

The Toxicology Investigators Consortium Case Registry—The 2011 Experience

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Abstract In 2010, the American College of Medical Toxicology established its Case Registry, the Toxicology Investigators Consortium (Toxic). Toxic is a prospective registry, which exclusively compiles suspected and confirmed toxic exposure cases cared for at the bedside by medical toxicologists at its participating sites. The Registry aims to fulfill two important gaps in the field: a real-time toxicosurveillance system to identify current poisoning trends and a powerful research tool in toxicology. Toxic allows extraction of information from medical records making it the most robust multicenter database on chemical toxicities in existence. All cases seen by medical toxicologists at participating institutions were entered in a database. Information characterizing patients entered in 2011 was

tabulated. 2010 data was also included so that cumulative total numbers could be described as well. The current report is a summary of the data collected in 2011 in comparison to 2010 entries and also includes cumulative data through December 31st, 2011. During 2011, 28 sites with 49 specific institutions contributed a total of 6,456 cases to the Registry. The total number of cases entered into the registry at the end of 2011 was 10,392. Emergency departments remained the most common source of consultations in 2011, accounting for 53 % of cases. The most common reason for consultation was for pharmaceutical overdoses, which occurred in 48 % of patients, including intentional (37 %) and unintentional (11 %) exposures. The most common classes of agents were sedative-hypnotics (1,492 entries in 23 % of cases), non-opioid analgesics (1,368 cases in 21 % of cases), opioids (17 %), antidepressants (16 %), stimulants/sympathomimetics (12 %), and ethanol (8 %). *N*-acetylcysteine was the most commonly administered antidote during 2011, similar to 2010, followed by the opioid antagonist naloxone, sodium bicarbonate, physostigmine and flumazenil. Anti-crotalid Fab fragments (CroFab) were administered in 106 out of 131 cases in which an envenomation occurred. There were 35 deaths recorded in the Registry during 2011. The most common associated agents, including when reported as sole agent or in combination with other agents, were opioids and analgesics (acetaminophen, aspirin, NSAIDs) with ten and eight deaths, respectively. Oxycodone was reported in six of the ten opioid-related deaths and heroin in three. Acetaminophen was the most common single agent reported overall being identified in all eight of the death cases attributed to analgesics. There were significant trends identified during 2011. Cases involving designer drugs including psychoactive bath salts and synthetic cannabinoids increased substantially from 2010 to 2011. The psychoactive bath salts were responsible for a large increase in stimulant/sympathomimetic-related

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cases reported to the Registry in 2011 with overall numbers doubling from 6 % of all Registry entries in 2010 to 12 % in 2011. Entries involving psychoactive drugs of abuse also increased twofold from 2010 to 2011 jumping 3 to 6 %, primarily due to increasing frequency of synthetic cannabinoid (“K2”) related intoxications as 2011 progressed. The 2011 Registry included over 600 ADR’s (10 % of Registry Cases) with 115 agents causing at least 2 ADR’s. This is up from only 3 % of cases (116 total cases) in 2010. The ToxIC Case Registry continues to grow. At the end of 2011, over 10,000 cases had been entered into the Registry. As demonstrated by the trends identified in psychoactive bath salt and synthetic cannabinoid reports, the Registry is a valuable toxicosurveillance and research tool. The ToxIC Registry is a unique tool for identifying and characterizing confirmed cases of significant or potential toxicity or complexity to require bedside consultation by a medical toxicologist.

Keywords Poisonings · Registry · Overdose · Toxicology · Medical toxicology

The Toxicology Investigators Consortium (ToxIC) Case Registry was established in 2010 by the American College of Medical Toxicology (ACMT) as a novel prospective toxico-surveillance and research tool. Participating sites record all cases cared for at the bedside or in clinics by medical toxicologists. Twenty-eight sites were actively contributing cases to the Registry in 2011. The Registry allows for identification and subsequent extraction and pooling of detailed clinical information from patients’ medical records across all centers. Through the use of expanded data collection on areas of particular interest the Registry serves as a source of prospective multi-center studies.

Because all cases on the Registry have had a formal consultation and care by a medical toxicologist, the cases recorded tend to be comprised of those with serious or potentially serious toxicities. A full description of the Registry has been previously published [1].

This is the second annual report and it includes comprehensive and comparative data from the first 2 years of Registry activity (2010–2011). Although data from 2010 Registry cases is included and compared to 2011 Registry cases, comprehensive information about the 2010 Registry experience is published elsewhere [2]. Total numbers of cases entered include 3,936 from 2010 and 6,456 in 2011, for a cumulative number of Registry cases of 10,392 by December 31st, 2011. The increase in the number of cases entered in 2011 occurred despite there being less sites participating overall (28 in 2011 vs. 33 in 2010). This increase is likely due to increased familiarity with the Registry and sites entering a greater percentage of their consults. The number of cases entered per site ranged from 3 to 847.

Table 1 Institutions contributing cases to the registry in 2011

Banner Good Samaritan Medical Center, Phoenix AZ
Bellevue Medical Center, New York, NY
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
Denver Health, Denver, CO
Doernbecher Children’s Hospital, Portland, OR
Evanston North Shore University Health System, Evanston, IL
Froedtert Memorial Lutheran Hospital, Milwaukee, WI
Harrisburg Hospital, Harrisburg, PA
Hartford Hospital, Hartford, CT
Hospital for Sick Children, Toronto, Canada
Indiana University Hospital, Indianapolis, IN
John Dempsey Hospital, Farmington, CT
Littleton Adventist Hospital, Littleton, CO
Methodist Hospital-Indianapolis, Indianapolis, IN
Morristown Memorial Hospital, Morristown, NJ
Mount Sinai Medical Center, New York, N
Newark Beth Israel Medical Center, Newark, NJ
New York City VA Hospital, New York, NY
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
Rambam Health Care Campus, Haifa, Israel
Regions Hospital, St Paul, MN
Riley Hospital for Children, Indianapolis, IN
Robert Wood Johnson University Hospital, New Brunswick, NJ
San Antonio Military Medical Center, San Antonio, TX
San Francisco General Hospital, San Francisco, CA
Spectrum Health Hospitals, Grand Rapids, MI
Strong Memorial Hospital, Rochester, NY
Swedish Medical Center, Denver, CO
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
UPMC Children’s Hospital of Pittsburgh, Pittsburgh, PA
UPMC Magee Women’s Hospital, Pittsburgh, PA
UPMC Presbyterian/Shadyside, Pittsburgh, PA
UT Southwestern University Hospital—St Paul, Dallas, TX
Virginia Commonwealth University Medical Center, Richmond, VA
Wishard Memorial Hospital, Indianapolis, IN

Methods

All participating centers aim to enter all of their medical toxicology consultations into the Registry. Case entry is done online using a password-protected user-friendly interface developed and maintained by ACMT and overseen by the ToxIC Steering Committee. No patient identifiers are provided on the database. Participation in the Registry is done pursuant to review by local institutional review board policies and procedures. A list of centers participating in the Registry during 2011 is provided in Table 1.

The information stored on the database includes demographic and detailed clinical data obtained through toxicology consultations on the patient's exposure, encounter, signs, symptoms, clinical course, treatment, and disposition. For this report, consultation refers to all patient encounters whether admitted directly to a medical toxicology service on an inpatient unit or when the toxicologist served as a consultant. Outpatient and Emergency Department encounters are also referred to as consultations as long as a formal medical toxicology consultation was done.

Information about a patient encounter is collected and subsequently entered into the online data interface form. Technically, 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 (i.e., envenomations) involved. More detailed queries require access to specific patient's charts pursuant IRB approval. 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.

During 2011 the Drug Abuse category was modified so that prescription, non-prescription, and other categories of drug abuse were recorded separately in order to identify different categories of drug abuse. Drug withdrawal syndromes were similarly modified.

For this report, a search was made of the database assessing the parameters in each field between the dates of 1 January, 2011 and 31 December, 2011. For comparative purposes, and when such data exists, the 2010 and cumulative 2010 and 2011 data are shown.

Results

Patient accrual throughout 2011 is included in Table 2. Demographic data about patients in the Registry are shown in Table 3; 69 % of consultations involved patients aged 19 to 64 years old, 26 % involved pediatric patients ages 18 years or less and 5 % involved ages >65 years old. As shown in Table 4, in 2011, just over half of the consultations came from emergency

Table 2 Number of cases enrolled by month 2010–2011

Month, year	Number of cases enrolled
January, 2010	46
February, 2010	98
March, 2010	155
April, 2010	276
May, 2010	206
June, 2010	311
July, 2010	363
August, 2010	555
September, 2010	500
October, 2010	471
November, 2010	573
December, 2010	382
January, 2011	474
February, 2011	504
March, 2011	774
April, 2011	616
May, 2011	322
June, 2011	500
July, 2011	684
August, 2011	572
September, 2011	429
October, 2011	635
November, 2011	477
December, 2011	502

departments and 12 % of the patients were transferred from other hospitals to ToxIC sites.

In 2011, intentional pharmaceutical exposure represented the most common type of encounter in the Registry, accounting for 37 % of cases in which "exposure type" identified. This is consistent with data obtained in 2010 where 42 % of cases involved intentional pharmaceutical exposure (Table 5). Drug abuse was also a common reason for case entry in 2011. Overall, drug and alcohol abuse

Table 3 Demographics of registry cases

	N 2010	N 2011	N total
Female (%)	48 %	51 %	
# pregnant	18	53	71
Age (%)			
<2 years	138 (4 %)	235 (4 %)	373 (4 %)
2–6 years	212 (6 %)	320 (5 %)	532 (5 %)
7–12 years	100 (3 %)	124 (2 %)	224 (2 %)
13–18 years	489 (13 %)	953 (15 %)	1442 (14 %)
19–64 years	2662 (70 %)	4490 (69 %)	7152 (69 %)
>65 years	183 (5 %)	378 (6 %)	561 (5 %)
Total entries	3,948	6,468	10,416

Table 4 Referral sources for medical toxicology consultations

Emergency department	2,037 (52 %)	3,431 (53 %)
Outside hospital transfer	522 (13 %)	804 (12 %)
Request from non-ED service	399 (10 %)	1043 (16 %)
Primary care physician/other outpatient treating physician ^c	262 (7 %)	NA
Poison Control Center	196 (5 %)	114 (2 %)
Self-referred ^c	93 (2 %)	63 (1 %)
Employer/IME/Work comp	32 (1 %)	67 (1 %)

^a Referral source was documented in 90 % of cases in 2010

^b Referral source was documented in 85 % of cases in 2011

^c In 2011 Primary Care Physician category changed to Primary Care Physician/All Outpatient Providers

^d In many cases multiple referral sources were selected

^e Refers to self-referral to out-patient clinic

accounted for about approximately a quarter of all entries. The agents of abuse were fairly evenly divided between

Table 5 Reasons for medical toxicology consultation

	2010 (%)	2011 (%)
Intentional exposure—pharmaceutical	1,675 (42)	2499 (39)
Intentional exposure—non-pharmaceutical	200 (5)	535 (9)
Unintentional exposure—pharmaceutical	557 (14)	761 (12)
Unintentional exposure—non-pharmaceutical	198 (5)	293 (5)
Drug abuse—illicit/non-prescription drug abuse ^a	NA	348 (5)
Drug abuse—prescription ^a	531 (13)	442 (7)
Nonprescription Drug Abuse	521 (13)	348 (5)
Ethanol abuse	NA	325 (5)
Withdrawal ^a	296 (7)	325 (5)
Adverse drug event ^{b,c}	35 (1)	95 (1)
Adverse drug reaction ^{c,d}	116 (3)	229 cases (4) and 601 (9) single agents
Envenomation	137 (3)	220 (3)
Organ system dysfunction (e.g. liver failure)	114 (3)	116 (2)
Interpretation of laboratory data	79 (2)	178 (3)
Occupational evaluation	116 (3)	137 (2)
Environmental evaluation	93 (3)	199 (3)
Occupational injury	4 (0)	58 (1)

Many cases had multiple reasons for medical toxicology consultation included

^a Medication error resulting in harm

^b Certain categories underwent modification from 2010 to 2011 including drug abuse and withdrawal categories.

^c Total number of Adverse Drug Reaction (ADR) cases 601 single agents and 229 cases

^d Undesirable effect of a medication used in a normal dose

prescription and nonprescription drugs in 2010; however in 2011 prescription drug abuse became a more frequent reason for toxicology consultation than non-prescription drug abuse. Table 5 also shows the frequency of medical toxicology consultations for other reasons.

Sedative–hypnotics, with 1,492 exposures (23 % of all Registry cases), were the most common class of agents responsible for medical toxicology consultations in 2011, with clonazepam being the most frequently encountered followed by alprazolam. They surpassed non-opioid

Table 6 Agent class involved in consultations

Agents	2010 N (%) ^a	2011 N (%) ^a	Total (%) ^a
Sedative–hypnotics/muscle relaxants	783 (20 %)	1492 (23 %)	2275 (21)
Non-opioid analgesics	854 (22 %)	1368 (21 %)	2222 (21)
Opioids	619 (16 %)	1100 (17 %)	1719(17 %)
Antidepressants	659 (17 %)	1029 (16 %)	1688(16 %)
Sympathomimetics	247 (6 %)	774 (12 %)	1021(10 %)
Cardiovascular	334 (8 %)	631 (10 %)	965 (9 %)
Antipsychotics	366 (9 %)	587 (9 %)	953 (9 %)
Ethanol	371 (10 %)	580 (9 %)	951 (9 %)
Anticholinergics/antihistamines	378 (10 %)	549 (8 %)	927 (9 %)
Anticonvulsants	218 (6 %)	451 (7 %)	669 (7 %)
Psychoactive drugs of abuse	135 (3 %)	360 (6 %)	495 (5 %)
Metals/metalloids/iron	154 (4 %)	322 (5 %)	476 (5 %)
Other—pharmaceutical/non-pharm	59 (2 %)	184 (3 %)	243 (2 %)
Envenomations	105 (3 %)	183 (3 %)	288 (3 %)
Gases/vapors/irritants/dusts	63 (2 %)	169 (3 %)	232 (2 %)
Other-non-pharmaceutical	12 (<1 %)	35 (<1 %)	47 (<1 %)
Unknown class	7 (<1 %)	92 (1 %)	99 (1 %)
Lithium	78 (2 %)	100 (2 %)	178 (2 %)
Non-ethanol alcohols and glycols	93 (2 %)	145 (2 %)	238 (2 %)
Diabetic medications	65 (2 %)	113 (2 %)	178 (2 %)
Plants and fungi	18 (<1 %)	78 (1 %)	96 (1 %)
Caustics	45 (1 %)	98 (2 %)	143 (1 %)
Hydrocarbons	50 (1 %)	67 (1 %)	117 (1 %)
Antimicrobials	38 (1 %)	105 (2 %)	143 (2 %)
Pesticides	18 (<1 %)	44 (1 %)	62 (1 %)
Herbals/dietary supplements/vitamins	48 (1 %)	76 (1 %)	124 (1 %)
Anesthetics (local and general)	16 (<1 %)	16 (<1 %)	23 (<1 %)
Household (not caustics)	Not included	136 (2 %)	136 (1 %)
Endocrine/hormones/steroids	9 (<1 %)	37 (1 %)	46 (<1 %)
Chemotherapeutic and immune	5 (<1 %)	13 (<1 %)	18 (<1 %)
Cough, cold, and decongestant cold meds	18 (<1 %)	42 (1 %)	60 (1 %)
GI	14 (<1 %)	50 (1 %)	64 (1 %)
Pulmonary	9 (<1 %)	17 (<1 %)	26 (<1 %)
WMD/NBC/Riot	0 (0 %)	3 (<1 %)	3 (<1 %)

^a Cases often have more than one agent class included in the entry during multi-drug exposures

Table 7 Cases with toxidrome identified

Sedative–hypnotic	327 (30)	653 (29)
Anticholinergic	175 (16)	407 (18)
Opioid	104 (9)	314 (14)
Other—not specified or other toxidrome	283 (26)	266 (12)
Sympathomimetic	73 (7)	205 (9)
Envenomation	62 (6)	220 (9)
Serotonin syndrome	54 (5)	148 (6)
Overlap syndromes (MCS, chronic fatigue)	13 (<1)	19 (<1)
Washout	0	9 (<1)
NMS	5 (<1)	7 (<1)
Cholinergic	3 (<1)	5 (<1)
Sympatholytic	0	2 (<1)
Totals	1,096	2,253

Toxidrome assigned in 35 % of cases in 2011

NMS neuroleptic malignant syndrome, MCS multiple chemical sensitivity

analgesics as the most common class of medications encountered during toxicology consultations in 2011. Exposure rates and Registry entries for different agent classes are included in Table 6. After sedative–hypnotics, non-opioid analgesics were reported 1,368 times (21 % of all Registry entries). Opioid analgesics were the third most common entry with 1,100 specific entries (17 %), and antidepressants were reported in 16 % of the cases.

Table 7 features specific toxidromes identified. Specific toxidromes were identified in 25 % of cases in 2010 and in 33 % of cases in 2011. Of cases with identifiable toxidromes in 2011, 653 (29 %) were sedative–hypnotic toxidrome and 407 (18 %) were anticholinergic toxidrome. The opioid toxidrome was identified in 314 (14 %) cases, 148 (6 %) cases were identified as serotonin syndrome, and 7 (<1 %) cases of neuroleptic malignant syndrome were identified in 2011.

During 2011, 35 cases involved patient deaths. These are listed in Table 8. The most common agent classes reported, either as sole agent or in combination, were opioids and non-opioid analgesics (acetaminophen, aspirin, and non-steroidal anti-inflammatory drugs (NSAIDs)) reported in ten and eight cases respectively. The most common opioids reported were oxycodone (identified in six of the ten cases) and heroin (identified in three of the ten cases, twice as a single agent). Among non-opioid analgesics, acetaminophen was the most common single agent overall, being reported in all eight deaths. Twenty-eight of the 35 death cases (78 %) were in ages 19–65. Males were reported in nearly two thirds of the deaths (21 of 35 cases). Most deaths involved multiple agents although 15 of 36 cases had only a single agent coded. Intentional exposure to pharmaceutical agents was the most common method of exposure associated with death although

in the >65 age group ADR/ADE was the cause of death in two of three cases, both deaths involving cardiovascular agents. Agents were unknown or unreported in four of the death cases.

Sedative–hypnotic agents and muscle relaxants are shown in Table 9. Agents in these classes were involved in 23 % of all cases entered into ToxIC in 2011. Benzodiazepines accounted for 56 % of cases in this category. Among the benzodiazepines, the most common was clonazepam, identified in 30 % of benzodiazepine cases, followed by alprazolam in 29 %, lorazepam in 18 %, and diazepam in 9 %. Zolpidem was the most common non-benzodiazepine sedative–hypnotic drug exposure entered into ToxIC in 2011. Muscle relaxants accounted for 18 % of cases in this category, with cyclobenzaprine encountered most frequently with 8 %, followed by carisoprodol with 6 %. Barbiturates accounted for approximately 4 % of entries, with butalbital representing 55 % of all barbiturates.

Non-opioid analgesic entries for 2011 are shown in Table 10. Acetaminophen was by far the most common, entered in 70 % of all cases in this category and thus 9 % of all Registry cases in 2011. Over the lifespan of the Registry there were 11 acetaminophen-related deaths, of which 7 (64 %) occurred in females. Non-salicylate NSAIDs made up 15 % of this category in 2011, of which ibuprofen was overwhelmingly the most common. 19 % of the cases were due to salicylates, the overwhelming majority of which involved aspirin.

Table 11 shows the antidepressant agents entered into the Registry. The most frequently entered antidepressant in 2011 was bupropion in 16 % of cases. Citalopram was the next most common antidepressant with 14 % of all cases. Citalopram made up 38 % of the 371 SSRI cases in 2011. Trazodone was also common, encountered in 13 % of cases. Amitriptyline was the most common tricyclic antidepressant with 114 entries constituting 11 % of all antidepressant entries and 64 % of all tricyclic antidepressant entries in 2011.

Opioids and opiates accounted for 1,100 Registry entries in 2011 (Table 12). The most common category was the semisynthetic agents with 35 % of all opioid entries. Oxycodone was the most common of the semisynthetic agents accounting for 66 % of all semisynthetic-related cases. The synthetic agents, fentanyl, methadone, and tramadol, made up 29 % of the cases overall, of which methadone was the most common, representing 48 % of synthetic agents. The partial opioid agonist buprenorphine was identified in just fewer than 5 % of all opioid cases in 2011. Heroin was seen with higher frequency in 2011 than 2010 with 134 specific entries (12.2 % of all opioid entries) in 2011 compared to 61 (9.9 %) in 2010. The use of opioid antagonists is also shown in Table 12.

Table 13 shows the antihistamine/anticholinergic agents; 549 cases were included in this category in 2011.

Table 8 Registry death reports—case information

Age	Gender	Reason for consult	Agent class/es involved in fatality	Specific agents involved in fatality
>65	M	ADR	Cardiovascular	Digoxin
>65	M	Environmental Evaluation	Gas/vapors/irritants/dusts	Carbon monoxide
13–18	M	Environmental Evaluation	Gas/vapors/irritants/dusts	Carbon monoxide
13–18	M	Intentional—pharmaceutical	Sympathomimetics/antidepressants; cardiovascular	Clonidine, methylphenidate ER, bupropion SR, melatonin
13–18	F	Intentional—pharmaceutical	Sedative–hypnotics/muscle relaxants	Alprazolam, oxycodone, codeine
19–65	F	Intentional—nonpharmaceutical	Gas/vapors/irritants/dusts	Carbon monoxide
19–65	M	Drug abuse—illicit	Opioids	Heroin
19–65	F	Intentional—pharmaceutical	Antidepressants, cardiovascular	Lamotrigine
19–65	M	Interpretation of lab data	Unknown	Unknown
19–65	F	Intentional—pharmaceutical	Analgesics (APAP, ASA, NSAIDs); antipsychotics; anticholinergics/ antihistamines	Acetaminophen, diphenhydramine, quetiapine
19–65	M	Intentional—nonpharmaceutical	Non-ethanol alcohols and ethers	Ethylene glycol
19–65	M	Intentional—pharmaceutical	Sedative–hypnotics/muscle relaxants	Cyclobenzaprine
19–65	F	Environmental evaluation	Gas/vapors/irritants/dusts	Carbon monoxide
19–65	M	Drug abuse—illicit	Opioids	Heroin
19–65	M	Drug abuse—illicit	Opioids, analgesics (ASA, APAP, NSAIDS)	Heroin, oxycodone acetaminophen
19–65	M	Drug abuse—illicit	Opioids, sympathomimetics	Morphine, psychoactive bath salts
19–65	F	Intentional—pharm/non-pharm	Unknown	Unknown
19–65	M	Intentional—pharm/non-pharm		Oxycodone, synthetic
2 to 6	M	Unintentional—pharmaceutical	Opioids	Methadone
19–65	F	Intentional—pharm/nonpharm	Antidepressants	Amirypiline
19–65	M	Unintentional—nonpharm	Gas/vapors/irritants/dusts	Carbon monoxide
13–18	M	Intentional—pharm/nonpharm	Opioids; sympathomimetics; sedative–hypnotics; antidepressants	Oxycodone, amphetamine, pregabalin, amirypiline
19–65	F	Intentional—pharmaceuticals	Analgesics (APAP, ASA, NSAIDs); sedative–hypnotics/muscle relaxants	Acetaminophen, diazepam
19–65	F	Interpretation lab data	Opioids, analgesics (ASA, APAP, NSAIDS), antihistamines/ anticholinergics, OTC	Oxycodone, dextromethorphan, diphenhydramine, brompheniramine, guaifenesin
>65	F	ADE	Cardiovascular	Nebivolol, amlodipine
19–65	M	Organ system dysfunction	Unknown	Unknown
19–65	M	Intentional exposure—pharmaceutical opioids; analgesics (APAP, ASA, NSAIDs); alcohols (ethanol); cardiovascular	Fentanyl patch (ingestion), oxycodone/APAP, ethanol, metoprolol, amlodipine	
19–65	F	Unintentional exposure—nonpharmaceutical	Antipsychotics; anticonvulsants (including non-antipsychotic mood stabilizers)	Quetiapine, lamotrigine
>65	F	Organ system dysfunction	Alcohols (toxic alcohols and glycols)	Methanol
19–65	M	Intentional exposure—Pharmaceutical	Analgesics (APAP, ASA, NSAIDs); diabetic Meds; anticholinergics/ antihistamines; cardiovascular	Amlodipine, metoprolol, diphenhydramine, metformin, acetaminophen
19–65	M	Intentional exposure—pharmaceutical	Analgesics (APAP, ASA, NSAIDs)	Acetaminophen
19–65	M	Intentional exposure—pharmaceutical	Lithium	Lithium
19–65	M	Interpretation of laboratory data	Unknown	Unknown
19–65	F	Intentional exposure—Pharmaceutical	Analgesics (APAP, ASA, NSAIDS)	Acetaminophen
19–65	F	ADR	Diabetic medications	Metformin, sitagliptin

Table 9 Sedative hypnotics/muscle relaxant agents

	Agent	2010 (%)	2011 (%)	Total (%)	
Benzo diazepines	Clonazepam	180 (21)	262 (18)	442 (19)	
	Alprazolam	145 (17)	253 (17)	398 (17)	
	Lorazepam	102 (12)	159 (11)	261 (11)	
	Diazepam	38 (5)	81 (5)	119 (5)	
	Unspecified BZDs	0	62 (4)	0	
	Temazepam	17 (2)	34 (2)	51 (2)	
	Midazolam	3 (<1)	10 (1)	13	
	Chlordiazepoxide	3 (<1)	4 (<1)	7	
	Triazolam	0	4 (<1)	0	
	Chlorazepate	1 (<1)	3 (<1)	4	
	Flurazepam	0	2 (<1)	0	
	Brotizolam	0	1 (<1)	0	
	Oxazepam	0	1 (<1)	0	
	Muscle relaxants	Cyclobenzaprine	66 (8)	118 (8)	184 (8)
		Carisoprodol	48 (6)	94 (6)	142 (6)
Baclofen		25 (3)	43 (3)	68 (3)	
Methocarbamol		5	9 (<1)	14	
Metaxalone		0	5 (<1)	1 (<1)	
Chlorzoxazone		0	1 (<1)	0	
Orphenadrine		2 (<1)	0	0	
Tizanidine		4 (<1)	0	0	
Unk muscle relaxant		0	0	0	
Barbiturates		Butalbital	25 (3)	34 (2)	59 (2)
	Phenobarbital	12 (1)	19 (1)	31	
	Unk Barb	0	6 (<1)	0	
	Butabarbital	0	2 (<1)	0	
	Pentobarbital	0	1 (<1)	0	
Other sedatives	Zolpidem	80 (10)	132 (9)	212 (9)	
	Gabapentin	43 (5)	89 (6)	132 (6)	
	Pregabalin	11 (1)	15 (1)	26	
	Buspirone	5 (1)	32 (2)	37	
	Eszopiclone	7 (1)	5 (<1)	12	
	Meprobamate	1 (<1)	4 (<1)	5	
	Aids	0	2 (<1)	0	
	Aminobutyric acid	0	1 (<1)	0	
	Chloral hydrate	1 (<1)	1 (<1)	2	
	Hypnotic	0	1 (<1)	0	
	Zaleplon	1 (<1)	1 (<1)	2	
	Zopiclone	10 (1)	1 (<1)	0	
	Dichloralphe nazone	1 (<1)	0	0	
	Ramelteon	1 (<1)	0	0	
	Total	837	1,492	2,329	

Diphenhydramine was the most common agent, reported in 54 % of the cases. The second most common agent was hydroxyzine with 13 %.

Table 10 Non-opioid analgesic agents (acetaminophen, aspirin, non-steroidal anti-inflammatory drugs)

	Agent	2010 (%)	2011 (%)	Total (%)
Acetaminophen	Acetaminophen	602 (70)	903 (66)	1,505 (70)
NSAIDS	Ibuprofen	82 (10)	154 (11)	236 (11)
	Naproxen	21 (2)	35 (3)	56 (2)
	Diclofenac	0	6 (<1)	6 (<1)
	Unidentified	NSAID	3 (<1)	6 (<1)
	Celecoxib	0	3 (<1)	3 (<1)
	Indomethacin	1 (<1)	2 (<1)	3 (<1)
	Nabumetone	2 (<1)	2 (<1)	4 (<1)
	Ketoprofen	0	1	1
	Ketorolac	0	1	1
	Meloxicam	0	1	1
Etodolac	2	0	0	
Flurbiprofen	1	0	0	
Piroxicam	1	0	0	
Salicylates	Acetylsalicylic acid	137 (15)	247 (18)	324 (17)
	Unspecified salicylates ^a	0	60 (4)	60 (17)
Other	Ziconotide	1	3	4
Totals		854	1,368	2,222

^aNon-aspirin (acetylsalicylic acid) salicylates

Cardiovascular agents were reported in 631 cases and are listed in Table 14. The most common categories of cardiovascular medications were the beta-blockers (21 %) and calcium-channel antagonists (19 %). Metoprolol was the most common beta blocker, accounting for 47 % of all beta blocker entries. Propranolol and atenolol each comprised approximately 20 % of beta-blocker entries. The most common calcium channel antagonist was amlodipine, comprising 40 % of these entries. Verapamil and diltiazem comprised another 28 and 22 % of cases, respectively. The most common statin was simvastatin comprising 56 % of the statin cases. Hydrochlorothiazide was the most common diuretic encountered.

Table 15 shows agents reported as stimulants or sympathomimetics. There was a large increase in this class of drugs from 2010 to 2011, primarily due to increased numbers of designer amphetamines including mephedrone, methylenedioxypyrovalerone (MDPV) and other drugs sold as “psychoactive bath salts”. Mephedrone, MDPV, and “other” psychoactive bath salts were reported in a total of 111 cases (14 %) in 2011 compared to only once in 2010. Despite these increases in designer drugs, cocaine remains most common sympathomimetic or stimulant substance, accounting for 31 % of cases reported in this category in 2011. Amphetamine

Table 11 Antidepressant agents

	Agent	2010 (%)	2011 (%)	Total (%)
Atypical	Bupropion	99 (14)	162 (15)	261 (15)
	Mirtazapine	10 (1)	46 (4)	56 (3)
	Nefazodone	1	0	1
	Trazodone	90 (13)	135 (13)	225 (13)
Unspecified		3	1	4
MAOIs	Phenelzine	3	1	4
	Tranylcypromine	0	1	1
SSRIs	Citalopram	106 (15)	142 (14)	248 (14)
	Escitalopram	23 (3)	38 (4)	61 (3)
	Fluoxetine	43 (4)	80 (8)	123 (6)
	Fluvoxamine	2	6	8
	Paroxetine	33(5)	32 (4)	64 (4)
	Sertraline	47 (4)	67 (7)	114 (7)
	Unspecified SSRI	1	6	7
Tricyclics	Amitriptyline	95 (14)	114 (11)	209 (12)
	Clomipramine	1	4	5
	Desipramine	0	6	6
	Doxepin	10 (1)	27 (2)	37 (2)
	Imipramine	6	7	13
	Nortriptyline	19 (3)	15 (1)	34 (1)
	Unspecified TCA	2	5	7
SNRIs	Duloxetine	24 (3)	42 (4)	66 (4)
	Venlafaxine	37 (5)	84 (8)	131 (8)
	Desvenlafaxine	5	7	12
	Milnacipran	0	1	1
Totals		694	1,029	1,725

and methamphetamine combined accounted for 27 % of cases, caffeine was reported in 9 % of cases, and methylphenidate in 4 % of cases.

Cases classified as involving psychoactive drugs of abuse are shown in Table 16. Marijuana was the most frequent entry in this category in 2011, with 123 cases representing 34 % of all entries in this group. Although synthetic cannabinoids showed a greater than threefold increase from 11 cases in 2010 to 40 cases in 2011, the increase in marijuana entries was even greater, from 27 to 123 cases. Dextromethorphan was the next most common, representing 33 % of cases in the psychoactive category. Phencyclidine was reported about half as often as dextromethorphan. *Salvia divinorum*, not reported in 2010, appears in the database 4 times in 2011.

Table 17 shows the number of cases involving ethanol. In 2011, there were a total of 580 ethanol cases reported. This compares to 371 cases in 2010.

Table 18 shows the antipsychotic exposures. The atypical antipsychotics were overwhelmingly the most

Table 12 Opioid agents

	Agent	2010 (%)	2011 (%)	Total (%)
Opiates	Morphine	37 (5)	56 (5)	93 (5)
	Codeine	23 (3)	12 (1)	35 (2)
	Unspecified	0	19 (2)	19
	Opium tincture	0	1	1
Semisynthetic	Oxycodone	142 (23)	252 (23)	394 (23)
	Hydrocodone	110 (18)	160 (15)	270 (16)
	Heroin	61 (10)	134 (12)	195 (11)
	Buprenorphine	20 (3)	49 (4)	69 (4)
Synthetic Opioids	Hydromorphone	14	24	38
	Oxymorphone	2	11	13
	Methadone	98 (16)	155 (14)	253 (15)
	Tramadol	49 (8)	98 (9)	147 (9)
	Fentanyl	36 (6)	50 (5)	86 (5)
	Propoxyphene	19	12	31
	Meperidine	2	3	5
	Loperamide	0	1	1
	Sufentanil	0	1	1
	Tapentadol	1	1	2
	Diphenoxylate	1	0	1
Unspecified	Pentazocine	1	0	1
	Naloxone	9	42 (4)	51 (3)
	Naltrexone	0	4	4
	Unspecified	19	15	34
Totals		619	1,100	1,719

common type of antipsychotics reported. Quetiapine was the most frequently reported comprising 44 % of all antipsychotic medication cases. Chlorpromazine was the most commonly reported “first generation” phenothiazine antipsychotic with 14 cases (2 %). Haloperidol was the only butyrophenone entered and it was included in 36 cases (4 %).

Lithium was listed separately from the antipsychotics. One hundred cases involving lithium were reported in 2011 compared to 78 cases in 2010 (Table 19).

Table 20 shows caustic agent entries. Acids make up 27 % of this group with hydrochloric acid being the most common. Bases including sodium hydroxide and sodium hypochlorite accounted for 20 % each in this category in 2011.

Table 21 shows non-ethanol alcohols (methanol and isopropyl alcohol), ethylene glycol, glycol ethers, and similar agents. Ethylene glycol was the most common agent included in this category in 2011 followed by isopropyl alcohol, methanol, and acetone.

Table 22 includes anticonvulsant case entries. The most common anticonvulsants reported were phenytoin, valproic acid, and lamotrigine.

Table 13 Antihistamines and anticholinergic agents

	Agent	2010 (%)	2011 (%)	Total (%)
Antihistamine	Diphenhydramine	234 (62)	299 (55)	533 (57)
	Hydroxyzine	34 (9)	62 (11)	96 (10)
	Chlopheniramine	11 (3)	27 (5)	38 (4)
	Prochlorperazine	3	7	10 (1)
	Pyrilamine	1	6	7
	Cetirizine	3	5	8
	Dimenhydrinate	5	5	10
	Loratadine	3	5	8
	Meclizine	4	4	8
	Promethazine	10 (3)	4	14
	Brompheniramine	0	3	3
	Cyproheptadine	1	3	4
	Fexofenadine	1	2	3
	Pheniramine	11 (3)	2	13
	Unspecified	1	23 (4)	24 (2)
	Anticholinergic	Benztropine	21 (6)	21 (4)
Hyoscyamine		3	7	10
Oxybutynin		3	6	9
Tolterodine		0	4	4
Atropine		3	2	5
Donnatol		1	2	3
Scopolamine		2	2	4
Clidinium		0	1	1
Dicyclomine		0	1	1
Fesoterodine		0	1	1
Glycopyrrolate		1	1	2
Trihexyphenidyl 2		0	0	
Total		378	549	927

Snakebites make up the majority of the envenomation cases (Table 23). Rattlesnakes were the most common type of envenomation in 2011 with 59 cases, most of them by unidentified rattlesnakes. 41 envenomations were reportedly due to copperhead bites. Scorpions accounted for 21 envenomations, and the Brown Recluse was the most commonly implicated spider with 19 cases.

Diabetic agents are shown in Table 24 with sulfonylureas (37 %), metformin (26 %), and insulin (30 %) being the most common medication types reported.

Table 25 includes cases involving hydrocarbons; 67 cases of hydrocarbon exposures were reported in 2011. The most commonly reported hydrocarbons included methane, tetrachloroethylene, methylene chloride, gasoline and kerosene.

Table 26 shows the number of cases involving metals and metalloids. A total of 322 entries were included in this category in 2011 with iron reported most frequently

Table 14 Cardiovascular agents including ACE inhibitors, alpha-2 agonists, alpha-1 antagonists, ARBs, antiarrhythmics; cardiovascular agents including anticoagulants, antiplatelet agents and antilipid agents; cardiovascular agents including beta-blocking agents, calcium channel antagonist agents, cardiac glycosides, diuretics, nitrates and vasodilator agents

	Agent	N 2010	N 2011	N total	
ACE inhibitors	Lisinopril	35	49	84	
	Benazepril	0	3	3	
	Captopril	0	1	1	
	Enalapril	3	1	4	
	Fosinopril	0	1	1	
	Quinapril	1	0	0	
	Ramipril	0	2	2	
	Sympatholytics (alpha-2 agonists)	Clonidine	63	93	156
		Guanfacine	7	17	24
	Combined alpha/beta blockers	Carvedilol	10	16	26
Labetalol		1	6	7	
Alpha-antagonists	Alfuzosin	1	0	0	
	Doxazosin	0	1	1	
	Prazosin	2	3	5	
	Tamsulosin	3	4	7	
	Terazosin	0	3	3	
Angiotensin II receptor antagonists	Eprosartan	0	1	1	
	Irbesartan	0	1	1	
	Olmesartan	1	1	2	
	Valsartan	2	8	10	
	Antiarrhythmics	Amiodarone	1	0	0
Dofetilide		0	1	1	
Flecainide		0	2	2	
Propafenone		0	1	1	
Quinidine		0	1	1	
Anticoagulants		Warfarin	11	25	36
		Dabigatran	0	1	1
	Enoxaparin	1	1	2	
	Fondaparinux	0	2	2	
	Unspecified	0	1	1	
	Antiplatelets	Argatroban	0	1	1
		Clopidogrel	0	4	4
	Antilipids	Simvastatin	5	14	19
Ezetimibe		0	1	1	
Atorvastatin		1	3	4	
Fenofibrate		1	1	2	
Gemfibrozil		1	1	2	
Lovastatin		0	3	3	
Pravastatin		1	1	2	
Rosuvastatin	1	2	3		
Beta-blocking agents	Metoprolol	31	62	93	
	Atenolol	25	28	53	
	Propranolol	16	31	47	

Table 14 (continued)

	Agent	N 2010	N 2011	N total
	Betaxolol	1	2	3
	Bisoprolol	0	2	2
	Nadolol	1	4	5
	Nebivolol	0	2	2
Calcium channel antagonists	Amlodipine	27	47	74
	Diltiazem	12	26	38
	Verapamil	13	33	46
	Nifedipine	4	9	13
	Sotolol	0	2	2
	Felodipine	1	0	1
Cardiac glycosides	Nicardipine	0	2	2
	Digoxin	35	44	79
	Digitoxin	0	1	1
	Natural glycosides	0	1	1
Diuretics	Hydrochlorothiazide	8	25	33
	Furosemide	0	8	8
	Acetazolamide	1	0	0
	Chlorothalidone	0	1	1
	Spironolactone	0	3	3
	Torsemide	1	1	2
	Triamterene	1	3	4
Nitrates	Isosorbide	1	1	2
	Nitroglycerin	0	4	4
Vasodilators	Hydralazine	1	3	4
	Minoxidil	1	1	2
	Nitroprusside	1	1	2
Totals		333	624	957

(15 %), followed by lead (14 %), chromium (13 %), cobalt (13 %), arsenic (10 %), cadmium (8 %), mercury (8 %), and selenium (8 %).

Table 27 shows cases involving gas, vapors dust, and irritant agents. Carbon monoxide, responsible for several deaths in 2011, accounts for 130 of 169 cases in this category.

Table 28 shows cases involving gastrointestinal (GI) agents including proton pump inhibitors, antacids and other GI agents. Table 29 shows pulmonary agent exposures of which guaifenesin was the most common. Additional tables are: Table 30 endocrine agents, Table 31 chemotherapeutic agents, Table 32 antimicrobial agents, Table 33 herbal and dietary supplements, and Table 34 plants, fungi, and mold entries. Household products were not listed separately in a table as most agents were included as specific names. The majority of the agents included detergents and cleaning agents.

Table 15 Stimulant and sympathomimetic agents

	Agents	N 2010 (%)	N 2011 (%)	N total
Amphetamine derivatives	Amphetamines	40 (13)	141 (18)	181 (17)
	Methamphetamine	38 (13)	70 (9)	108 (10)
	Dextroamphetamine	26 (6)	35 (5)	61 (5)
	Lisdexamfetamine	6	12	18
	MDMA	12 (2)	14 (2)	26 (2)
	Pseudoephedrine	7	10	17 (2)
	Phenylpropanolamine	0	4	4
	Ephedrine	0	1	1
	Phenylephrine	4	14 (2)	18 (2)
	Psychoactive bath salts	MDPV	0	14 (2)
Mephedrone		1	49 (6)	50 (5)
Desoxypropylolol		0	1	1
Other “non-specified” psychoactive bath salts		0	48 (6)	48 (4)
Others	Caffeine	31 (10)	67 (9)	98 (9)
	Cocaine	102 (34)	237 (31)	339 (32)
	Methylphenidate	24 (8)	34 (5)	58 (5)
	Atomoxetine	2	6	8
	Dexmethylphenidate	2	3	5
	Phentermine	2	2	4
	Ethylphenidate	0	1	1
	Isometheptene	1	1	2
Unspecified or other	0	4	4	
Total		298	769	1,067

Additional, Non-agent Tables

Adverse Drug Reaction related consultations increased in 2011; 115 specific agents were identified at least twice in ADRs during 2011. As many ADRs involved several agents or were the result of a combination of medications, when each medication was counted separately there were 603 specific instances of a medication contributing to an ADR in 2011. The total number of separate ADR cases in 2011, however, was 229.

Lithium was the most frequent agent involved in an ADR (24 cases). Digoxin, acetaminophen, trazodone, citalopram, quetiapine and oxycodone are also common with >12 ADR cases during 2011. Agents with at least two entries documented involving ADRs are shown in Table 35.

Antidotes used are shown in Table 36. N-acetylcysteine (NAC) was the most frequently reported antidote administered in 2011 making up 30 % of all antidote entries. Naloxone was the next most frequently used (19 %), followed by sodium bicarbonate (12 %),

Table 16 Psychoactive agents including dextromethorphan, cannabinoids, GHB, hallucinogen and dissociative agents

Agent		N 2010 (%)	N 2011 (%)	Total (%)
Cannabinoids	Marijuana	27 (20)	123 (34)	150 (30)
	Synthetic cannabinoids (K2)	11 (10)	40 (11)	51 (10)
	Pharmaceutical THC ^a	0	1	1
	Dissociatives dextromethorphan	65 (48)	120 (33)	185 (37)
	Phencyclidine	22 (16)	57 (16)	79 (16)
	Ketamine	1	2	3
	Gamma hydroxybutyrate and related agents	0	4	4
Gamma hydroxybutyrate and related agents	Gamma hydroxybutyrate	0	4	4
	1,4 BD ^b	1	1	1
	Hallucinogens LSD ^c	6	4	10
	DMT ^d	0	1	1
	Mescaline	1	0	1
Other	Salvia divinorum	0	4	4
	Unspecified psychoactive	1	2	3
	Unknown	0	2	2
Totals	135	360	495	

^a Tetrahydrocannabinol

^b 1,4 Butanediol

^c Lysergic acid diethylamide

^d Dimethyltryptamine

physostigmine (9 %), and flumazenil (6 %). Antivenom was administered in 131 cases. CroFab, used for crota-line snake bites, was the most common antivenom administered and accounted for 80 % of the cases in which antivenom was used. The other antivenoms used include other snake antivenom (not CroFab) in 5 cases, scorpion antivenom in 18 cases, and spider antivenom in 2 cases. Hyperinsulinemia/euglycemia therapy and intravenous lipid emulsion, two relatively new and controversial antidotal therapies, represented a small percentage of this category with 28 (1 %) and 20 (<1 %) administrations recorded, respectively.

Pharmacological support was documented in 1,661 cases. The majority (73 %) received benzodiazepines. Antipsychotics were administered in 9 % and anticonvulsants in 5 %. Dextrose (>5 % glucose) was administered in 4 %. Additional pharmacologic was reported infrequently.

Table 17 Ethanol

Agent	N 2010	N 2011	N total
Ethanol	371	580	951
Totals	371	580	951

Table 18 Antipsychotic agents

Agent		N 2010 (%)	N 2011 (%)	N total
Atypical	Quetiapine	178 (49)	260 (44)	438 (46)
	Risperidone	43 (12)	72 (12)	115 (12)
	Olanzapine	37 (10)	69 (12)	106 (11)
	Aripiprazole	23 (6)	63 (11)	86 (9)
	Ziprasidone	17 (5)	28 (5)	45 (5)
	Clozapine	13 (4)	21 (4)	34 (4)
	Paliperidone	0	3	3
	Asenapine	1	2	3
	Iloperidone	1	0	1
	First -Generation	Chlorpromazine	11 (3)	14 (3)
Perphenazine		6	7	13
Loxapine		2	5	7
Thiothixene		0	3	3
Fluphenazine		2	1	3
Pericyazine		2	1	3
Pimozide		0	1	1
Butyrophenones	Thioridazine	2	1	3
	Haloperidol	30 (8)	36 (6)	66 (7)
Totals	366	587	953	

The most common form of non-pharmacologic support was intubation and ventilator management being reported in 648 entries. Hyperbaric oxygen was reported in only 48 cases, cardiopulmonary resuscitation in 4, cardioversion in 4, and ECHMO once.

Very few patients received GI decontamination. Activated charcoal was entered only 285 times, whole bowel irrigation 49 times and gastric lavage 18 times. GI decontamination was documented in just over 5 % of all Registry cases.

Extracorporeal treatment in poisoning was also rare with 109 patients receiving hemodialysis. Continuous renal replacement therapy was performed in 28 cases, exchange transfusion in 5 cases. Urinary alkalinization was documented 52 times and multi-dose activated charcoal was given 18 times.

Discussion

The ACMT ToxIC Registry continues to develop as 2011 began the second year of data collection. Over 10,000 cases

Table 19 Lithium

Agent	N 2010	N 2011	N total
Lithium	78	100	178

Table 20 Caustic agents

Agent		2010	2011	Total
Acids	Hydrochloric acid	4	14	18
	Citric acid	0	4	4
	Acetic acid	4	2	6
	Hydrofluoric acid	0	2	2
	Alkyl benzosulfonic acid	0	1	1
	Callous removal	0	1	1
	Phenol	2	1	3
	Phosphoric acid	0	1	2
	Sulfuric acid	1	1	2
	Bases	Sodium hydroxide	5	21
Sodium hypochlorite		13	20	33
Ammonia		4	7	11
Alkaline substance		1	5	6
Potassium hydroxide		3	3	6
Ammonium chloride		3	0	0
Ammonium nitrates		1	0	0
Other		Hydrogen peroxide	3	11
	Unknown caustics	0	3	3
	Hydrogen fluoride	0	1	1
	Na-hypoborate	0	0	0
	Total	45	98	139

Table 21 Non-ethanol alcohols (methanol, isopropyl alcohol), ethylene glycol and similar agents

Agent	2010	2011	Total
Ethylene glycol	41	68	109
Isopropanol	20	34	54
Methanol	17	19	36
Acetone	3	8	11
Propylene glycol	0	5	5
Glycol ether	4	3	7
Toxic alcohol	0	3	3
Butyl alcohol	0	1	1
Butyl-ethylene glycol	0	1	1
Denatured ethanol	1	1	2
Diethylether	0	1	1
Methyl ethyl ketone	0	1	1
Butanol	1	0	1
Diethylene glycol	3	0	3
Other denatured	1	0	1
Triethylene glycol monobutyl ether	1	0	1
Unknown	1	0	1
Total	93	145	238

Table 22 Anticonvulsants and non-antipsychotic mood stabilizers

Agents	N 2010 (%)	N 2011 (%)	N total (%)
Carbamazepine	25 (11)	38 (8)	63 (9)
Felbamate	1	1	1
Lacosamide	1	1	1
Lamotrigine	35 (16)	65 (14)	100 (15)
Levetiracetam	2	6	8
Oxcarbazepine	9 (4)	26 (6)	35 (5)
Phenytoin	23 (11)	88 (20)	111 (17)
Primidone	1	2	3
Tiagabine	1	1	1
Topiramate	19 (9)	32 (7)	51 (8)
Valproic acid	46 (21)	86 (19)	132 (20)
Zonisamide	1	1	1
Totals	218	451	669

Table 23 Envenomations

		N 2010	N 2011	N total
Scorpions	Unspecified scorpion	26	21	47
	Bark	0	3	3
	<i>Centruroides sculpturatus</i>	0	1	1
	<i>Centruroides</i> —unspecified	0	2	2
Snakes				
Viperidae	Copperhead	20	41	61
	<i>Vipera palaestinae</i>	0	4	4
	Unspecified crotalid	0	2	2
	Water moccasin	0	2	2
	Cottonmouth	0	1	1
Rattlesnake	<i>Bitis gabonica</i>	0	1	1
	Unspecified Rattlesnake	39	53	92
	<i>Crotalus atrox</i>	0	2	2
	<i>Crotalus mitchellii</i>	0	1	1
	<i>Sistrurus miliarius</i>	0	1	1
Colubridae	<i>Coluber jugularis</i>	0	1	1
	Unspecified family	2	9	11
Spider	Snake non-venomous	0	2	2
	Brown recluse	9	19	28
	<i>Latrodectus mactans</i>	0	7	7
	Unspecified spider	1	3	4
	<i>Latrodectus</i>	0	1	1
Gila monster	Wolf spider	0	1	1
	Unspecified	0	2	2
	Portuguese man-of-war	0	1	1
Rabies	0	1	1	
Totals		185	105	290

Table 24 Diabetic agents

	Agent	2010	2011	Total	
Biguanides	Metformin	22	29	51	
	Insulin	16	35	51	
	Sulfonylureas	Glyburide	10	20	30
		Glipizide	7	14	21
		Glimepiride	8	6	14
	Unspecified Sulfonylurea	0	2	2	
	Tolbutamide	0	1	1	
Other agents	Pioglitazone	1	3	4	
	Nateglinide	0	2	2	
	Sitagliptin	0	1	1	
	Liraglutide	1	0	0	
	Total	65	113	178	

had been entered onto the Registry by the end of 2011. In addition to ongoing development and enhancement of the Registry infrastructure many accomplishments occurred and initiatives were developed. The Registry continues to grow in terms of publication and research applications.

A number of interesting trends are immediately evident looking at these data. In 2011, sedative hypnotics

Table 25 Hydrocarbons

	Agent	2010	2011	Total
Aliphatic	Methane	2	6	8
	Hexane	2	2	4
	Benzene	3	3	6
	Other aliphatic	0	4	4
Aromatic	Naphthalene	0	3	3
	Xylene	3	3	6
	Ethylbenzene	0	2	2
	Toluene	0	1	1
Other	Gasoline	1	4	5
	Kerosine	2	3	5
	Mineral oil	0	1	1
	Paraffin oil	0	1	1
	Tetrachloroethylene	1	5	6
	Methylene chloride	1	4	5
	Other halogenated	0	3	3
	Trichloroethylene	4	2	6
	Chlorofluorocarbons	0	1	1
	Dichloroethane	0	1	1
	Difluoroethane	3	1	4
	Ethyl chloride	0	1	1
	Other hydrocarbon	28	16	44
	Total	50	67	117

Table 26 Metals and metalloids

	2010	2011	Total
Lead	30	46	76
Iron	12	48	60
Chromium	4	41	45
Cobalt	1	40	41
Arsenic	14	32	46
Cadmium	31	25	56
Mercury	21	25	46
Selenium	31	24	55
Coppers	1	6	7
Aluminum	2	4	6
Cesium	0	4	4
Thallium	0	4	4
Magnesium	0	3	3
Manganese	4	3	7
Gadolinium	1	2	3
Gold	1	2	3
Nickel	1	2	3
Barium chromate	0	1	1
Beryllium	0	1	1
Platinum	0	1	1
Rhodium	0	1	1
Other metals	0	1	1
Other metals	0	5	5
Total	154	320	474

(particularly benzodiazepines), with nearly 1,500 cases, emerged as the most common agents provoking a medial toxicology consultation. These numbers, and the 1-

Table 27 Gas (including carbon monoxide), vapors, dusts and irritant agents

Agent	2010	2011	Total
Carbon monoxide	44	130	174
Chlorine	9	9	18
Smoke	0	9	9
Oxides of nitrogen	0	3	3
Cyanide	3	2	5
Hydrogen sulfide	2	2	4
Natural gas	0	2	2
Arsine gas	0	1	1
Bromine	0	1	1
Duster (canned air)	0	1	1
Liquified petroleum gases	0	1	1
Petroleum vapors	0	2	2
Polyurethane vapors	0	1	1
Dust	5	4	9
Soot	0	1	1
Total	63	169	232

Table 28 GI agents including antacids, PPIs, and other gastrointestinal medications

Agent	2010	2011	
Antacids and PPIs ^a	Omeprazole	3	9
	Ranitidine	2	9
	Famotidine	0	3
	Esomeprazole	1	2
	Lansoprazole	0	2
	Pantoprazole	0	1
Other	Metoclopramide	2	6
	Ondansetron	2	4
	Dicyclomine	1	3
	Bismuth subsalicylate	0	2
	Docusate	1	2
	Polyethylene glycol	0	2
	Balsalazide disodium	2	1
	Simethicone	0	1
	Sucralfate	0	1
	Sulfasalazine	0	1
	Total	14	49

^aProton pump inhibitors

year time period, are both too small to postulate the existence of a developing trend. Nevertheless, this is an area that warrants continued toxicosurveillance by the Registry and by other relevant toxicosurveillance systems. That this may indeed represent a trend is suggested by the fact that the sedative–hypnotic toxidrome was the most frequently encountered of all toxidromes. Much of the current concerns about prescription drug abuse have centered on opioids, and while opioids are certainly of greater concern in regards to morbidity and mortality related to overdose, the data reported herein suggest that emphasis should also be placed on the sedative hypnotics. Clonazepam was the most common sedative hypnotic reported.

Our data also suggest that while medication abuse is a major problem, restricting our concerns to prescription drug abuse fails to acknowledge the major role of OTC

Table 29 Pulmonary agents

Agent	2010	2011	Total
Guaifenesin	6	8	14
Albuterol	1	4	5
Theophylline	2	2	4
Diphylline	0	1	1
Montelukast	0	1	1
Terbutaline	0	1	1
Total	9	17	26

Table 30 Endocrine agents

Agent	2010	2011	Total
Levothyroxine and thyroxine	3	15	18
Prednisone	3	8	11
Desmopressin	1	2	3
Finasteride	0	2	2
Anabolic steroids	0	1	1
Calcitonin	0	1	1
Fludrocortisone	0	1	1
Glucagon-like-peptide-1	0	1	1
Hydrocortisone	0	1	1
Methimazole	0	1	1
Methylprednisolone	1	1	2
Progesterone	1	1	2
Thyroid hormone (veterinary)	0	1	1
Triiodothyronine	0	1	1
Total	9	37	46

agents. Dextromethorphan, readily available over-the-counter, was shown to be one of the most commonly abused psychoactive substances. Modifications to the Registry data entry form will allow for better identification and surveillance involving drugs of abuse.

Oxycodone was the most common opioid medication encountered. There appeared to be an increase in the encounters involving heroin over the last two years, from 9.9 % of all opioid cases in 2010 to 12.2 % in 2011. There is concern about the reformulation of oxycodone to a preparation that is difficult to convert illicitly to a parenteral form causing an increase in heroin use. It is too early, however, to conclude that this is the reason for the increase in heroin cases the medical toxicology community is encountering. This too is an area of continued toxicosurveillance by the Registry.

Table 31 Chemotherapeutic agents

Agent	2010	2011	Total
Cyclosporine	2	3	5
Interferon alpha	1	2	3
Methotrexate	0	2	2
Sunitinib	2	2	4
Sorafenib	0	1	1
Tacrolimus	0	1	1
Tamoxifen	0	1	1
Topotecan	0	1	1
Total	5	13	18

Table 32 Antimicrobials (antibiotics and antivirals)

Agent	2010	2011	Total
Abacavir	0	2	2
Acyclovir	2	1	3
Amantadine	1	3	4
Amoxicillin	0	7	7
Atazanavir	0	1	1
Azithromycin	0	2	2
Ceftriaxone	1	1	2
Cephalexin	3	5	8
Ciprofloxacin	1	2	3
Clindamycin	0	5	5
Dapsone	0	3	3
Darunavir	0	1	1
Doxycycline	2	1	3
Efavirenz	0	2	2
Emtricitabine	0	3	3
Erythromycin	1	2	3
Isoniazid	11	7	18
Lamivudine	0	1	1
Levofloxacin	0	1	1
Linezolid	2	2	4
Maraviroc	0	1	1
Metronidazole	2	5	7
Minocycline	0	2	2
Moxifloxacin	0	1	1
Nafcillin	0	1	1
Nevirapine	0	1	1
Nitrofurantoin	0	1	1
Penicillin	2	2	4
Piperacillin	0	2	2
Raltegravir	0	1	1
Ritonavir	2	3	5
Sulfamethoxazole and sulfonamides	3	14	17
Iazobactam	0	1	1
Tenofovir	0	3	3
Trimethoprim	4	12	16
Vancomycin	1	1	2
Total	38	105	143

Table 33 Herbal, dietary supplements, and vitamin agents

Agent	2010	2011	Total
Senna	0	3	3
Echinacea	1	2	3
Unspecified herb	5	2	7
Caper bush	0	1	1
Chicory	0	1	1
Citronella oil	1	1	2
Elderberry extract	0	1	1
Ephedra	0	1	1
Eucalyptus oil	0	1	1
Fragrant lemongrass oil	0	1	1
Ginseng royal jelly	0	1	1
Grapefruit extract	0	1	1
Jojoba oil	0	1	1
Probiotics	0	1	1
Yohimbine	0	1	1
St. John's wort	0	1	1
Tamarisk	0	1	1
Tea tree oil	0	1	1
Yarrow	0	1	1
Yerba mate green tea extract	0	1	1
Melatonin	1	10	11
Unspecified dietary supplements	0	5	5
1,3-dimethylamylamine	0	2	2
Omega-3-acid ethyl esters	0	2	2
Ruta	6	0	1
Soy lecithin	0	1	1
Whey protein concentrate	0	1	1
Multivitamins	1	11	12
Vitamin D	1	9	10
Calcium	1	8	9
Potassium	4	5	9
Zinc	5	5	10
Ascorbic acid	1	3	4
Folic acid	0	3	3
Niacin	1	2	3
Prenatal vitamins	0	2	2
Biotin	0	1	1
Hydroxocobalamin	0	1	1
Thiamine	2	1	3
Vitamin K	0	1	1
Vitamin A	1	0	1
Total	25	98	123

The data in Table 15 demonstrates that illicit psychostimulants are a growing area of toxicologic morbidity. This appears to be driven by the growing number of cases of designer amphetamines. Agents in the psychoactive bath salts category increased dramatically from 2010 to 2011. The specific agents and the syndromes they engender is clearly a dynamic area and we expect that the multi-center nature of the Registry will allow it to play a vital role in identifying these

newly emerging agents and characterizing their syndromes. Similar to the Registry experience with psychoactive amphetamines, there was a greater than threefold increase in the frequency of encounters with synthetic cannabinoids. Nevertheless, cocaine remained the most commonly encountered psychostimulant,

Table 34 Plants and fungi (mushroom) agents

	Agent	2010	2011	Total
Plants	Senna	0	2	2
	Yohimbine	0	2	2
	Acai fruit	0	1	1
	Betel nut	0	1	1
	Cascara	0	1	1
	Dioscorae	0	1	1
	Ebony	0	1	1
	Fox nut	0	1	1
	Goldenseal	0	1	1
	Hordenine	0	1	1
	Kanna	0	1	1
	Peuraria	0	1	1
	Laetrile	0	1	1
	Moonflower	0	1	1
	Nut/seed suspected cardiac glycoside	0	1	1
	<i>Saccaromyces boulardii</i>	0	1	1
	Strychnine	0	1	1
	<i>Thevetia peruviana</i>	0	1	1
	Tuckahoe	0	1	1
	Unknown leaf	0	1	1
Valerian root	0	1	1	
Mold	Mold	13	37	50
Mushroom	Cyclopeptide	2	6	8
	Psilocybin	1	1	2
	Other mushroom	2	11	13
	Total	18	78	96

Table 35 Adverse drug reactions in 2011 registry

Agent	N 2011	Agent	N 2011
Lithium	24	Aspirin	4
Digoxin	22	Cyclobenzepine	4
Acetaminophen	21	Duloxetine	4
Trazodone	15	Hydroxyzine	4
Citalopram	14	Ibuprofen	4
Quetiapine	14	Promethazine	4
Valproic acid	14	Trimethoprim	4
Oxycodone	13	Verapamil	4
Risperidone	12	Amlodipine	3
Venlafaxine	12	Atenolol	3
Bupropion	11	Buprenorphine	3
Olanzapine	11	Carvedilol	3
Diphenhydramine	10	Codeine	3
Lamotrigine	10	Dextroamphetamine	3
Lisinopril	10	Diazepam	3
Clonazepam	9	Escitalopram	3
Fluoxetine	9	Loxapine	3
Haloperidol	9	Metronidazole	3
Aripiprazole	8	Prochlorperazine	3
Clozapine	8	Propofol	3
Fentanyl	8	Ranitidine	3
Lorazepam	8	Topiramate	3
Metoprolol	8	Amoxicillin	2
Phenytoin	8	Atomoxetine	2
Baclofen	7	Azithromycin	2
Buspirone	7	Chromium	2
Ethanol	7	Cobalt	2
Hydrocodone	7	Cocaine	2
Methadone	7	Dapsone	2
Hydromorphone	7	Dilantin	2
Benztrapine	6	Disulfiram	2
Caffeine	6	Doxylamine	2
Carbamazepine	6	Famotidine	2
Dextromethorphan	6	Fluvoxamine	2
Glyburide	6	Fondaparinux	2
Metformin	6	Furosemide	2
Mirtazepine	8	Guanfacine	2
Sertraline	6	Hyoscyamine	2
Tramadol	6	Isoniazid	2
Alprazolam	5	Linezolid	2
Carisoprodol	5	Naloxone	2
Clonidine	5	Other	2
Diltiazem	5	Oxcarbazepine	2
Gabapentin	5	Perphenazine	2
Hydrochlorothiazide	5	Phenylephrine	2
Morphine	5	Piperacillin	2
Omeprazole	5	Polyethylene glycol	2
Prednisone	5	Pregabalin	2
Propranolol	5	Pseudoephedrine	2

comprising approximately 1/3 of the cases in this category over both 2010 and 2011.

The data reported herein is subject to several important limitations. The numbers and trends should not be taken as representative of the use of these agents in the general population. These data reflect only those cases cared for by medical toxicologists making it probable that they represent cases where there was likely to be significant morbidity. Cases with little or no clinical effect are probably under-represented in the Registry. As a result, the Registry is more of a marker of significant toxicities than it is of general population exposures.

A second limitation is that the history of exposure in most patients is either self-reported or comes from a third party. This raises the potential for inaccurate reporting, and is a limitation of any data set like this one.

Quality assurance for data entered into the Registry is currently the responsibility of the individual reporting sites. The data given here represent those that were

Table 35 (continued)

Agent	N 2011	Agent	N 2011
Sulfamethoxazole	5	Ritonavir	2
Ziprasidone	5	Senna	2
Zolpidem	5	Tolterodine	2
Amitriptyline	4	Triamterene	2
Amphetamine	4	Warfarin	2
		Total	459

reported. The Registry has initiated a quality assurance program that will provide a secondary level of monitoring the data. There may, however, be some data that is incompletely reported. To the extent that this may be

Table 36 Antidote entries for 2011 registry

Agent	2010 (%)	N 2011 (%)
2-PAM		1 (<1)
Atropine	1	30 (<1)
Botulinum antitoxin		0
Bromocriptine		1 (<1)
Calcium	2	65 (3)
Carnitine		14 (<1)
Cyproheptadine		24 (<1)
Dantrolene		2 (<1)
Ethanol		5 (<1)
Fab for digoxin	1	20 (1)
Factor replacement		0
Flumazenil	9	155 (6)
Folate	1	54 (2)
Fomepizole	4	103 (4)
Glucagon	2	66 (2)
Hydroxocobalamin		8 (<1)
Insulin euglycemia	1	28 (1)
Lipid resuscitation	1	20 (<1)
Methylene blue		5 (<1)
<i>N</i> -acetylcysteine (NAC)	27	798 (30)
Naloxone (opioid antagonists)	17	498 (19)
Nitrites		2 (<1)
Octreotide	1	19 (<1)
Physostigmine	11	228 (9)
Pyridoxine	1	28 (1)
Sodium bicarbonate	14	315 (12)
Thiamine	3	109 (4)
Thiosulfate		3 (<1)
Vitamin K	3	48 (2)
Total (2011 only)		2,651

Antidotes reported as overall % of total administered in 2010. Only non-zero use reported in 2010

the case it is most likely the outcome data that may be incomplete. Currently, the default outcome is that the patient survived without sequelae. If a death occurs after the patient has been entered in the registry it is the responsibility of the site caring for that patient to edit the record to reflect this outcome. Registry guidelines and site responsibilities have recently been strengthened reinforcing the mandatory nature of recording outcomes. This should make the possibility of incomplete data reporting less likely in subsequent years.

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Conflicts of interest None

Appendix

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