J. Med. Toxicol. (2011) 7:266–276
DOI 10.1007/s13181-011-0185-z

TOXICOLOGY INVESTIGATION

The Toxicology Investigators Consortium Case Registry—The 2010 Experience

Jeffrey Brent · Paul M. Wax · Tayler Schwartz · Kurt C. Kleinschmidt · Kristin Engebretsen · Michael Beuhler · on Behalf of the Toxicology Investigators Consortium Case Registry Investigators

Published online: 9 November 2011

Abstract
Introduction The American College of Medical Toxicology Case Registry was established in 2010 as a method of identifying cases cared for by medical toxicologists at participating institutions. The Registry allows for the extraction of information from medical records making it the most robust multicenter database on chemical toxicities in existence. The current report is a summary of the data collected in 2010.
Methods All cases seen by medical toxicologists at participating institutions were entered on a database. Information characterizing patients entered in 2010 was tabulated.
Results Over the course of 2010, the number of institutions contributing cases grew from 4 to 50. Three thousand nine hundred forty-eight cases were entered. Emergency departments were the most common source of consultations, accounting for approximately 50% of the cases. The most common reason for consultations was for pharmaceutical overdoses, which occurred in 42% of the patients. The most common classes of agents were non-opioid analgesics (14%), sedative/hypnotics/muscle relaxants (10%), ethanol (8%), and opioids (8%). N-acetylcysteine was the most common antidote used, followed by opioid antagonists, sodium bicarbonate, and physostigmine. Anti-crotalidae Fab fragments were administered in 72% of the cases in which an antivenin was used. Signals were detected suggesting the possibility that amlodipine and metoprolol were associated with greater toxicity than had been previously recognized.
Conclusions The Registry can identify and characterize patients who have sufficient toxicity to require a consultation by a medical toxicologist. Hypotheses for further investigation emerged from the data. The Registry appears to be a potentially powerful tool for toxicovigilance and research.

Keywords Poisonings · Registry · Overdose · Toxicology · Medical toxicology

J. Brent (✉)
Toxicology Associates, University of Colorado,
School of Medicine,
Denver, CO, USA
e-mail: Jeffrey.Brent@UCDenver.edu

J. Brent
Colorado School of Public Health,
Denver, CO, USA

P. M. Wax · K. C. Kleinschmidt
University of Texas, Southwestern Medical Center,
Dallas, TX, USA

T. Schwartz
Brown University,
Providence, RI, USA

K. Engebretsen
Regions Hospital,
St. Paul, MN, USA

M. Beuhler
Carolinas Poison Center, Carolinas Medical Center,
Charlotte, NC, USA

The American College of Medical Toxicology (ACMT) Case Registry was established in early 2010 as a method of recording all cases cared for by medical toxicologists in the USA. This information was deemed important for both toxicosurveillance and research. The Case Registry is unique in that it contains information on patients who have all been evaluated at the bedside in hospitals or in clinics by

medical toxicologists. The Registry allows for the identification and subsequent extraction of detailed clinical information from patients' medical records making it the most robust multicenter clinical toxicology database in existence. Because all cases in the Registry are there by virtue of a medical toxicologist evaluation of the patient, the cases contained therein tend to be those with more serious toxicities.

A full description of the Registry has been published [1]. This is the first annual report and it is based on an analysis of 3,948 patients cared for by participating medical toxicologists at participating institutions during 2010. In 2010, there were 50 hospitals and clinics contributing cases to the Registry.

Methods

All participating centers, by agreement, enter all of their medical toxicology consultation cases into the Case Registry. Case entry is done online using a password-protected database maintained by ACMT. No patient identifiers are provided on the database [1]. Participation in the Case Registry is done pursuant to local institutional review board policies and procedures. A list of centers participating in the Case Registry during 2010 is listed in Table 1.

The information stored on the database is strictly descriptive and statistical. A number of fields are populated for each patient involving check offs or drop-down boxes. There are free text fields for signaling new, unusual, or sentinel cases, as well as for entry of the substances or species involved. More detailed queries require access to specific patient's charts. This is done only in the context of an approved study or as allowed by statute, such as reporting the details of an adverse drug reaction to the FDA.

For this report, a search was made of the database assessing the parameters in each field between the dates of 10 January 2010, when the database was initially started with four centers, and 31 December 31 2010, when 50 institutions were contributing data. The patient accrual over time is shown in Table 2. Only data fields with significant numbers of cases are shown.

Hospitalized cases in the Case Registry were either admitted directly to medical toxicology services or cared for by virtue of a consultation request. In this report, all types of patient encounters, as well as outpatient visits, are referred to as consultations.

Over the course of 2010, as more experience was gained, the specific statistical data collected on each patient evolved. This was due to the addition of several data fields. Because of these additions, some of the data reported by us are based on only a partial year collection and thus expressed only as the percentage of use over that period.

Table 1 Institutions contributing cases to the Case Registry in 2010

Banner Good Samaritan Medical Center, Phoenix, AZ
Bellevue Medical Center, New York, NY
Beth Israel Medical Center, Boston, MA
Carolinas Medical Center, Charlotte, NC
Children's Hospital Boston, Boston, MA
Children's Medical Center Dallas, Dallas, TX
Children's Mercy Hospitals & Clinics, Kansas City, MO
Children's Hospital of Wisconsin, Milwaukee, WI
Connecticut Children's Medical Center, Hartford, CN
Doernbecher Children's Hospital, Portland, OR
Elmhurst Hospital Center, Elmhurst, NY
Evanston North Shore University Health System, Evanston, IL
Froedtert Memorial Lutheran Hospital, Milwaukee, WI
Harrisburg Hospital, Harrisburg, PA
Hartford Hospital, Hartford, CT
Indiana University Hospital, Indianapolis, IN
John Dempsey Hospital, Farmington, CT
Littleton Adventist Hospital, Littleton, CO
Loma Linda University Medical Center, Loma Linda, CA
Maine Medical Center, Portland, MA
Methodist Hospital-Indianapolis, Indianapolis, IN
Mount Sinai Medical Center, New York, NY
Newark Beth Israel Medical Center, Newark, NJ
NJMS-University Hospital, Newark, NJ
North Shore University Hospital—Manhasset, NY
NYU Langone Medical Center, New York, NY
Oregon Health and Science University Hospital, Portland, OR
Parkland Memorial Hospital, Dallas, TX
Phoenix Children's Hospital, Phoenix, AZ
Porter Adventist Hospital, Denver, CO
Primary Children's Medical Center Salt Lake, Salt Lake City, UT
Regions Hospital, St. Paul, MN
Riley Hospital for Children, Indianapolis, IN
Robert Wood Johnson University Hospital, New Brunswick, NJ
SMDC Medical Center, Duluth, MN
Spectrum Health Hospitals—Grand Rapids, MI
St. Lukes Hospital, Duluth, MN
St. Mary's Medical Center, Duluth, MN
Strong Memorial Hospital, Rochester, NY
Swedish Medical Center, Denver, CO
UIC-Rush-Cook, Chicago, IL
University of Colorado Medical Center, Denver, CO
University of Connecticut Health Center, Farmington CT
University of Massachusetts Memorial Medical Center, Worcester, MA
University of Nebraska Medical Center, Omaha, NE
University of Utah Hospital, Salt Lake City, UT
UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA
UPMC Presbyterian/Shadyside, Pittsburgh, PA
UT Southwestern University Hospital—St. Paul, Dallas, TX
Wishard Memorial Hospital, Indianapolis, IN

Table 2 Case accrual by month in the 2010 ToxIC Case Registry

Month	Number of cases enrolled
January	46
February	99
March	156
April	277
May	207
June	312
July	364
August	556
September	502
October	472
November	574
December	383

Results

Demographic data about patients in the Case Registry are shown in Table 3. Most cases were in the age category 19 to 64 years old, although approximately one quarter of the patients were in the pediatric age group. As shown in Table 4, approximately half of the consultations came from emergency departments. Thirteen percent of the patients were transferred from other hospitals.

Intentional pharmaceutical overdose represents the most common type of patient in the Case Registry, accounting for 42% of the cases (Table 5). The next most common category was drug abuse, accounting for approximately one quarter of the patients. The agents of abuse were evenly divided between prescription and nonprescription drugs. Table 5 also shows the frequency of medical toxicology consultations for other reasons.

Table 6 shows the classes of agents responsible for medical toxicology consultations. The most common were non-opioid analgesics. Specific toxidromes were identified in 25% (997/3948) of the cases. The most common was the sedative-hypnotic, followed by anticholinergic toxidromes.

Table 3 Demographics of 3,948 Case Registry patients in 2010

	N
Female (%)[a]	48
Number pregnant	18
Age[b]	(%)
<2	138 (4)
2–6	212 (6)
7–12	100 (3)
12–18	489 (13)
19–64	2,662 (70)
>65	183 (5)

[a] Sex of patient was recorded in 90% of cases

[b] Patient age was documented in 96% of cases

Table 4 Referral sources for medical toxicology consultations for cases in the Case Registry in 2010

Emergency Department	2,037	52%
Outside hospital transfer	522	13%
Request from another hospital service (not Emergency Department)	399	10%
Primary care physician	262	7%
Poison control center	196	5%
Self-referred	93	2%
Employer/independent medical evaluation/workmens compensation	32	1%

Referral source was documented in 90% of the cases

The agents responsible for the 856 cases involving non-opioid analgesics are shown in Table 7. Acetaminophen was by far the most common, responsible for 70% of all cases in this category and thus 15% of Registry cases in 2010. Non-salicylate nonsteroidal anti-inflammatory agents (NSAIDS) made up, in the aggregate, 13% of the cases, of which ibuprofen was overwhelmingly the most common. Sixteen percent of cases were due to salicylates, 99% of which involved aspirin.

Sedative-hypnotic agents and muscle relaxants accounted for 826 cases in the Registry (Table 8). Of these, approximately two thirds were due to benzodiazepines, with

Table 5 Reason for medical toxicology consultation in cases entered into the Case Registry in 2010

	N (%)
Pharmaceutical overdose—intentional	1,675 (42)
Pharmaceutical overdose—unintentional	557 (14)
Nonprescription drug abuse	521 (13)
Prescription drug abuse	531 (13)
Non-pharmaceutical toxicant—intentional	200 (5)
Withdrawal	296 (7)
Non-pharmaceutical toxicant—unintentional	198 (5)
Adverse drug reaction[a]	116 (3)
Envenomation	137 (3)
Environmental evaluation	93 (2)
Interpretation of laboratory data	79 (2)
Occupational evaluation	116 (3)
Organ system dysfunction (e.g., liver failure)	114 (3)
Adverse drug event[b]	35 (1)
Occupational injury	4 (0)

Respondents could list more than one reason; thus, percentages add up to great than 100%

[a] Undesirable effect of a medication used in a normal dose

[b] Medication error resulting in harm

Table 6 Agents responsible for medical toxicology consultations for cases entered into the Case Registry in 2010

Agents	*N* (%)
Non-opioid analgesics	533 (14)
Sedative-hypnotics/muscle relaxants	413 (10)
Antidepressants	333 (8)
Ethanol	322 (8)
Opioids	284 (7)
Anticholinergics/antihistamines	212 (5)
Antipsychotics	200 (5)
Cardiovascular	148 (4)
Sympathomimetics	127 (3)
Anticonvulsants	117 (3)
Metals/metalloids/iron	90 (2)
Other—pharmaceutical	88 (2)
Envenomations	77 (2)
Gases/vapors/irritants/dusts	62 (2)
Other—nonpharmaceutical	60 (2)
Psychoactive drugs of abuse	48 (1)
Unknown class	57 (2)
Lithium	47 (1)
Non-ethanol alcohols and glycols	46 (1)
Diabetic medications	44 (1)
Plants and fungi	29 (1)
Caustics	28 (1)
Hydrocarbons	24 (1)
Antimicrobials	18 (<1)
Pesticides	15 (<1)
Herbals/dietary supplements/vitamins	16 (<1)
Anesthetics (local and general)	15 (<1)
Household (not caustics)	10 (<1)
Endocrine/hormones/steroids	6 (<1)
Chemotherapeutic and immune	6 (<1)

Not recorded for all cases, so the total is less than 100%

clonazepam being the most common. Muscle relaxants, particularly cyclobenzaprine and carisoprodol, accounted for 18% of cases. Barbiturates were responsible for only 5% of the cases, of which two thirds were due to butalbital.

As shown in Table 9, approximately equal numbers of atypical antidepressants and selective serotonin reuptake inhibitors were recorded. Almost one quarter of the cases were due to tricyclic agents. The most common agents in each class were bupropion, citalopram, and amitriptyline.

Opioids and opiates accounted for 620 cases (Table 10). The most common category was semisynthetic agents, primarily oxycodone. The synthetic agents made up approximately one third of the cases, of which methadone was the most common.

Table 7 Non-opioid analgesic agents in cases in the 2010 Case Registry

	N (%)
Total	856
Acetaminophen	602 (70)
NSAIDS	113 (13)
Ibuprofen	82 (73)
Unidentified NSAID	21 (19)
Nabumetone	3 (3)
Indomethacin	2 (2)
Naproxen	2 (2)
Etodolac	1 (<1)
Flurbiprofen	1 (<1)
Piroxicam	1 (<1)
Salicylates	139 (16)
Aspirin	137 (99)
Oil of wintergreen	1 (<1)
Salicylamide	1 (<1)
Other	2 (1)
Pain medication—unidentified	1 (50)
Ziconotide	1 (50)

NSAID nonsteroidal anti-inflammatory agent

As shown in Table 11, 366 cases were due to anticholinergic/antihistamine toxicity, most commonly diphenhydramine, followed by hydoxyzine. Table 12 shows the antipsychotic agent cases. Eighty-five percent of these cases involved atypical agents, particularly quetiapine and risperidone.

The 240 cases involving cardiovascular agents are shown in Table 13. As can be seen in the table, this category represents a diverse group of medications. The most common categories were beta blockers (36%) and calcium channel blockers (24%). Metoprolol was the most common beta blocker, accounting for 36% of the cases. This was followed by atenolol and propranolol. Amlodipine was responsible for almost half of the cases of calcium channel blocker toxicity. Verapamil accounted for approximately one quarter of the cases.

Table 14 shows the agents involved in sympathomimetic cases. Methamphetamine and cocaine were the most common, each accounting for nearly one third of the cases. Cases classified as involving psychoactive drugs of abuse are shown in Table 15. Fifty-nine percent of these were related to the use of dissociative agents, primarily dextromethorphan. The second most common group of agents in this category was cannabinoids, for which there were 11 cases involving synthetics.

Table 8 Sedative-hypnotics and muscle relaxants in cases in the 2010 Case Registry

	N (%)
Total	826
Benzodiazepines	521 (63)
Clonazepam	180 (34)
Alprazolam	145 (27)
Lorazepam	102 (19)
Diazepam	38 (7)
"Benzodiazepine"	31 (6)
Temazepam	17 (3)
Zopiclone	10 (2)
Chlordiazepoxide	3 (1)
Midazolam	3 (1)
Bromazepam	1 (<1)
Chlorazepate	1 (<1)
Muscle relaxants	152 (18)
Cyclobenzaprine	66 (43)
Carisoprodol	48 (32)
Baclofen	25 (16)
Methocarbamol	5 (3)
Tizanidine	4 (3)
Metaxolone	2 (1)
Orphenadrine	2 (1)
Barbiturates	38 (5)
Butalbital	25 (66)
Phenobarbital	12 (32)
"Barb"	1 (3)
Sedatives/hypnotics—other	103 (12)
Zolpidem	80 (86)
Zopiclone	10 (92)
Eszopiclone	7 (8)
Sleep aid	3 (3)
Chloral hydrate	1 (1)
Ramelteon	1 (1)
Zaleplon	1 (1)
Other	12 (1)
Buspirone	5 (42)
Dichloralphenazone	1 (8)
Meprobamate	1 (8)

Snakebites made up two thirds of the envenomation cases (Table 16). Most of these involved rattlesnakes. Twenty-eight percent of the cases involved copperhead bites.

Table 9 Antidepressant agents responsible for cases in the 2010 Case Registry

	N (%)
Total	653
Atypical	238 (36)
Bupropion	99 (42)
Trazodone	90 (38)
Venlafaxine	32 (13)
Mirtazapine	10 (4)
Desvenlafaxine	5 (2)
Nefazodone	1 (<1)
Selective serotonin norepinephrine reuptake inhibitor—unspecified	1 (<1)
Monoamine oxidase inhibitors	3 (<1)
Phenelzine	3 (100)
Selective serotonin reuptake inhibitors	253 (39%)
Citalopram	84 (13 %)
Sertraline	47 (19)
Fluoxetine	43 (17)
Paroxetine	33 (13)
Escitalopram	23 (9)
Nortriptyline	19 (7.5)
Fluvoxamine	2 (<1)
Unknown SSRI	2 (<1)
Tricyclic antidepressants	157 (24)
Amitriptyline	95 (61)
Duloxetine	24 (15)
Nortriptyline	19 (12)
Doxepin	10 (6)
Imipramine	6 (4)
Tricyclic antidepressant (unspecified)	2 (1)
Clomipramine	1 (<1)
Unknown	2 (<1)

SSRI selective serotonin reuptake inhibitor

Table 17 shows the number of cases involving alcohols and glycols. Ethylene glycol represented almost one half of the non-ethanol-related cases, followed by isopropanol and methanol.

Anti-diabetic medication-related cases are shown in Table 18. The sulfonylureas were the most common agents, accounting for 40% of cases. Metformin accounted for almost one third of cases while insulin was responsible for an additional approximately one quarter of the cases.

As shown in Table 19, basic substances, primarily sodium hypochlorite, made up nearly 50% of the caustic

Table 10 Opioids and opiates in 610 cases in the 2010 Case Registry

	N (%)
Total	610
Naturally occurring	110 (18)
Heroin	61 (55)
Morphine	37 (34)
Codeine	12 (11)
Opioids not otherwise specified	19 (3)
Opioids	19 (100)
Semisynthetic	268 (44)
Oxycodone	142 (53)
Hydrocodone	110 (41)
Hydromorphone	14 (5)
Oxymorphone	2 (1)
Synthetic	213 (35)
Methadone	98 (46)
Tramadol	49 (23)
Fentanyl	36 (17)
Buprenorphine	25 (12)
Meperidine	2 (1)
Diphenoxylate	1 (<1)
Pentazocine	1 (<1)
Tapentadol	1 (<1)

Table 11 Anticholinergic/antihistamine agents in cases in the 2010 Case Registry

	N (%)
Anticholinergics	35 (10)
Benztropine	21 (60)
Hyoscyamine	4 (11)
Atropine	3 (9)
Oxybutynin	3 (9)
Trihexyphenidyl	2 (6)
Glycopyrrolate	1 (3)
Unknown antihistamine	1 (3)
Antihistamines	331 (90)
Diphenhydramine	234 (71)
Hydroxyzine	34 (10)
Doxylamine	20 (6)
Chlorpheniramine	11 (3)
Promethazine	10 (3)
Dimenhydrinate	5 (2)
Meclizine	4 (1)
Antihistamine	3 (1)
Cetirizine	3 (1)
Loratadine	3 (1)
Cyproheptadine	1 (<1)
Dicyclomine	1 (<1)
Fexofenadine	1 (<1)
Pyrilamine	1 (<1)

Table 12 Antipsychotic agents in cases on the 2010 Case Registry

	N (%)
Total	369
Atypical	313 (85)
Quetiapine	178 (57)
Risperidone	43 (14)
Olanzapine	37 (12)
Aripiprazole	23 (7)
Ziprasidone	17 (5)
Clozapine	13 (4)
Asenapine	1 (<1)
Lloperidone	1 (<1)
First-generation antipsychotics	56 (15)
Haloperidol	30 (54)
Chlorpromazine	11 (20)
Perphenazine	6 (11)
Prochlorperazine	3 (5)
Fluphenazine	2 (4)
Loxapine	2 (4)
Thioridazine	2 (4)

cases. Acids made up 22%, the most common being acetic, hydrochloric, and hydrofluoric. Each of these was responsible for almost one third of the acid cases.

Specific antidotes used are shown in Table 20. Because these data are only from a part of the year they are expressed as percentages of use. The most commonly administered antidotes were N-acetylcysteine, opioid antagonists, sodium bicarbonate, and physostigmine. Ovine crotalidae Fab snake antivenin was the most commonly used antivenin and succimer was the most frequently administered chelator.

Of the cases in which an enhanced elimination technique was utilized, hemodialysis constituted over half (53%). The latter was used much more frequently than continuous renal replacement therapy, which was done in 9% of these cases. Urinary alkalinization was done in 24% and multi-dose activated charcoal was used in 14% of the cases in which an enhanced elimination technique was recorded.

Three 3% of cases in the Registry were listed as adverse drug reactions (ADRs). Detailed categorization of the ADRs is shown in Table 21. Eighty-four different medications were implicated. The most common were

Table 13 Cardiovascular medications responsible for cases in the 2010 Case Registry

	N (%)
Total	240
ACE inhibitors	3 (1)
Enalapril	1 (33)
Lisinopril	1 (33)
Quinapril	1 (33)
Alpha-2 agonists	2 (<1)
Clonidine	1 (50)
Guanfacine	1 (50)
Alpha-blockers	3 (1)
Alfuzosin	1 (33)
Prazosin	1 (33)
Tamsulosin	1 (33)
Angiotensin II receptor antagonists	4 (2)
Valsartan	2 (50)
Olmesartan	1 (25)
Losartan	1 (25)
Antiarrhythmics	1 (<1)
Amiodarone	1 (100)
Anticoagulants	12 (5)
Coumadin	11 (92)
Enoxaparin	1 (8)
Antilipids	10 (4)
Simvastatin	5 (50)
Atorvastatin	1 (10)
Fenofibrate	1 (10)
Gemfibrozil	1 (10)
Pravastatin	1 (10)
Rosuvastatin	1 (10)
Beta-blockers	87 (36)
Metoprolol	31 (36)
Atenolol	25 (29)
Propranolol	16 (18)
Carvedilol	10 (11)
Beta blockers	2 (2)
Betaxolol	1 (1)
Labetalol	1 (1)
Nadolol	1 (1)
Calcium-channel blockers	57 (24)
Amlodipine	27 (47)
Verapamil	13 (23)
Diltiazem	12 (21)
Nifedipine	4 (7)
Felodipine	1 (2)
Digoxin	35 (15)
Diuretics	22 (9)
Chlorothiazide	9 (41)
Hydrochlorothiazide	8 (36)
Acetazolamide	1 (5)
Parabrom	1 (5)
Suspected diuretic abuse	1 (5)
Torsemide	1 (5)
Triamterene	1 (5)
Nitrates	1 (<1)
Isosorbide	1 (100)
Vasodilators	3 (1)
Hydralazine	1 (33)
Minoxidil (Topical)	1 (33)
Nitroprusside	1 (33)

ACE angiotensin-converting enzyme

acetaminophen occurring in 13% of cases and lithium in 12%.

Discussion

The ACMT Case Registry was developed because there is no other multicenter data collection system that could lead to detailed medical record-validated information on patients experiencing adverse toxicological or pharmacological effects. The data from the patients in the Case Registry are unique in that these are of high quality specifically related to toxicological issues because the patients were directly evaluated and cared for by a medical toxicologist.

The Case Registry collects de-identified patient data on all medical toxicology consultations by participating institutions. This dataset provides an important profile of those patients requiring care by medical toxicologists. Because of this, the Case Registry does not provide incidence data on all poisonings. Patients with minor exposures are less likely than those with serious toxicities to receive care by medical toxicologists. Thus, the Registry provides information biased towards sicker

Table 14 Sympathomimetic agents responsible for cases in the 2010 Case Registry

	N (%)
Total	346
Amphetamines	155 (45)
Amphetamine	51 (33)
Methamphetamine	99 (64)
Lisdexamfetamine	6 (6)
Caffeine	37 (11)
Cocaine	102 (29)
Methylphenidates	26 (8)
Methylphenidate	24 (92)
Dexmethylphenidate	2 (8)
Mephedrone	1 (<1)
Methylenedioxymethamphetamine	12 (3)
Other	13 (4)
Phenylephrine	4 (31)
Tetrahydrozoline	3 (23)
Atomoxetine	2 (15)
Epinephrine injection	2 (15)
Isometheptene	1 (8)
Methylone	1 (8)

Table 15 Psychoactive drugs of abuse responsible for cases in the 2010 Case Registry

	N (%)
Total	149
Cannabinoids	38 (26)
Non-synthetic cannabinoids	27 (71)
Synthetic cannabinoids	11 (29)
Dissociative agents	88 (59)
Dextromethorphan	65 (74)
Phencyclidine	22 (25)
Ketamine	1 (1)
Gamma hydroxybutyrate and related agents	14 (9)
Gamma hydroxybutyrate	12 (86)
4-Butanediol	1 (7)
Gamma butyrolactone	1 (7)
Hallucinogens	8 (5)
LSD	6 (75)
Hallucinogen—unknown	1 (13)
Mescaline	1 (13)
Other	1 (<1)
Acetylate	1 (100)

LSD lysergic acid diethylamide

Table 16 Envenomations responsible for cases in the 2010 Case Registry

	N (%)
Total	107
Scorpion	26 (24)
Scorpion	26 (100)
Snakes	71 (66)
Crotaline	
Rattlesnake	39 (55)
Copperhead	20 (28)
“Crotalid”	8 (11)
Eyelash viper	1 (1)
Elapidae	
Coral snake	1 (1)
Other	
Dry bite	1 (1)
Unknown snake	1 (1)
Spiders	10 (9)
Brown recluse spider	9 (90)
Spider bite—unknown type	1 (10)

patients and can be used, therefore, to extract information on more serious toxicities.

The Case Registry began in 2010 with only four centers [1]. Over the course of the year, progressively more centers joined the Registry so that by 31 December 2010 there were 50 participating institutions. Therefore, the rate of patient accrual increased as the year progressed. The fact that case accrual was not random over the year, but was weighted towards the latter part of 2010, is unlikely to have a major effect on most of the data points in the Registry. However, for toxicities in which there is a seasonal predominance, such as carbon monoxide poisoning, or geographical predominance, such as crotaline envenomation, the frequencies presented here may not be representative of what would have been collected by all centers over a 12-month period.

A number of interesting trends can be gleaned from the data we present. Serious poisonings appear to be least common in the 7–12 year age group. Children in this age range are beyond the stage where they are vulnerable to the accidental toxicities seen in younger

Table 17 Alcohols and glycols responsible for cases in the 2010 Case Registry

	N (%)
Total	478
Ethanol	386 (81)
Non-ethanol alcohols and glycols	92 (19)
Ethylene glycol	43 (47)
Isopropyl alcohol	20 (22)
Methanol	16 (17)
Acetone	3 (3)
Glycol ethers	3 (3)
Diethylene glycol	3 (3)
Butanol	1 (1)
Industrial denatured alcohol	1 (1)
Triethylene glycol monobutyl ether	1 (1)
Unknown—suspected ethylene glycol or methanol	1 (1)

patients and many have not yet begun the patterns of possible drug abuse and attempts at self-harm which become more common in teenagers. The pattern of few exposures in this age group is mirrored in the data collected by poison centers [2].

A truly unique aspect of the Registry is that for the first time we have data on the bedside practice patterns of medical toxicologists, as seen in Tables 4 and 5. Such information may be useful to individual medical toxicologists as they strategize on building a successful practice.

Table 18 Diabetic medications responsible for cases in the 2010 Case Registry

	N (%)
Total	72
Biguanides	22 (31)
Metformin	22 (100)
Insulin	16 (22)
Other	4 (6)
Liraglutide	4 (100)
Sulfonylurea derivatives	29 (40)
Glyburide	10 (34)
Glimepiride	8 (26)
Glipizide	7 (24)
Sulfonylurea—unspecified	4 (33)
Thiazolidinediones	1 (1)
Pioglitazone	1 (100)

Table 19 Caustic agents responsible for cases in the 2010 Case Registry

	N (%)
Total	59
Acids	13 (22)
Acetic acid	4 (31)
Hydrochloric acid	4 (31)
Hydrofluoric acid	4 (31)
Sulfuric acid	1 (8)
Bases	29 (49)
Sodium hypochlorite	13 (45)
Sodium hydroxide	5 (17)
Ammonia	4 (14)
Ammonium chloride	3 (10)
Potassium hydroxide	3 (10)
Ammonium nitrates	1 (3)
Other	17 (29)
Hydrogen peroxide	3 (10)
Phenol	2 (7)
Surfactant	2 (7)
Unknown name caustic degreaser	2 (7)
Zinc chloride	2 (7)
Alcohol ethoxylates	1 (3)
“Caustic”	1 (3)
Dishwashing detergent	1 (3)
Multiple cleaning agents identities unknown	1 (3)
Sodium hydroborate	1 (3)
Unknown toilet bowel cleaner	1 (3)

The most common type of patients cared for by medical toxicologists are those who have intentionally overdosed on a pharmaceutical agent and for whom the consultation arose from an emergency department. However, there is a broad diversity of reasons that medical toxicologists are consulted (Table 5) and intentional pharmaceutical overdoses account for less than half of all patients. N-acetylcysteine was the most commonly used antidote, a fact consistent with the high frequency of acetaminophen-related consultations.

Of all cases involving non-opioid analgesics, acetaminophen comprised 70% and non-salicylate NSAIDS 13%. Because of the possibility of acetaminophen-induced hepatic injury, patients ingesting this agent are often admitted for antidotal therapy with N-acetylcysteine. The decreased late toxicity of NSAIDS compared to acetaminophen likely results in fewer hospital admissions and medical toxicology consultations for this group of medications.

Table 20 Antidotes administered to patients in the Case Registry in 2010

	(%)[a]
Non-antivenin, non-chelator	
N-acetylcysteine	27
Naloxone/nalmefene	17
Sodium bicarbonate	14
Physostigmine	11
Flumazenil	9
Fomepizole	4
Thiamine	3
Vitamin K	3
Glucagon	2
Calcium	2
Folate	1
Pyridoxine	1
Fab for digoxin	1
Atropine	1
Insulin—euglycemic therapy	1
Octreotide	1
Lipid resuscitation therapy	1
Antivenin	
Ovine crotalidae polyvalent immune fab snake antivenin	72
Scorpion	18
Other snake antivenin	10

Data on the use of other antidotes were collected. Only those with non-zero use are shown in the table

[a] Percents given are those for patients who received an antidote or for those who received an antivenin

Table 21 Adverse drug reaction cases in the 2010 registry

	N (%)
Total	174
Acetaminophen	10 (13)
Lithium	9 (12)
Digoxin	7 (9)
Ethanol	5 (6)
Haloperidol	5 (6)
Morphine	4 (5)
Oxycodone	4 (5)
Valproic acid	4 (5)
Amphetamine	3 (4)
Benzodiazepines	3 (4)
Bupropion	3 (4)
Lisinopril	3 (4)
Lorazepam	3 (4)
Olanzapine	3 (4)
Phenytoin	3 (4)
Alprazolam	2 (3)
Atenolol	2 (3)
Citalopram	2 (3)
Clonazepam	2 (3)
Clozapine	2 (3)
Diphenhydramine	2 (3)
Fentanyl	2 (3)
Hydrocodone	2 (3)
Lidocaine	2 (3)
Metformin	2 (3)
Methadone	2 (3)
Methamphetamine	2 (3)
Nortriptyline	2 (3)
Paroxetine	2 (3)
Quetiapine	2 (3)
Risperidone	2 (3)
Sertraline	2 (3)

Only medications listed more than once are included. One hundred and seventy-four substances were reported in 116 patients

It is clear that there is a major difference in the frequency with which cases appear on the Case Registry and their market share. This is dramatically demonstrated with the cardiovascular agents where angiotensin-converting enzyme inhibitors accounted for only 1% of the cases and statins only 4%. In contrast, there was an overrepresentation of beta blockers and calcium channel blockers, the two categories of cardiovascular agents associated with the most significant acute toxicity. Although propranolol and verapamil are generally thought of as the most toxic agents in this category, the predominance of metoprolol and amlodipine cases suggest that these agents may have a greater likelihood of causing toxicity than has been previously recognized. However, the difference in submissions to the Registry may reflect a difference in the number of dispensed prescriptions. For example, in 2009, metoprolol ranked number 9 and amlodipine ranked number 15 in number of prescriptions. Conversely, verapamil SR was ranked number 198 and propranolol was not among the top 200 prescribed medications [3]. This is an example of how the Registry can generate important hypothesis-driven studies.

It is interesting to note that ethanol and fomepizole are both used for the same indication—inhibition of alcohol dehydrogenase after the ingestion of a potentially toxic alcohol or glycol. In 100% of the cases in which an alcohol dehydrogenase inhibitor was used, fomepizole was chosen. This suggests that medical toxicologists, or the pharmacies in the institutions in which they practice, appear to have a strong preference for using fomepizole over ethanol.

One hundred and sixteen cases were classified as ADRs, representing 3% of all cases in the Registry. This is important as medical toxicologists are consulted for primarily serious adverse reactions. Simple rashes (non-blistering, non-bullous) make up a very large group of non-serious adverse drug reactions, yet there were only two such ADR cases in the Registry in 2010. Thus, ADRs potentially constitute a major area for toxicosurveillance for the Case Registry.

Interestingly, acetaminophen and lithium were the two medications most implicated in causing ADRs. Although it is possible that the acetaminophen-related ADRs are from liver function test abnormalities with therapeutic use, and the lithium cases involve such known therapeutic side effects as hypothyroidism or nephrogenic diabetes insipidus, these deserve further study.

The Case Registry has certain limitations. It provides real world prospective data on cases seen by medical toxicologists. However, as in the real world, many clinical conclusions are more diagnostic impressions than absolute truths. For example, in many cases, the substances implicated in the patients' clinical presentation have not been verified by full analytical confirmation.

Categorization of some of the specific substances is subject to debate. In several cases, there was no absolute right answer. For example, should diphenhydramine be classified as an antihistamine or an anticholinergic? In cases of controversy, the substances were categorized by consensus.

Despite the Case Registry collecting nearly 4,000 cases in 2010, the number of cases in individual cells can be small. The Case Registry should be viewed as a constantly growing body of data. For purposes of aggregating cases together for research studies, the 2010 cases will be added to those subsequently collected. Given that the Registry's current accrual rate is approximately 150 entries per week, the number of individual cases in the various cells should grow considerably over time.

This report is based only on statistical data from patients entered into the Case Registry. Therefore, these data are best viewed as providing information about the agents that cause serious poisonings, the reasons for such poisonings, and commonly used therapies. No attempt was made to correlate specific exposures with specific reasons for poisonings or with any age group. Because the Registry is continuing to collect cases, and at the time of publication of this report 57 institutions are contributing cases, it is expected that these further analyses will be forthcoming.

The strongest data available through the Case Registry are contained in the patients' medical records. No attempt was made to mine any data from these records for this report. It is expected that as issues of toxicosurveillance or research questions arise, more in-depth analyses using individual patient medical records will be done.

Acknowledgments Funding for this project comes from the American College of Medical Toxicology.

Conflicts of interest None

References

1. Wax PM, Kleinschmidt K, Brent J (2011) The toxicology investigators consortium (ToxIC) registry. J Med Toxicol. doi:10.1007/s13181-011-0177-z
2. Bronstein AC, Spyker DA, Cantilena LR, Green JL, Rumack BH, Griffin SL (2010) 2009 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th annual report. Clin Toxicol 48(10):979
3. Pharmacy Times. May 11, 2011 posting. http://www.pharmacytimes.com/publications/issue/2010/May2010/RxFocusTopDrugs-0510. Accessed 28 August 2011