174. (Don't) DIY: YouTube, chemistry texts, and down home chloroform synthesis

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Introduction: Chloroform (trichloromethane) is a halogenated hydrocarbon used historically as an inhaled anesthetic. Hepatotoxicity has been noted with therapeutic and recreational inhalational exposures, and significant hepatic necrosis is reported following oral ingestions. Recreational inhalation for its euphoric effect is well-documented; oral ingestions are far less common.
Case Report: A 14-year old male contacted the Poison Center (PC) to report that he had just ingested 32mL of chloroform that he had synthesized at home based on reactions that he had studied in his chemistry textbook. PC immediately communicated with EMS, and an ambulance was immediately dispatched to his home. Medics arrived 10 minutes after ingestion and encountered a patient who appeared agitated, complained of nausea and was hyperventilating, unable to speak. A complex chemical "filtration" system consistent with his report of on-site chemical synthesis was noted at his residence. His level of consciousness rapidly declined. PC recommended supportive cares en route to the receiving hospital; prehospital vital signs were not available. On arrival to the receiving hospital, the patient was profoundly somnolent, with a calculated GCS of 8. He was promptly intubated for airway protection, and initial assessment demonstrated a normothermic, obtunded, flushed, diaphoretic patient with midrange & reactive pupils with tachycardia to the 130s, with reportedly "normal" respiratory rate and blood pressure. Baseline hepatic transaminases were ordered, and the PC recommended prompt gastric aspiration and initiation of n-acetylcysteine (NAC) therapy for anticipated glutathione depletion and resultant hepatotoxicity. He was transferred to a pediatric center for further cares, arriving with vital signs of 98.7 °F, pulse 77, and blood pressure 106/45 sedated with 40μg/kg/minute propofol infusion. The patient was extubated uneventfully overnight. NAC was continued for 72 hours. He remained hemodynamically stable and appropriate and was transferred to inpatient psychiatry on hospital day (HD) #4 following 72 hours of NAC therapy. Transaminases slowly peaked on hospital day #8 (Table). Chloroform, drawn on HD#5, was in process at the time of writing.
Case Discussion: Large chloroform ingestions are unusual, and despite easily accessed do-it-yourself (DIY) videos describing its home manufacture, this case is particularly unique inasmuch as it involved the home manufacture of chloroform for suicidal purposes. Despite some similarity to acetaminophen-induced hepatotoxicity (via depletion of glutathione), no clear standard of care characterizes the optimal regimen to mitigate hepatotoxicity resulting from the cytochrome P450-mediated oxidation of chloroform to chloromethanol, and the subsequent dechlorination to phosgene and hydrochloric acid. In this case, a 72-hour course of intravenous NAC was chosen noting an anticipated delay to glutathione nadir following metabolism of the parent compound to its toxic metabolites.
Conclusions: We report the large volume ingestion of trichloromethane synthesized at home for suicidal purposes. The delay in hepatotoxicity is expected in these instances is attributable to a nontoxic parent compound with toxic metabolites. Glutathione depletion must occur prior to the onset of toxicity. Early NAC, in conjunction with early gastric content aspiration, may have mitigated the hepatotoxicity associated with this large oral chloroform ingestion by providing a substrate for the repletion of glutathione.

KEYWORDS Chloroform; hepatitis; n-acetylcysteine

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175. Multistate response to an outbreak of T3 thyroid storm following 1,000-fold compounding pharmacy error

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Background: A compounding pharmacy notified the Poison Center (PC) that a batch of 15mcg liothyronine (T3) capsules incorrectly contained 15,000mcg after a 1:1000 stock solution was replaced with undiluted T3 solution. The resulting capsules reached 10-15 patients; three patients ingested them and developed thyroid storm. Two of three cases were available to report.
Case Reports: Case 1 - A 64-year old female presented to the emergency department (ED) with chest and back pain 4 days after ingesting 30,000mcg of T3, reportedly prescribed to treat "Wilson's Temperature Syndrome." Intravenous lorazepam and nitroglycerine were administered; PC was consulted. Vital signs were: pulse 120, temperature 36.9 °C, blood pressure (BP) 121/80mmHg. Free T3 was immeasurably elevated (>30pg/mL, ref: 2.0-3.5pg/mL); troponin and TSH were undetectable, and metabolic panel revealed hypokalemia (3.2mEq/L). PC recommended an esmolol infusion and transfer to a facility with plasmapheresis capabilities. At transfer the patient was awake and alert with BP 111/77mmHg, pulse 107, and respiratory rate 18. Emergent plasmapheresis was undertaken at the receiving facility on hospital day (HD)#2; free T3 levels fell sequentially (see Table). The patient discharged on HD#4, but ill-defined symptoms persisted 6 weeks later. Case 2 - A 53-year old female with hypothyroidism and history of chronic Lyme disease developed flu-like symptoms after filling a prescription for compounded T3/T4 capsules. She presented to the ED 6 days after symptom onset, confused with "word salad" speech; she was discharged with tramadol and ondansetron. Symptoms persisted, and the next day she returned to the ED and was admitted. Head CT, MRI, EEG, lumbar puncture, chest CT, MRCP and echocardiogram were normal. She discharged on HD#7 following improvement in encephalopathic symptoms. No specific diagnosis was made; thyroid hormones were resumed. She was readmitted for erratic behavior and recurrent delirium 3 days later. Total serum T3 returned elevated (>500ng/dL, ref: 80-200ng/dL). Concurrent PC investigation revealed the compounding error and 1,000-fold overdose (15,000mcg). She was intubated, transferred to a facility capable of plasmapheresis. PC advised the receiving team of the outbreak. Initial vital signs were: temperature 38.5 °C; pulse 120; BP 121/71mmHg; respiratory rate 33/minute; SpO2 91%. Atrial fibrillation with a reduced ejection fraction developed. Endocrinology initiated cholestyramine and corticosteroids; Cardiology initiated propranolol. Repeat cerebral MRI and lumbar puncture were unrevealing. Plasmapheresis on HD#2 correlated with decreasing T3 concentrations (see Table). She was extubated on HD#5. Following hormone normalization, levothyroxine was restarted. She discharged on HD#9 with endocrinology follow-up and PT/OT services. "Non-distributional" weakness, gait difficulty, and muscle stiffness persisted. Echocardiographic

Summary of laboratory parameters in two cases of iatrogenic T3 thyrotoxicosis

Patient #1												
HD	1	2*	3	4	5	6						
Free T3 (jjg/mL)	35	32.6	13.8	5.7		2.4						
Patient #2												
HD (time)	1 (2317)	2* (0455)	2 (1733)	2 (2053)	3 (0456)	3 (1108)	3 (1650)	3 (2331)	4 (0553)	4 (1309)	4 (1757)	6 (0535)
Total T3 Ing/dL]	525	525	504	331	227		181	148	124	123	102	79
Free T3 (jgg/mL)	28		12.7	9	5.9	439	4.8					
Free T4 (rig/dL)	0.4	0.4	0.4	0. 5	0.4		0.3		<0.3			<0.3

*plasmapheresis initiated

ejection fraction was normal 7 weeks later, with grade II diastolic dysfunction.
Case Discussion: Hemoperfusion, exchange transfusion, and plasmapheresis have been implemented for T3 thyrotoxicosis, with variable results. PC response to this outbreak included consultations for the critically ill and collaboration with the state board of pharmacy, multiple state health departments and neighboring PCs.
Conclusions: This iatrogenic outbreak required PC guidance and outreach to identify exposures and ongoing risk to the public. These data suggest plasmapheresis may enhance the elimination of liothryonine in massive T3 overdose.

KEYWORDS Thyrotoxicosis; compounding error; plasmapheresis

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176. Uridine triacetate is a lifesaving antidote for overdoses and severe early-onset 5-fluorouracil and capecitabine toxicities

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Background: Uridine triacetate was approved by FDA in 2015 for adult and pediatric patients who exhibit early-onset, severe or life-threatening toxicities or who receive an overdose of 5-fluorouracil or capecitabine. Uridine triacetate is an oral prodrug of uridine, a direct antagonist of 5-FU, that dilutes and competes with toxic 5-FU metabolites, particularly FUTP incorporation into RNA, reducing morbidity and mortality due to 5-FU and capecitabine.
Increased susceptibility to 5-FU/capecitabine can lead to rapid, early-onset toxicity caused by factors such as: impaired clearance; DPD deficiency (3-5% of the population); and elevated OPRT (which converts 5-FU to toxic intracellular 5-fluorouridine nucleotides). Life-threatening or lethal 5-FU overdose occurs due to infusion pump errors, dosage miscalculations, accidental and suicidal ingestion of capecitabine.
Methods: 173 patients overdosed with 5-FU or capecitabine (n = 147); or who showed early onset of severe toxicities (n = 26) were treated with uridine triacetate in 2 clinical trials. Patients were to receive uridine triacetate (10g q6h for 20 doses) starting up to 96h post-5-FU/capecitabine. Clinical endpoints included survival, time to resumption of chemotherapy, and safety.
Results: A total of 163/173 (94%) patients treated with uridine triacetate recovered fully (within 30 days), including rapid reversal of severe cardiotoxicity (e.g. multiple cardiac arrests; LVEF of 5%) and neurotoxicity (e.g. coma, encephalopathy, ataxia), in addition to recovery from mucositis and leukopenias. Historical comparators for overdose patients (n = 47) were obtained from publicly-available sources. Of those with outcome data, 38/42 (90%) died. Of the 166 uridine triacetate-treated patients with a diagnosis of cancer, 53 resumed chemotherapy in <30 days (median 19.5 days post-5-FU), indicating rapid recovery from toxicity. Adverse reactions in patients receiving uridine triacetate were vomiting (10%), nausea (5%), and diarrhea (3%).
Conclusions: In these studies, uridine triacetate was a safe and effective life-saving antidote for capecitabine and 5-FU overexposure, and facilitated rapid resumption of chemotherapy.

KEYWORDS Uridine triacetate; 5-fluorouracil; overdose

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177. *Withdrawn*

178. Anaphylactic Shock to IV Patent Blue Dye

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Background: Patent blue dye was historically used to colour lymphatic vessels for lymphangiography and is currently used mostly for sentinel lymph node biopsy. Hypersensitivity reactions occur at rates as high as 1-2%. These are likely IgE-mediated and are usually mild with erythema, hives, urticaria and angioedema. Rarely, hypotension, pulmonary edema and cardiopulmonary arrest have been reported. Intense blue staining of the tissues and urine occur for multiple days. Allergic sensitization may occur through nonmedical exposure to patent blue dye in food colouring (E131), cosmetics and textiles. Some authors suggest preoperative skin testing for patent blue hypersensitivity prior to planned administration and avoidance of in patients with known allergy to food colorant E131.
Case Report: A 25-year-old female was undergoing an elective laparoscopic hysterectomy. Due to a difficult dissection, the gynecologist administered 1 mL of intravenous (IV) patent blue dye to assess for bladder integrity. The patient immediately became profoundly hypotensive to 70/30 and tachycardic to 115. Her face became grossly edematous with tongue and eyelid swelling and was notable for a grey-blue discoloration. The anesthesiologist administered boluses of epinephrine, phenylephrine and vasopressin and initiated an epinephrine infusion. The patient was admitted to the ICU post-operatively for persistent hypotension and an elevated lactate to 8.9. Her anaphylaxis was treated with an epinephrine infusion, methylprednisolone and diphenhydramine. The provincial toxicology service was consulted and advised administration of a 20% lipid emulsion bolus, which produced some hemodynamic stabilization. The patient was gradually