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Drug & Poison Center Information Center's Newsletter

Spring 2017

DPIC Celebrates National Poison Prevention Week (NPPW)

Alysia Longmire, Prevention Education Specialist

Each year Poison Control Centers around the country focus on sharing tips, information and materials to help decrease the incidence of poisoning and minimize exposure to harmful chemicals. National Poison Prevention Week took place Sunday, March 19– Saturday, March 25, 2017.

Including our Northeast Ohio service area, DPIC reached over 3 million households and families and published articles in over 18 newspapers or other print media. Certified Specialist in Poison Information, Jerry Wiesenhahn, Jr., provided an informative interview on Fox 19 news. Click the link to see this interview for yourself. http://www.fox19.com/clip/13195347/poison-prevention-awareness-week

In addition, 32 radio stations aired interviews or public service announcements encouraging poison proofing the home and the safe use and disposal of household chemicals. In addition, DPIC launched the Text. Save. Share. campaign. Detailed instructions to text and save the poison control center contact to your cell phone are in the infographic above.

In this issue:

Food for Thought

Deborah Donald, MSN, RNII, CSPI

The lychee berry is a unique and interesting fruit that originated in China. It is from the Soapberry family: Sapindaceae and Genus: Litchi. This fruit has a few variations, and it is found in tropical regions all over the world. The lychee fruit hangs in bunches like grapes with an outer casing that is red, hard, and bumpy (Figure 1). A white sweet juice filled berry surrounds a brown seed; the outer casing and the brown seed are inedible (Figure 2). The state of Bihar in Northern India is well known for this unique fruit. Lychee orchards are harvested from May through June in the Muzaffarpur district of Bihar. Every year approximately 200 children develop an unknown illness, die or experience brain damage during the lychee fruit harvesting season. Since 1995, it has been a mystery why children were getting ill and dying during that time (Pulla, 2015; CDC, 2015).

The illness was initially thought to be caused by pesticides or infectious encephalitis. Over the years, researchers and investigators followed many leads, but they were unable to determine the cause this mysterious illness. The U.S. Center for Disease Control and Prevention (CDC) and the Indian National Centre for Disease Control (NCDC) conducted an investigational study in 2013 and 2014 solely on the lychee berry. The findings indicated that an unknown toxin in lychee caused hypoglycemia in rats (Table 1), and an unknown lychee toxin that caused hypoglycemia levels in children initially, later developed Acute Non-inflammatory Encephalopathy (Table 2). The affected children in Muzaffarpur were less than 15 years of age, and they usually awakened abruptly between 4:00 - 8:00 a.m. with seizures, memory loss, and confusion. Coma and death occurred in approximately 67 of 200 children studied . Similar toxicity was reported in other countries including Vietnam and Bangladesh. In Vietnam, all affected children developed a fever, and in India some of the children developed a fever. After the CDC and NCDC data was presented, it was advised that symptomatic patients should have their blood glucose levels monitored and intravenous dextrose be administered to suspected and hospitalized patients. Following adoption of these guidelines, there was a 29% decrease in the mortality rate in 2014 compared to 2013 (Pulla, 2015; CDC, 2015).

Table 1. Rats

Toxin	Symptom	Illness
Unknown Lychee toxin	Hypoglycemia	Neurological

Table 2. Children (6 months -14 years)

Toxin	Symptom	Outbreak Illness
Unknown Lychee toxin	Hypoglycemia	Acute Non-inflammatory Encephalo-pathy

Ackee fruit found in the Caribbean is a variation of the lychee fruit. Children who ate the unripened fruit developed "Jamaican vomiting sickness." The ackee fruit toxin is hypoglycin; the lychee fruit toxin is methylenecyclopropylglycine (MCPG). The toxins are structurally similar. In 1991, a research article indicated that rats fed MCPG developed hypoglycemia. The CDC and NCDC investigators are currently studying MCPG and its metabolites. In addition to testing environmental samples, they also are testing the blood and urine samples of patients who died from the unknown illness. The inedible brown lychee seed does contain the MCPG toxin. Investigators are attempting to find out (1) How does MCPG get in the body? (2) Is MCPG in the white berry flesh of some lychee varieties? (3) Why are some geographical regions affected and others not? Currently, no risk factors have been identified by the NCDC (Pulla, 2015; CDC, 2015).

Lychee fruit imported to the United States is currently unregulated with no screening for MCPG. It is an expensive imported fruit. Canned ackee fruit is also imported, but it is regulated and screened for hypoglycin. As commercial production increases in Bangladesh, China, India, Philippines, Thailand, and Vietnam to meet increased demand for lychee fruit, it will become increasingly important for investigators and the lychee industry to collaborate to prevent additional poisonings from lychee fruit ingestion. Continued research may allow lychee fruit toxin or a derivative to be developed as a treatment for metabolic disorders. (Spencer & Palmer, 2015).

Figure 1. Lychee fruit

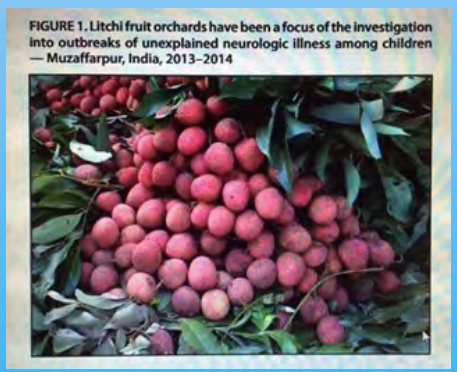

Figure 2. Lychee Berry with seed

(CDC, 2015)

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A New Approach to Substance Abuse: The Icelandic Model

Shannon Staton-Growcock, MSN, RN, CSPI

Substance use continues to be a global public health concern in many countries with advanced economies. Twenty years ago teens in Iceland were among the heaviest substance abusers in Europe — with more than 40 percent of 15- and 16-year-olds reporting being drunk in a given month. Here it is now 2017, and the country boasts the fewest drinking, smoking and drug-taking youth on the continent. The turnaround is credited, partly, to an American psychologist and drug researcher, Harvey Milkman, who was convinced that replacing artificial highs with natural highs, before addiction began, could change a society. Harvey Milkman is a visiting professor at the University of Reykjavik, and a professor of psychology at the Metropolitan State University of Denver. He worked closely with the implementation of the Icelandic Model.

"we had that 'aha' moment that it was the style of coping that they were becoming addicted to."

Harvey Milkman, on what he learned studying drugs and drug users in the 1970's

Icelandic social scientists at the Icelandic Centre for Social Research and Analysis (ICSRA), a non-profit research institute in the City of Reykjavik and now affiliated with Reykjavik University, along with policy makers and practitioners in the field, began collaborating in 1990s in an effort to better understand the societal factors influencing substance use among adolescents and potential approaches to prevention.

Icelandic Prevention Model

Step 1.) a coalition of social scientists and policy makers use national data to identify the scope of the problem and the broad outlines of the approach to be pursued.
Step 2.) action shifts to the local level as team members 'hit the road', discussing the national data in communities and neighborhoods throughout the country. By design, these local level discussions are inclusive, mobilizing an ever-widening group of researchers, policy makers, practitioners and community members, including parents, school personnel, sports facilitators, recreational and extracurricular youth workers.
Step 3.) local action in multiple sites, informed by the national data but animated by the uniquely different spirit, talents, and imaginations of neighborhoods, towns and regions.
Step 4.) integrative reflection; as local activities are reviewed by participants, process and outcome dimensions of the aggregate activity are explored, and then analyzed with the new round of national data.

The model is based on quick and confident action, supported by the Icelandic values of independence, cooperation and roles for everyone. Preventing adolescent substance use remains a challenge for both European and North-American societies. The Icelandic Model of Adolescent Substance Use Prevention focuses on both risk reduction and the enhancement of protective factors at various levels of prevention.

Parental support and monitoring not only directly decrease the likelihood of substance use, they also affect friendship choices. Thus, adolescents who perceive that their parents provide substantial support are less likely to associate with friends who use drugs, and those who acquire friends who use drugs are less likely to start using drugs themselves. In schools where parents know the friends of their adolescent children and develop and maintain relationships with the parents of their children's friends—a social-capital indicator known as 'intergenerational closure'develops.

In Iceland, the relationship between people and the state has allowed an effective national program to cut the rates of teenagers smoking and drinking to excess – and, in the process, brought families closer and helped kids become healthier. In Iceland "It's really a combination of government support, corporate support and tax support. The cost is estimated to be $250 a year per individual, which is a very small price compared to what it costs when a kid becomes adjudicated and requires probation or incarceration or something. It's a minor expense" (Milkman, 1995). Will no other country decide these benefits are worth the costs?

Substance use amongst Icelandic adolescents has become the lowest in Europe in 2013. In 1998 42% of 15 to 16 year old Icelanders had become drunk during the past 30 days whereas in 2013, only 5% of students report the same. Daily smoking and the use of cannabis had also decreased dramatically.

Michael O'Toole, CEO of Mentor, a charity that works to reduce alcohol and drug misuse in children and young people in the UK, fully endorses the Icelandic focus on parents, school and the community all coming together to help support kids, and on parents or caregivers being engaged in young people's lives. Improving support for kids could help in so many ways, he stresses. Even when it comes just to alcohol and smoking, there is plenty of data to show that the older a child is when they have their first drink or cigarette, the healthier they will be over the course of their life.

Preventing adolescent substance use remains a challenge for both European and North-American societies. The Icelandic Model of Adolescent Substance Use Prevention focuses on both risk reduction and the enhancement of protective factors at various levels of prevention. Substance use among Icelandic adolescents over a decade during which the Icelandic Model was implemented demonstrates that it is possible to define and implement well- organized steps in promoting adolescent emotional well-being by capitalizing on opportunities at several community levels to reduce substance use nationally.

The Icelandic Model is a promising example of such an approach. Harvey Milkman noted that you can't prescribe a generic model to every community because they don't all have the same resources. Any move towards giving kids in the US the opportunities to participate in the kinds of activities now common in Iceland, depends on what already exists. "You have to rely on the resources of the community (1995)."

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A review of "The Secret History of Lead" by Jamie Lincoln Kitman

Sara K. Pinkston, RNII, MSN, CSPI

In March of 2000 Jamie Lincoln Kitman wrote and published an article entitled "The Secret History of Lead" supported by the Investigative Fund of The Nation Institute – "a nonprofit media center dedicated to strengthening the independent press and advancing social justice and civil rights" (www.nationinstitute.org). The Investigative Fund of The Nation Institute "supports the costs associated with investigative journalism to help improve the scope and quality of investigative reporting in the independent press and beyond" (www.theinvestigativefund.org).

The article gave a compelling look at the history of lead as an additive in gasoline beginning with its commercial inception in 1927 through its demise in 1986 when catalytic converters came into being to reduce emissions. Lead would contaminate & make catalytic converters ineffective. Otherwise, we would still be using lead as an additive in gasoline. Three of America's leading corporations - General Motors, DuPont, and Standard Oil of New Jersey (now known as Exxon) - were instrumental in promoting Tetraethyl Lead (TEL) as an additive in gasoline (p. 1, The Secret History of Lead).

Here is a brief timeline of the "life and times" of TEL:

1854 - TEL was first discovered by a German chemist in 1854. It was known to be highly poisonous and was not used commercially because of its known deadliness.

1911 - Charles Kettering (yes, that Charles Kettering - known for half of the famous Memorial Sloan-Kettering Cancer Institute) invented an electric self-starter engine. It eliminated the sometimes dangerous hand cranking of engines helping many Americans drive for the first time.

Kettering then started his own firm, Dayton Engineering Laboratories Company, or DELCO. It received its first big order for $10 million from General Motors Corporation which had been founded only 3 years earlier.

General Motors' Cadillac was equipped with DELCO's self-starter and battery ignition, but customers reported the engine of the vehicle had a tendency to knock – a sharp, metallic sound which some believed hinted at damage being done inside the engine. Critics began blaming Kettering's electrical components. Kettering, however, was certain that the knocking was a result of the engine's fuel rather than his electrical ignition components.

1916 - Kettering sold DELCO to GM and its new partner, Alfred Sloan, (we now have the first part of Memorial Sloan-Kettering Cancer Institute). Kettering was on the search for a cure for this engine knock. His new firm, the Dayton Research Laboratories, employed an assistant Thomas Midgley to study this problem.

1918 - Kettering and his staff concluded that ethyl alcohol could be blended with gasoline to get rid of the knock; therefore, making it suitable for motor fuel in aircraft or automobile engines.

1919 – General Motors purchased Kettering's Dayton Research Laboratory.

1920 – General Motors named Charles Kettering vice president of research for General Motors Research Corporation (p. 5, The Secret History of Lead). Thomas Midgley, now working for General Motors, filed a patent for a blend of alcohol and cracked (olefin) gasoline as an antiknock fuel. GM had been temporarily concerned about an imminent disruption in oil supply. So, for a short time, they were all for ethanol as an additive in gasoline.

The DuPont family controlled more than 35% of GM shares and packed the board with a DuPont faction successfully taking control of the finance committee. After the recession of 1920, GM's former head, W.C. Durant lost his stake in the company and was forced to leave. Pierre DuPont would now run the company and Alfred Sloan became executive vice president.

Following an unfortunate decision by Kettering to champion an air-cooled engine which proved to be a costly disaster for GM, Kettering gave his trusted assistant, Thomas Midgley, two weeks to find something to dazzle new management's interests and continue funding of his lab's fuel research.

1921 - Thomas Midgley reportedly discovered tetraethyl lead or TEL's ability to stop the knock when added to gasoline. In spite of lead's known toxicity and in spite of safer, alternative antiknock (ethyl alcohol) additives, TEL was on its way to becoming the additive of choice. Kettering proposed the name "Ethyl" for the new antiknock fluid.

From the corporation's perspective, ethyl alcohol could not be made in the volumes needed, and it was too easily made by anyone with a still. Ethanol, unlike TEL, could not be patented.

1922 – An agreement was made with Irenee DuPont (Pierre's brother) to supply GM with TEL. Pierre signed for GM while Irenee signed for the DuPont company.

1923 – Manufacturing began with a small operation in Dayton, OH. The US Surgeon General, H.S. Cumming, wrote a letter to Pierre DuPont expressing concern regarding the health hazard associated with extensive use of TEL in engines.

Kettering submitted his resignation feeling defeated in the aftermath of the air cooled engine debacle. It was declined by Sloan who was now GM's president (p. 7, The Secret History of Lead). Midgley sent a letter to Kettering detailing possible profits from manufacturing of TEL. One month later The General Motors Chemical Company was established to produce TEL. Charles Kettering was made president and Thomas Midgley vice president.

Kettering marketed TEL to GM as not only an antiknock additive, but also as a way to make cars faster and more powerful due to the high compression it enabled in engines. Thus, it paved the way for the sale of more cars.

Kettering signed contracts with Standard Oil of New Jersey (now Exxon), Standard Oil of Indiana (later Amoco and now merged with BP), and Gulf Oil (owned by Mellon) for East Coast, Midwest, and Southern distribution of leaded gasoline

TEL plant opened in Deepwater, New Jersey, where the first of several deaths of workers there occurred 30 days after plant opening.

GM signed a contract with the Bureau of Mines to "refute any false propaganda" regarding the safety of TEL. As part of the contract with GM, The Bureau of Mines was required to submit any of their research papers or articles regarding the safety of TEL to them for comment, criticism, and approval before publication.

1924 – Two GM employees at a pilot plant in Dayton responsible for manufacturing of TEL, died of lead poisoning. Two months later, production of TEL increased. GM president, Sloan, appointed a medical committee to investigate deaths at Deepwater and Dayton.

Standard Oil of New Jersey developed a faster, cheaper method to produce TEL. They now had better manufacturing technology with a patent of their own. GM and Standard Oil of New Jersey formed a joint venture called the Ethyl Gasoline Corporation.

On October 26, 1924, the first of five deaths occurred at Standard Oil's Bayway TEL works after experiencing "fits of violent insanity". Four more deaths followed in quick succession. More than 80% of Bayway's employees would die or suffer severe poisoning.

In order to demonstrate the safety of TEL, Midgley rubbed it on his hands during numerous exhibits. Midgley was soon diagnosed with lead poisoning.

A review of "The Secret History of Lead" by Jamie Lincoln Kitman (contd.)

Sara K. Pinkston, RNII, MSN, CSPI

New York City Board of Health banned the sale of TEL enhanced gasoline. Soon after, Philadelphia, Pittsburgh, and the State of New Jersey also banned the sale of gasoline containing TEL.

The Bureau of Mines released a report giving TEL a thumbs up based on limited animal testing.

Three months after the Bayway deaths, Standard Oil is acquitted of criminal responsibility.

1925 – Ethyl was withdrawn from the market.

The Surgeon General's conference began. TEL referred as a "Gift of God" by Standard Oil's Frank Howard during the hearing.

More TEL deaths were reported at Deepwater plant.

Robert Kehoe of the University of Cincinnati hired by Kettering was appointed chief medical consultant of the Ethyl Corporation. He remained in that post for 33 years.

1926 – The Surgeon General's Committee found "no good grounds" for prohibiting the sale of Ethyl. Dr. Robert Kehoe was a member of the committee.

1927 – Advertising began plugging the benefits of TEL including increased speed and more power on hills and heavy roads.

1930s - Late 1930s – US market essentially saturated with leaded gasoline. Now, it was making major progress in Europe .

1962 – Standard Oil and GM sold their interests in the Ethyl Corporation. It was bought by the Albermarle Paper Manufacturing Company of Richmond, VA .

1963 – 98% of all gasoline sold in US contained TEL. Now, it was sold worldwide.

1969 – Mounting awareness of the nation's smog problems put pressure on Congress to enact air pollution laws that would eventually put lead out of business in the US.

1970 – GM president, Ed Cole, announced the company would meet pending clean-air laws with catalytic converters beginning in 1974.

1974 – EPA announced phase out of ethyl in gasoline and was promptly sued by Ethyl Corporation and DuPont stating they were denied property rights. A panel of the US Court of Appeals for the District of Columbia Circuit ruled against the EPA's lead regulations as "arbitrary and capricious" .

1976 – The full US Court of Appeals for the DC Circuit overturned the earlier decision against the EPA. They ruled that "significant risk" was adequate for the EPAs restrictions regarding lead and within its authority.

1986 - Phase out of Ethyl essentially complete in United States.

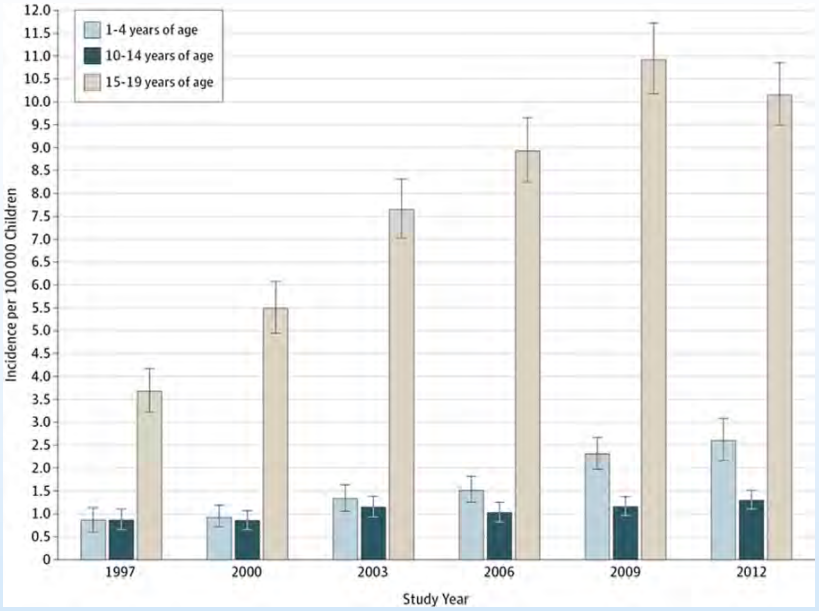
Various statistics were given by the author regarding decline of mean blood lead levels in the United States. One such statistic "based on data collected in more than 60 US cities by the Centers for Disease Control (CDC), the Department of Health & Human Services reported that blood-lead levels in Americans aged 1-74 declined 78% between 1978 and 1991".

One of the more interesting aspects of this article was Kehoe's testimony to the Surgeon General's Committee. He essentially stated TEL was safe because it could not be proven to be unsafe. This reasoning has now developed into the Kehoe Rule.

Reference: Kitman, J.L. (2000). The secret history of lead. *The Nation.* Retrieved April 2017 from: https://www.thenation.com/article/secret-history-lead/

Opioid Poisoning Increase in Children

Heidi Frondorf RN, BSN



As the opioid epidemic is increasing, so is the news coverage surrounding the epidemic. Many of you are probably familiar with the image of a mother and father seated in the front seat of the car passed out, while their 4 year old is strapped in the back seat. After seeing this picture, one would not be surprised that these children often deal with mental health issues. However, according to a new study, published in the JAMA pediatrics (Gaither et al., 2016, Vol 170, No 12), it has been shown that the opioid epidemic is affecting children far beyond mental health. The epidemic has caused an increase in hospitalizations for children due to opioid poisonings.

Although data has shown that in 2011 to 2013, physicians have been prescribing opioids less frequently; there were still 259 million prescriptions written for opioid painkillers. In 2012, according to Julie Gaither, the study lead author and an epidemiologist and post-doctoral fellow at Yale, opioid poisonings are increasing with more opioids being prescribed. In addition, poisonings are increasing as parents and other adults are leaving pills within easy reach for children.

Between 1997 and 2012, 13,052 children were hospitalized for poisonings from opioid prescriptions of Oxycodone, Codeine and similar drugs. This number was doubled from previous years. The most affected ages (1 to 4 years) have access to parents or adults medications. There is a gap between those ages 5 to 9 years, who are not affected by the poisonings, which according to Gaither could be due to this age group learning to differentiate between pills and candy. Ages 10 and up continue to be affected by opioid poisonings, but these poisonings are likely to be a cause of suicide or self-inflicted injury rather than accidental ingestion. Surprisingly, there has been a slight decrease in opioid poisoning hospitalizations in age groups 15-19 years. Instead this age group has seen a rise in hospitalizations involving heroin, an indicator that opioid abuse may lead to heroin abuse.

This data infers that doctors should only prescribe the amount of opioids necessary to treat initial pain. It also shows the need for physicians to include teaching methods to parents and adults on how to keep medications out of reach of children and how to properly dispose of opioids. CS Mott took a poll this year of nearly 1200 patient's ages 5 to 17, and found that 1/3 of the parents stated their child was prescribed an opioid and about half of them had left over medication. According to the study, 8 percent of those with unused medication returned it to their doctor or pharmacy, 47 percent kept the leftover drugs, 30 percent threw the drugs in the trash or down the toilet, 6 percent said another family member took the medication, and 9 percent did not remember what they had done with the medication. Based on this data, proper disposal of opioids is something that needs to be addressed, as it can ultimately impact the number of hospitalizations in children caused by opioid poisoning.

55,622

OPIOID EXPOSURES*

Jan. 1 - October 31, 2016
**These numbers reflect multiple substance exposures to opioids reported to poison centers*

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Journal of the American Medical Association. Image: http://jamanetwork.com/data/Journals/PEDS/935880/m_poi160061f1.png

Cuyahoga County: Opioid Epidemic

Tisha Carson RPh, CSPI

A frantic 911 call by a father, "For some reason, my son's not breathing…his lips are turning blue…" A parent's nightmare. The call was made just before 9:30 pm when the father found his 8 year old son in bed not breathing. He thought the child had turned over into a pillow and suffocated. He performed CPR on the child until the police arrived and took over. When the child was revived, he was rushed to the hospital. Testing revealed that he had opiates and benzodiazepines in his system. Those drugs were discovered to be heroin, fentanyl and Xanax. Thankfully, he survived. Needles and drugs were found in the home, and police suspected the parents were high. During a search, police found a bag of heroin and prescription pills hidden inside a toy watch kept inside the boy's sock. No one seems to know how it got there. Now this couple from Berea, Ohio have been indicted by a grand jury in the Cuyahoga County Common Pleas Court on charges of child endangering and drug possession. These parents didn't set out to place their child in harm's way, but it happened anyway.

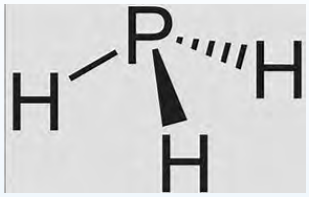
There are so many children impacted in multiple ways through addiction: from abuse, neglect, accidental overdose of the child, to becoming an orphan. The Cuyahoga County Medical Examiner's Office reported deaths from heroin, fentanyl and other opiates rose from 64 in 2011 to 517 last year. In total, at least 663 people died of drug overdoses in the county last year. When those 663 lost their lives, the lives of their families, especially their children, were turned upside down.

Reference: Ohio parents charged after 8-year-old son overdoses on heroin. *Daily News*. Retrieved April 2017 from: http://www.nydailynews.com/news/national/ohio-parents-charged-8-year-old-son-overdoses-heroin-article-1.2978464

Phosphine Gas

Robert Henry EMT-B, PIP

Phosphine can come in multiple forms including aluminum, calcium, and magnesium phosphide; often solids are used as fumigants, and zinc phosphide is a common rodenticide. Phosphine gas develops when the solid comes in contact with either water or an acid. It is a colorless, flammable, and toxic gas with an odor of garlic or decaying fish. The odor is not always an adequate indicator of the presence of phosphine gas.



Symptoms of exposure to phosphine gas may include restlessness, irritability, drowsiness, tremors, ataxia, cough, shortness of breath, abdominal pain, and vomiting. A person exposed only to phosphine gas does not pose a risk of secondary contamination. Exposure to metallic phosphides on clothes, skin, or hair can react with water or moisture to generate phosphine gas. Vomitus after ingestion of phosphides can "off-gas" phosphine which may be a significant concern for medical staff. Veterinary hospital staff should take this into consideration when inducing vomiting after an animal has ingested a zinc phosphide rodenticide.

Reference: Centers for Disease Control. (April 27, 2017). *Morbidity and Mortality Weekly Report, p.* 286-288.

Poison Center Snapshot—2015

American Association of Poison Control Centers (AAPCC)

Who calls the poison center? Anyone can experience a poison emergency. Poison centers take calls from and manage cases about people of all ages, and can provide live, tailored help to callers in 150 languages. In 2015, just under half of exposure cases managed by poison centers involved children younger than six, but as in previous years, many of the more serious cases occurred among adolescents and adults.

When do people call the poison center? Experts answer calls to the poison center 24 hours a day, 7 days a week, every day of the year. Similar to previous years, in 2015 higher call volumes were observed in the warmer months.

Where do the most poison exposures occur? In 2015, 93% of human exposures reported to poison centers occurred at a residence, but they can also occur in the workplace, schools, outdoors, and anywhere else! About 67% of the 2.2 million exposures reported to poison centers were treated at the exposure site, saving millions of dollars in medical expenses. In fact, poison centers save Americans more than $1.8 billion every year in medical costs and lost productivity!

About what kinds of things do people call the poison center? In 2015, 57% of human exposures involved medications, or pharmaceuticals. Other exposures were to household products, plants, mushrooms, pesticides, animal bits and stings, carbon monoxide, and many other types of nonpharmaceutical substances.

Why do people call the poison center? People call the poison center when they think someone may have been exposed to something that could hurt them. People also call the poison center for information about medications, pesticides, chemicals, bites and stings, carbon monoxide, and many other topics. In 2015, 80% of exposures involved people who swallowed a substance. However, people were also exposed through the lungs, skin, eyes and in other ways. Most poison exposures were unintentional (78%). Poison centers also received calls about medication side effects, substance abuse, malicious poisonings, and suicide attempts.

Cincinnati Children's
changing the outcome together

DRIPPING

Sheila Goertemoeller PharmD, DABAT

A recent study published by the American Academy of Pediatrics found that 1 in 4 high school youth who use e-cigarettes have tried "dripping" with them. This vaping method involves dripping the e-cigarette liquid directly onto the hot coils of the apparatus, which can produce smoke that is more potent. There are at least 4 potential risks from "dripping" :

1. **Exposure to more potent and potentially toxic substances**. A higher e-liquid temperature can produce more harmful chemicals which can be inhaled into the lungs. This includes formaldehyde and acetaldehyde, which are carcinogenic. Formaldehyde may cause asthma, contact dermatitis or adverse side effects on the central nervous system such as mood changes, depression, headache, insomnia, irritability, and attention and memory issues.
2. **Potential for skin contact**. Dripping the e-liquid directly onto the coil, versus the traditional method of vaping, could raise the risk for accidental exposure to the skin. Nicotine is rapidly absorbed through the skin. The e-liquid, if hot, may burn the skin.
3. **Safety for younger children.** Our poison control center receives calls about kids' exposures to e-liquids, using traditional vaping methods. Both toddlers and children accidentally ingest the liquid when it has been left within their reach.
4. **Potential for explosions.** There have been reports of e-cigarettes exploding, causing **chemical burns, blast injuries, and thermal burns.**

Hysingla ER® (Hydrocodone Bitartrate Extended-Release tablets)

Alexis Mundy , DPIA, Paramedic

Indication

New to the ever-growing chronic pain management drug class, Hysingla ER, a brand of extended release hydrocodone was recently released. Hysingla ER is a single-entity hydrocodone product intended for once daily administration, and is reported to last for 24 hours. The medication is intended for severe pain that requires daily, round-the clock, long-term opioid treatment; especially when alternative treatment options are inadequate. Safety and efficacy of this medication was primarily evaluated in a study conducted for people with chronic lower back pain.

Dosing

Hysingla ER 20mg is the recommended starting dose for patients who are not opioid tolerant. Per the drug insert for Hysingla, some examples of opioid tolerant patients would be those that receive 60mg oral morphine, 25mg oral oxymorphone or equianalgesic doses of other opioids daily. Hysingla ER doses are available at 20, 30, 40, 60, 80, 100, and 120mg of extended release hydrocodone. This makes the largest available dose of Hysingla ER more than twenty times more potent than the typical starting dose of most hydrocodone preparations containing 5mg of the opioid.

These tablets are intended to be taken whole, one at a time. Crushing, chewing or dissolving the Hysingla tablets will result in an un-controlled release of hydrocodone that can lead to overdose and/or death.

Formulation

In the midst of the nationwide opioid epidemic Hysingla ER's manufacturer has taken measures to reduce the potential for abuse. One of these properties is the difficulty of crushing, breaking or dissolving the tablet. It forms a thick gel when crushed and cannot be easily prepared for injection.

For patients with chronic pain management issues, Hysingla offers steady-state hydrocodone concentrations around the clock. Hysingla ER is now available to be prescribed nationwide. For more information on this drug, visit the manufacturer's website at https://hysinglaer.com.

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Caralluma Fimbriata versus Obesity

Amanda Sothard, UC PharmD Candidate 2017, Robert Goetz PharmD, D ABAT

http://carallumafimbriataactives.org/wp-content/uploads/2014/02/Caralluma-Fimbriata-plant.png

A plant that has been used as an appetite suppressant in the traditional medicine of India is now starting to show up more frequently in the United States as a possible tool to combat obesity. *Caralluma fimbriata*, or *Kullee moofiyan,* as it is commonly known in some regions of the world, is an edible cactus. It grows wild in India and is also found in Africa, the Canary Islands, the Arabian Peninsula, parts of southern Europe, Ceylon, and Afghanistan. Its stems are covered in spines and may contain foul smelling star shaped blooms that typically appear in late summer. It can be consumed in a variety of ways including being eaten raw, cooked with spices, or used in chutneys. Historically, hunters would chew raw chunks of the plant when they were on particularly long hunts, and it was frequently consumed as a vegetable during times of famine. *Caralluma* extracts are increasingly available online and in health food stores as a dietary supplement tablet.

The mechanism of *Caralluma*'s appetite suppression is unknown, but is thought to stem from its ability to block ghrelin release and regulate neuropeptide Y activity. Ghrelin is released when the stomach is empty with resulting appetite suppression. Studies evaluating the efficacy of *Caralluma both* as an appetite suppressant and to treat abdominal obesity have produced conflicting results. A 2006 study conducted in India found that 500 mg of *Caralluma* twice a day was effective at suppressing appetite, but did not produce statistically significant weight loss. Conversely, a 2013 study found that it did not suppress appetite, but did help to reduce abdominal obesity.

Information regarding the long term safety of Caralluma is not available. However, in a randomized placebo controlled study of its use in healthy volunteers an extract of Caralluma was given as two 500 mg capsules of daily (1 g/day) for 60 days. Adverse effects were limited to mild abdominal distention, flatulence, constipation and gastritis with an incidence similar to that seen in the placebo group. A second similar study by the same researchers followed obese patients for twelve weeks. Reported adverse effects were again mild and transient with similar incidence in patients receiving active drug or placebo.

Whether *Caralluma* will help patients lose weight is still unclear, especially considering that obesity is not always linked to increased appetite. However, despite conflicting evidence of efficacy in controlled trials *Caralluma* is increasingly available and anecdotal evidence of its long use as an appetite suppressant in Indian traditional medicine is intriguing. While compelling information on its efficacy is sparse, short term use for up to 12 weeks appears to be well tolerated with only mild transient side effects.

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Vraylar® (Cariprazine) Drug Review

Alyssa Nichols, UC PharmD Candidate 2017, Robert Goetz PharmD, D ABAT

Cariprazine is an antipsychotic medication that received FDA approval in September 2015 for the treatment of schizophrenia and acute mania or mixed episodes associated with bipolar disorder. It is a dopamine D_3 and D_2 receptor partial agonist, with a preference for the D_3 receptor. Cariprazine is also a partial agonist of serotonin 5-HT_{1A} and an antagonist of serotonin 5-HT_{2A} and 5-HT_{2B}. Its major metabolites are desmethyl cariprazine (DCAR) and didesmethyl cariprazine (DDCAR). These metabolites both have *in vitro* binding profiles similar to cariprazine and they are equipotent to the parent compound.

The dose for schizophrenia is 1.5 mg – 6 mg once daily. A starting dose of 1.5 mg can be increased to 3 mg on day 2. Dosing for acute treatment of manic or mixed episodes associated with bipolar disorder is 3 mg – 6 mg once daily, with a starting dose of 1.5 mg which should be increased to 3 mg on day 2. Dosing should be adjusted using 1.5 – 3 mg increments.

Peak plasma	3-6 hours
Steady state	Cariprazine & DCAR: 1-2 weeks DDCAR: 4-8 weeks
Protein binding	91-97%
Half-life elimination	Cariprazine: 2-4 days DDCAR: 1-3 weeks
Metabolism	CYP3A4 and, to lesser extent, CYP2D6
Excretion	Urine (21%; 1.2% unchanged)

Cariprazine's pharmacodynamics properties include high D_3, D_2, 5-HT_{1A}, and 5-HT_{2B} binding affinity (Ki = 0.085 nM, 0.69 nM, 2.6 nM, and 0.58 nM respectively). It also includes moderate 5-HT_{2A} and H_1 binding affinity (18.8 nM and 23.2 nM respectively). Lastly, it includes low 5-HT_{2C} and α_{1A}-adrenergic binding affinity (134 nM and 155 nM respectively). **Cariprazine has no cholinergic muscarinic activity and does not appear to prolong QT_C interval.**

There is a **Black Box Warning** for cariprazine stating that elderly patients with dementia-related psychosis are at **increased risk of death** (due to cardiovascular complications or infections). Other warnings included are related to the atypical antipsychotic class, but cariprazine has **fewer incidences** of hyperprolactinemia and **extrapyramidal symptoms**. Cariprazine is believed to have drug interactions with strong CYP3A4 inhibitors and inducers as this is the same enzyme that metabolizes cariprazine. The only current treatment for overdose is supportive care.

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Supervised Injection Facilities

Robyn Davis MSN, RNII, CSPI

http://www.treatment4addiction.com/addiction/iv-drug-use-infection/

Supervised Injection facilities (SIFs) are exactly what the name describes: they are a designated place for drug users to prepare and use drugs under the supervision of health care professionals. Nurses are on site and able to implement lifesaving treatments such as naloxone in the event of an overdose. Currently there are 66 cities in 9 different countries operating these types of facilities. As of today there are no operating SIFs in the United States. The closest SIF to the United States is in Vancouver, Canada.

Last summer Seattle, San Francisco, and Ithaca began considering opening SIFs. In January, Seattle Mayor Ed Murray announced Seattle/King County Public Health would be tasked with setting up two supervised injection facilities in Seattle. They are still working to secure funding to build these 2 facilities.

The purpose of SIFs is not to encourage or enable drug use but to provide a safe environment for users, prevent loss of life from overdoses, and to provide addiction resources when users are ready for treatment. These facilities do not provide drugs to users.

Heroin use is a growing epidemic that cannot be ignored and eradicating heroin use is unlikely. SIFs are considered an alternative solution to the heroin epidemic as they allow drug use in a controlled environment with sterile supplies in the hopes to decrease disease transmission and prevent overdose fatalities. SIF's encourage addiction recovery resources to all users through face to face interactions with healthcare providers.

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Tamiflu Psychosis

Gretchen Shoemaker, UC PharmD Candidate 2017, Robert Goetz PharmD, D ABAT

Since Tamiflu's approval in 1999, there have been post-marketing reports of neuropsychiatric adverse events occurring in individuals taking Tamiflu (oseltamivir), particularly in Japan. **Most of these case reports involve adolescents and the reactions can include insomnia, confusion, delirium, and hallucinations.** In a small number of cases, patients have died as a result of reckless behavior. These reports led Japanese health officials to prohibit the use of Tamiflu in patients 10-19 years old. In 2006 the FDA recommended the addition of a warning to the prescribing information for Tamiflu, however the agency stated that it was uncertain whether the neuropsychiatric events are related to the drug, influenza, or some combination of both. This distinction still remains unclear, but there does appear to be a link between Tamiflu and abnormal behaviors.

It is important to consider that Japan consumes approximately 75% of the world's Tamiflu and has more intensive adverse event reporting requirements in the period following drug approval. Both of these factors could contribute to a greater number of cases seen in Japan. Several large studies in the U.S. and Europe have found no significant difference in neuropsychiatric events in patients receiving Tamiflu. On the other hand, a meta-analysis and observational cohort study performed in Japan both found an association between Tamiflu and abnormal behaviors. Additionally, almost all of the case reports involve otherwise healthy individuals with no psychiatric history who develop neuropsychiatric symptoms within hours of taking a dose of Tamiflu.

Various mechanisms for Tamiflu causing psychiatric issues have been suggested. Certain genetic polymorphisms could lead to increased concentrations of drug in the central nervous system. Animal studies have also implicated Tamiflu as an inhibitor of several different receptors in the body. These factors either alone or in combination could potentially lead to the abnormal behaviors, but further study is needed.

Although the mechanism is unclear, Tamiflu has been associated with strange and dangerous behaviors in some patients. It is unclear if there are any lasting effects, although the acute symptoms have resolved in a matter of days after stopping the drug for patients in case reports. It is important to monitor patients, particularly children, taking Tamiflu and report the emergence of unusual behaviors to a healthcare professional immediately.

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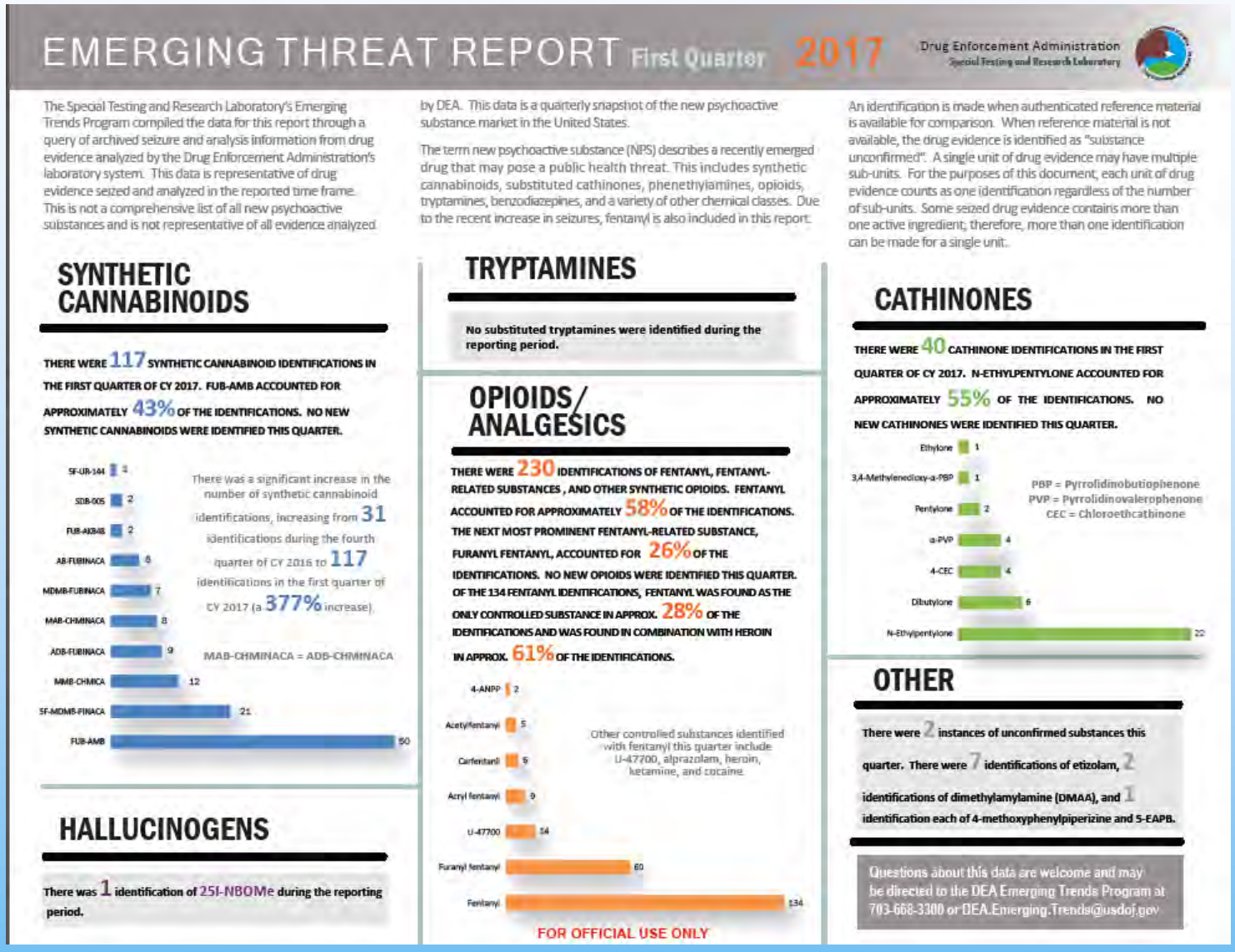
Emerging Threat Report

Drug Enforcement Administration (reprinted)



EMERGING THREAT REPORT First Quarter 2017

Drug Enforcement Administration
Special Testing and Research Laboratory

The Special Testing and Research Laboratory's Emerging Trends Program compiled the data for this report through a query of archived seizure and analysis information from drug evidence analyzed by the Drug Enforcement Administration's laboratory system. This data is representative of drug evidence seized and analyzed in the reported time frame. This is not a comprehensive list of all new psychoactive substances and is not representative of all evidence analyzed by DEA. This data is a quarterly snapshot of the new psychoactive substance market in the United States.

The term new psychoactive substance (NPS) describes a recently emerged drug that may pose a public health threat. This includes synthetic cannabinoids, substituted cathinones, phenethylamines, opioids, tryptamines, benzodiazepines, and a variety of other chemical classes. Due to the recent increase in seizures, fentanyl is also included in this report.

An identification is made when authenticated reference material is available for comparison. When reference material is not available, the drug evidence is identified as "substance unconfirmed". A single unit of drug evidence may have multiple sub-units. For the purposes of this document, each unit of drug evidence counts as one identification regardless of the number of sub-units. Some seized drug evidence contains more than one active ingredient; therefore, more than one identification can be made for a single unit.

SYNTHETIC CANNABINOIDS

THERE WERE 117 SYNTHETIC CANNABINOID IDENTIFICATIONS IN THE FIRST QUARTER OF CY 2017. FUB-AMB ACCOUNTED FOR APPROXIMATELY 43% OF THE IDENTIFICATIONS. NO NEW SYNTHETIC CANNABINOIDS WERE IDENTIFIED THIS QUARTER.

There was a significant increase in the number of synthetic cannabinoid identifications, increasing from 31 identifications during the fourth quarter of CY 2016 to 117 identifications in the first quarter of CY 2017 (a 377% increase).

MAB-CHMINACA = ADB-CHMINACA

HALLUCINOGENS

There was 1 identification of 25I-NBOMe during the reporting period.

TRYPTAMINES

No substituted tryptamines were identified during the reporting period.

OPIOIDS/ ANALGESICS

THERE WERE 230 IDENTIFICATIONS OF FENTANYL, FENTANYL-RELATED SUBSTANCES, AND OTHER SYNTHETIC OPIOIDS. FENTANYL ACCOUNTED FOR APPROXIMATELY 58% OF THE IDENTIFICATIONS. THE NEXT MOST PROMINENT FENTANYL-RELATED SUBSTANCE, FURANYL FENTANYL, ACCOUNTED FOR 26% OF THE IDENTIFICATIONS. NO NEW OPIOIDS WERE IDENTIFIED THIS QUARTER. OF THE 134 FENTANYL IDENTIFICATIONS, FENTANYL WAS FOUND AS THE ONLY CONTROLLED SUBSTANCE IN APPROX. 28% OF THE IDENTIFICATIONS AND WAS FOUND IN COMBINATION WITH HEROIN IN APPROX. 61% OF THE IDENTIFICATIONS.

Other controlled substances identified with fentanyl this quarter include U-47700, alprazolam, heroin, ketamine, and cocaine.

FOR OFFICIAL USE ONLY

CATHINONES

THERE WERE 40 CATHINONE IDENTIFICATIONS IN THE FIRST QUARTER OF CY 2017. N-ETHYLPENTYLONE ACCOUNTED FOR APPROXIMATELY 55% OF THE IDENTIFICATIONS. NO NEW CATHINONES WERE IDENTIFIED THIS QUARTER.

PBP = Pyrrolidinobutiophenone
PVP = Pyrrolidinovalerophenone
CEC = Chloroethcathinone

OTHER

There were 2 instances of unconfirmed substances this quarter. There were 7 identifications of etizolam, 2 identifications of dimethylamylamine (DMAA), and 1 identification each of 4-methoxyphenylpiperizine and 5-EAPB.

Questions about this data are welcome and may be directed to the DEA Emerging Trends Program at 703-668-3300 or DEA.Emerging.Trends@usdoj.gov

http://www.cincinnatichildrens.org/service/d/dpic/default/

http://cincinnatichildrensblog.org/category/safety-and-prevention/

Spotlight on a Poison Specialist—Debra Roll RPh, CSPI

How did you come to work here? Tisha Carson and I have been friends since our freshman year at UC – we both lived on the 11th floor of Siddall Hall. She started in the pharmacy track while I started in Business School, switching to pharmacy a year later Tisha interned at Good Sam her first year of pharmacy school and then found out about DPIC when Dr. Earl Siegel (the managing director) came and spoke to their class. She let me know that her Good Sam position would become vacant if I was looking for an internship. I applied to Good Sam but after a couple of weeks of not hearing back I reached out to Tisha to ask if she was enjoying DPIC and were there any other intern positions – 27 years later as they say 'the rest is history'.

What is your favorite thing about your job? No two days are the same – each day comes with new challenges and new learning opportunities. If I think back to the hundreds of students and professionals that I have worked with over the years I am amazed by the diversity of talent and contributions that so many have made to the success of the center. I celebrated the 25th year of DPIC in 1991 and now we have just passed 50 years! DPIC is not only a collective of great minds, but great hearts as well. Both professionally and personally my co-workers have surprised me with so many acts of kindness at some of the most needed times. DPIC is really a family.

What is your most memorable call? I don't know if I have a single most memorable call - and maybe after 27 years my brain can't even hold them all! I think my most memorable calls are collectively those from a frantic mother or caregiver calling from home. I have said to many callers (only when I am certain☺) 'you did the right thing by calling, I can reassure you before we go any further that you child is going to be OK'. The sigh of relief is almost always audible through the phone. We can't safely manage all of our cases at home but those interactions are probably the most satisfying.

What are your other interests? I love cooking, traveling, working out, hanging out with family and friends. We have made two big moves (Coast to Coast) in the last 7 years – and I love exploring all that our area has to offer.

What is your biggest personal accomplishment? Uncovering my mom's NPH diagnosis. After the death of my dad in 2003 my mom's health quickly declined in a period of about 14 months. After exhausting all possible resources for a curable diagnosis I was devastated when a gerontologist diagnosed her with vascular dementia. My sister and I were planning to arrange for my mom to transition to a nursing home when I just happened to see a teaser on the Today Show 'do you have a loved one who has recently been diagnosed with dementia or Alzheimer's? Stay tuned – it may be something else'. The segment was about Normal Pressure Hydrocephalus (NPH) a treatable condition that can mimic dementia and is the true diagnosis in 5-10% of all dementia patients. We immediately switched gears, asked the doctor for an MRI, and 10 days later found out my mom did in fact have NPH. A month later she had shunt surgery and weeks later she was back to living independently at home. We became spokespeople for NPH, appearing on local TV shows, traveling to NYC with the makers of the shunt, and appearing in Women's Day Magazine. I got my mom back for 4 more years, and we helped many other families. My mom's story can still be found on the NPH website (https://www.lifenph.com/docs/AANPH/Support/Edythe_story.html). I'm happy to share the Women's Day article, too! I had all the support of my DPIC family through this difficult time.

What is your biggest professional accomplishment? Each year that I have sat for the CSPI exam I have enjoyed the process of learning and re-learning 'all things toxicology'. I appreciate being a resource to the staff and students and get a great deal of satisfaction in being able to provide (in my little way) to the continued success and growth of the center.

Who inspires you? I am inspired by my husband - Kevin, my family, friends and co-workers – it takes a village and I am truly blessed with mine.

Debbie Roll on the left, Julie Crawford on the right

Poisoning is a very real public health problem

According to the U.S. Centers for Disease Control and Prevention, more than 40,000 people die every year from poisonings; of those, about 15,000 die from prescription painkiller overdoses. Every day in the U.S., more than 80 people die as a result of unintentional poisoning and about 2,000 are treated in emergency departments.

While almost all categories of childhood injuries decreased over the last decade, poisonings rose dramatically. Most of the poison exposure cases managed by poison centers involve children; however, most poison exposure deaths occur to adults.

The AAPCC works with local poison centers and other partners to develop programs designed to prevent poisonings and promote use of the toll-free Poison Help line for poison emergencies or information.

Reference: AAPCC brochure accessed: https://aapcc.s3.amazonaws.com/files/library/PocketBrochureFINALpdf.pdf

Addendum to House Bill 388 "Annie's Law" article written by Deborah A. Donald MSN, RNII, CSPI for the Winter 2017 DPICtions issue:

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American Association of Poison Control Centers

This newsletter is brought to you by the Cincinnati Drug and Poison Information Center and was produced with assistance from the American Association of Poison Control Centers and local poison centers across the country.

When you dial 1-800-222-1222, your call is answered by a medical professional with special training in poison management. Help is fast, free, confidential and available 24 hours a day, every day.