Cough and cold products

	N (%)
Dextromethorphan	109 (81.3)
Cough and cold product unspecified	20 (14.9)
Miscellaneous ^a	5 (3.7)

^a Includes guaifenesin and camphor

Table 22 Gases, irritants, vapors, and dusts

	N (%)
Carbon monoxide	57 (45.2)
Cyanide	12 (9.5)
Smoke	7 (5.6)
Nitrogen oxides	6 (4.8)
Hydrogen sulfide	5 (4.0)
Petroleum vapors	5 (4.0)
Unspecified gas	5 (4.0)
Miscellaneous ^a	29 (23.0)

^a Includes dust, spray duster (canned air), asbestos, tungsten hexafluoride, boron hydride, acetonitrile, chlorine, radon, carbon dioxide, chloramine, fiberglass, liquefied petroleum gas, silica, and sulfur dioxide

Table 23 Herbal products and dietary supplements

	N (%)
Caffeine	56 (47.1)
Melatonin	15 (12.6)
Herbal product unspecified	10 (8.4)
Menthol	6 (5.0)
Multiple vitamin	6 (5.0)
Miscellaneous ^a	26 (21.8)

^a Includes 1,3-dimethylamine, thymol, eucalyptus oil, *Garcinia cambogia*, calcium, prenatal vitamins, zinc, arginine, St. John's Wort, tea tree oil, vitamin D, niacin, and garlic

Table 24 Antimicrobials

	N (%)
Antibiotics	65 (57.5)
Trimethoprim/sulfamethoxazole	14 (12.4)
Amoxicillin	9 (8.0)
Metronidazole	6 (5.3)
Penicillin	5 (4.4)
Miscellaneous ^a	31 (27.4)
Antivirals	27 (23.9)
Emtricitabine	6 (5.3)
Tenofovir	6 (5.3)
Miscellaneous ^b	15 (13.3)
Antifungals ^c	6 (5.3)
Other antimicrobials	15 (13.2)
Levamisole	5 (4.4)
Miscellaneous ^d	10 (8.8)

^a Includes cephalixin, dapsone, daptomycin, doxycycline, levofloxacin, linezolid, azithromycin, cefidinin, ceftriaxone, cefuroxime, isoniazid, meropenem, nitrofurantoin, vancomycin, cefepime, cefpodoxime, ciprofloxacin, and minocycline

^b Includes amantadine, efavirenz, lamivudine, oseltamivir, zidovudine, ribavirin, ritonavir, and valacyclovir

^c Includes fluconazole, terbinafine, griseofulvin, and itraconazole

^d Includes antimicrobial unspecified, chloroquine, benzoic acid, chlorhexidine, primaquine, and silver sulfadiazine

Table 25 Household products

	N (%)
Detergent pods	33 (29.2)
Cleaning solutions and disinfectants	25 (22.1)
Sodium hypochlorite (concentration <6 %)	21 (18.6)
Detergents	17 (15.0)
Household product unspecified	11 (9.7)
Miscellaneous ^a	6 (5.3)

^a Includes ammonia (concentration <10 %), paints, and talc

Table 26 Alcohols and glycols

	N (%)
Ethanol ^a	737 (100.0)
Nonethanol alcohols and glycols	
Ethylene glycol	39 (41.0)
Isopropanol	34 (35.8)
Methanol	12 (12.6)
Miscellaneous ^b	10 (10.5)

^a Ethanol is considered a separate category

^b Includes glycol ethers, acetone, butanol, methyl ethyl ketone, and propylene glycol

Table 27 Caustics

	N (%)
Caustic Unspecified	16 (18.0)
Sodium hypochlorite (unknown concentration)	16 (18.0)
Sodium hydroxide	12 (13.5)
Hydrochloric acid	7 (7.9)
Potassium hydroxide	7 (13.5)
Sulfuric acid	5 (5.6)
Miscellaneous ^a	27 (30.7)

^a Includes acetic acid, boric acid, hydrogen peroxide (>10 %), sodium hypochlorite (>6 %), ammonium bifluoride, ammonium chloride, ammonium nitrate, formaldehyde, nitric acid, peroxyacetic acid, potassium permanganate, and zinc chloride

Table 28 Hydrocarbons

	N (%)
Hydrocarbon unspecified	40 (47.6)
Carbon tetrachloride	10 (11.9)
Toluene	5 (6.0)
Gasoline	4 (4.8)
Methylene chloride	3 (3.6)
Miscellaneous (<3 cases) ^a	22 (26.2)

^a Includes methylene chloride, chlorofluorocarbons, difluoroethane, kerosene, methane, mineral oil, paraffin oil, tetrachloroethylene, vinyl chloride, mineral spirits (Stoddard solvent), naphthalene, pine oil, polychlorinated biphenyls (PCB), xylene, and trichloroethylene

Table 29 Plants and fungi

	N (%)
Mold	28 (39.4)
Mushroom unspecified	16 (22.5)
<i>Nerium oleander</i>	5 (7.0)
Mushroom (<i>Psilocybe</i> spp.)	4 (5.6)
<i>Atropa belladonna</i> (deadly nightshade)	3 (4.2)
Miscellaneous (<3 cases) ^a	15 (21.1)

^a Includes *Piper methysticum* (kava), *Dieffenbachia* spp., *Digitalis* spp., *Illicium* spp. (star anise), *Mentha pulegium* (pennyroyal), *Rhododendron* spp., *Ricinus communis* (castor bean), *Solanum dulcamara* (bitter nightshade), *Sophora* spp. (kowhai), strychnine, valerian root, *Phytolacca americana* (pokeweed), *Taxus* spp. (yew), and *Toxicodendron* spp. (poison ivy)

Table 30 Anticoagulants

	N (%)
Warfarin	46 (79.3)
Rivoroxaban	4 (6.9)
Enoxaparin	3 (5.2)
Miscellaneous (<3 cases) ^a	5 (8.6)

^a Includes unspecified anticoagulant, clopidogrel, and dabigatran

Table 31 Gastrointestinal agents

	N (%)
Ondansetron	8 (22.9)
Ranitidine	6 (17.1)
Metoclopramide	5 (14.3)
Miscellaneous ^a	15 (44.1)

^a Includes bismuth subsalicylate, sodium bicarbonate, omeprazole, bisacodyl, docusate, pancrelipase, sennosides, sulfasalazine, famotidine, dexlansoprazole, esomeprazole, and cimetidine

Table 32 Endocrine

	N (%)
Levothyroxine	17 (50.0)
Dexamethasone	3 (8.8)
Prednisone	3 (8.8)
Miscellaneous (<3 cases) ^a	11 (32.4)

^a Includes methimazole, anabolic steroid unspecified, hydrocortisone, medroxyprogesterone, mestranol, methylprednisolone, progesterone, triiodothyronine, androsterone, and ethinyl estradiol

Table 33 Other pharmaceutical products

	N (%)
Hydrogen peroxide (concentration <10 %)	6 (20.0)
Tadalafil	3 (10.0)
Miscellaneous (<3 cases) ^a	21 (70.0)

^a Includes modafinil, pyridostigmine, radiological contrast dye, succinylcholine, sumatriptan, memantine, sildenafil, ursodiol, filgrastim, hyaluronic acid, methylethylglycyl-L-homocysteine, and rivastigmine

Table 34 Pesticides

	<i>N</i> (%)
Insecticides	
Pyrethroid unspecified	9 (33.3)
Aldicarb	2 (7.4)
Insecticide unspecified	2 (7.4)
Pentachlorophenol	2 (7.4)
Terbufos	2 (7.4)
Cyhalothrin	2 (7.4)
Miscellaneous (<2 cases) ^a	8 (29.6)
Herbicides	
Dicamba	3 (27.3)
Glyphosate	3 (27.3)
Diquat	2 (18.2)
Miscellaneous (<2 cases) ^b	3 (27.3)
Rodenticides	
Brodifacoum	10 (66.7)
Unspecified rodenticide	5 (33.3)
Fungicides ^c	1 (100.0)

^a Includes abamectin, chlorfenapyr, dimethoate, esfenvalerate, permethrin, phenothrin, bifenthrin, and hydropene

^b Includes triclopyr, iprodione, and 2,4,5-trichlorophenoxyacetic acid

^c Includes daconil

Table 35 Chemotherapeutic and immunological agents

	<i>N</i> (%)
Hydroxychloroquine	6 (26.1)
Methotrexate	5 (21.4)
Colchicine	3 (13.0)
Miscellaneous (<3 cases) ^a	9 (39.1)

^a Includes psoralen, bicalutamine, bosutinib, diphtheria/tetanus/pertussis vaccine, isotretinoin, tacrolimus, dimethylfumarate, and pazopanib

Table 36 Antiparkinsonism drugs

	<i>N</i> (%)
Levodopa/carbidopa	9 (47.4)
Ropinirole	5 (26.3)
Miscellaneous ^a	5 (26.3)

^a Includes entacapone, rasagiline, selegiline, and pramipexole

Table 37 Other nonpharmaceutical products

	<i>N</i> (%)
Nitrates	5 (35.7)
Miscellaneous ^a	9 (64.3)

^a Includes citric acid, iodine monochloride, isocyanates, methacrylates, silicone, tetrabenazine, tetrodotoxin, water, and sodium carbonate

Table 38 Anesthetics

	<i>N</i> (%)
Benzonatate	6 (54.5)
Lidocaine	2 (18.2)
Miscellaneous (<2 cases) ^a	3 (27.3)

^a Includes bupivacaine, mepivacaine, and sevoflurane

Table 39 Pulmonary agents

	<i>N</i> (%)
Albuterol	5 (55.6)
Clenbuterol	2 (22.2)
Miscellaneous (<2 cases) ^a	2 (22.2)

^a Includes theophylline and treprostinil

Table 40 Miscellaneous nonpharmaceuticals

	<i>N</i> (%)
Ingested foreign object	
Batteries	3 (100.0)
WMD/riot agents/radiological	
Mace	2 (66.7)
Botulinum toxin	1 (33.3)

WMD weapons of mass destruction

Table 41 Antidotal therapy

	N (%) ^a
<i>N</i> -acetylcysteine	861 (30.5)
Naloxone/nalmefene	573 (20.3)
Sodium bicarbonate	337 (11.9)
Physostigmine	186 (6.6)
Flumazenil	154 (5.5)
Glucagon	89 (3.2)
Thiamine	82 (2.9)
Fomepizole	79 (2.8)
Calcium	76 (2.7)
Folate	46 (1.6)
Atropine	43 (1.5)
L-carnitine	42 (1.5)
Octreotide	42 (1.5)
Vitamin K	42 (1.5)
Fab for digoxin	36 (1.3)
Lipid resuscitation	34 (1.2)
Insulin-euglycemic therapy	33 (1.2)
Cyproheptadine	24 (0.8)
Methylene Blue	13 (0.5)
Hydroxocobalamin	11 (0.4)
Pyridoxine	5 (0.2)
Bromocriptine	4 (0.1)
Coagulation factor replacement	3 (0.1)
2-PAM	2 (0.1)
Botulinum antitoxin	2 (0.1)
Dantrolene	2 (0.1)
Ethanol	2 (0.1)
Anticoagulation reversal	1 (0.0)
Nitrites	1 (0.0)

^a Percentages are out of the total number antidotes administered (2,825); 4.1 % of registry cases received more than one antidote

in a substantial fraction of entries. Another limitation is that other than fatality, there is no mechanism to determine the relative severity of outcome. In fatal cases where toxic exposure is responsible for clinical symptoms or findings, it is likely that death is attributable to poisoning. However, the current data collection methods do not allow for distinguishing whether a secondary, nontoxic etiology is responsible for death.

Table 42 Antivenom therapy

	N (%)
Polyvalent anti-Crotalidae Fab fragments	112 (91.8)
Scorpion antivenom	4 (3.3)
Spider antivenom	4 (3.3)
Other snake antivenom	2 (1.6)

Table 43 Chelation therapy

	N (%)
DMSA	15 (53.6)
Deferoxamine	6 (21.4)
Dimercaprol (BAL)	3 (10.7)
EDTA	3 (10.7)
Penicillamine	1 (3.6)

DMSA dimercaptosuccinic acid, *EDTA* ethylenediamine-tetraacetic acid

Table 44 Supportive care (pharmacological)

	N (%) ^a
Benzodiazepines	1,170 (56.0)
Vasopressors	206 (9.9)
Antipsychotics	165 (7.9)
Anticonvulsants	141 (6.7)
Opioids	122 (5.8)
Glucose (concentration > 5 %)	105 (5.0)
Albuterol (or other bronchodilator)	48 (2.3)
Neuromuscular blockers	41 (2.0)
Corticosteroids	37 (1.8)
Antiarrhythmics	19 (0.9)
Antihypertensives	16 (0.8)
Vasodilators	11 (0.5)
Beta blockers	8 (0.4)

^a Percentages are out of the total number of treatments administered (2,089); 3.9 % of registry cases received more than one form of treatment.

Table 45 Supportive care (nonpharmacological)

	N (%) ^a
IV fluid resuscitation	1,207 (62.0)
Intubation/ventilatory management	615 (31.6)
CPR	55 (2.8)
Pacemaker	19 (1.0)
Transfusion	15 (0.8)
Hyperbaric oxygen	13 (0.7)
ECMO	11 (0.6)
Cardioversion	10 (0.5)
Organ transplantation	2 (0.1)
Aortic balloon pump	1 (0.1)

^a Percentages are out of the total number of treatments administered (1,948); 4.1 % of registry cases received more than one form of treatment
CPR Cardiopulmonary resuscitation, *ECMO* extracorporeal membrane oxygenation

Table 46 Decontamination

	<i>N</i> (%) ^a
Activated charcoal	332 (79.4)
Whole bowel irrigation	48 (11.5)
Gastric lavage	23 (5.5)
External irrigation	15 (3.6)

^a Percentages are out of the total number of treatments administered (418); 28 registry cases received more than one form of treatment

The ToxIC Registry is not population based and has a specific ascertainment bias, which is present by design. The key inclusion criterion for entry into the Registry is the consultation by a medical toxicologist. Thus, Registry cases represent patients for whom there was a concern for significant toxicity. Cases of no, or mild, toxicity are likely to be underrepresented.

Discussion

This report of the ToxIC Registry serves as a comprehensive overview of cases involving medical toxicology consultations. The number of cases (Fig. 1) and number of participating institutions have grown steadily since the Registry's inception in 2010.

For the most part, the patterns seen in this report are similar to the trends seen in prior years [3]. The pattern of ADRs deserves further discussion. Adverse drug reactions are a considerable patient safety issue. Overall, ADRs ranked as the fourth most common reason for consultation. It is interesting that of the most common drugs associated with ADRs, only three, acetaminophen, oxycodone, and fentanyl, belong to the top three agent classes found in Table 5. Rather ADRs were dominated by antidepressants, antipsychotics, and anticonvulsants. The reason for this pattern is not clear. However, the medication types presented in Table 48 may indicate a disproportionate representation of psychiatric patients in ADR consultations. Nevertheless, these medications have a significant intrinsic potential for toxicity. Since the ADRs represented in this Registry are likely to be serious, future studies should be focused on evaluating their causes and clinical syndromes in more detail.

Table 47 Enhanced elimination

	<i>N</i> (%) ^a
Hemodialysis (toxin removal)	70 (29.7)
Urinary alkalization	61 (25.8)
Continuous renal replacement therapy	41 (17.4)
Hemodialysis (other indication)	36 (15.3)
Multiple-dose activated charcoal	27 (11.4)
Exchange transfusion	1 (0.4)

^a Percentages are out of the total number of treatments administered (236); 22 registry cases received more than one form of treatment

Table 48 Most common drugs associated with ADRs

	<i>N</i> (%)
Lithium	40 (6.9)
Valproic acid	26 (4.5)
Risperidone	18 (3.1)
Phenytoin	17 (2.9)
Bupropion	14 (2.4)
Digoxin	14 (2.4)
Citalopram	13 (2.2)
Acetaminophen	12 (2.1)
Haloperidol	12 (2.1)
Oxycodone	12 (2.1)
Lamotrigine	11 (1.9)
Methylphenidate	11 (1.9)
Sertraline	11 (1.9)
Fentanyl	10 (1.7)
Quetiapine	10 (1.7)

There have been a number of upgrades to the Registry in 2014 which should be evident in next year's annual report. Because most of the cases involve intentional pharmaceutical ingestions, we are evaluating the reasons for taking the medication in more detail. This includes an assessment of intent to determine if the medication was taken for therapeutic purposes, for attempts at self-harm, or for other reasons, such as to generate a pleasurable effect. Additional information about intent is being collected within each of these categories. Furthermore, this year, we are also beginning to obtain ethnic and racial data to refine the demographic profile for patients with the various kinds of toxicologic disease enumerated in this report.

Another factor of considerable interest to medical toxicologists involves the decision to terminate life support. This decision is especially complicated because of the difficulties in assessing brain death or neurological function when central nervous system-active medications are present, particularly in the high concentrations that are often found in these patients. In 2014, we began collecting additional information regarding the decision to terminate life support, and these data should be reflected in next year's report.

Conclusions

Cases requiring medical toxicology consultation in 2013 predominantly involved pharmaceuticals and illicit drugs. Reasons for these drug exposures were diverse and included intentional overdose, unintentional exposure, withdrawal syndromes, and ADRs. Nonopioid analgesics, sedative-hypnotic agents, and opioids remained the most frequently encountered agent classes. While over half of cases required some form of medical treatment, fatalities were uncommon.

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