The Unappetizing Truth of Toxic Ingestion –
A Little IV Fat May Do the Body Good

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Learning Objectives:

1. Define the morbidity and mortality of poisoning in the United States
2. Explain proposed mechanisms of action of intravenous fat emulsion for toxic ingestion
3. Compare literature and case reports of reversal of toxic ingestion with intravenous fat emulsion
4. Describe proposed algorithm for using intravenous fat emulsion during Advanced Cardiac Life Support
Current Trends in US Toxic Ingestion

I. Number of emergency department visits due to drug use and abuse increased 98.4% from 2004 to 2009\(^1,2\)

II. Over half of visit due to legal pharmaceutical products compared to illicit drugs\(^3\)

Figure 1: ED Visits Due to Drug Use and Abuse in the US, 2009*
(n = 2.1 million)*

*Excludes visits due to underage drinking and EtOH combined with other drugs

III. Fatalities from toxic ingestion have more than tripled since 1990\(^4\)

IV. 36,450 deaths from drug overdoses in the United States in 2008\(^1\)

Figure 2: Drug Overdose Death Rates per 100,000 people by State, 2008\(^1\)
V. Increased number of deaths due to unintentional poisoning
   a. Defined as accidental poisoning from drug misuse, drug abuse, or taking too much of a prescription drug in error

   Figure 3: Death Rate of Unintentional Drug Poisoning in United States

VI. Antidotes to treat poisoning do exist
   a. N-acetylcysteine - acetaminophen
   b. Hydroxocobalamin – cyanide
   c. Pralidoxime (2-PAM)/atropine – organophosphates or acetylcholinesterase inhibitors

VII. Not every toxin has a specific antidote, and adverse events can be deadly

VIII. Intravenous fat emulsions (IVFE) are a potential antidote for toxic ingestion

Table 1: Adverse events of toxins without antidotes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect of Overdose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic Antidepressants</td>
<td>Hallucinations, confusion, coma, seizures, respiratory failure, QRS prolongation and ventricular dysrhythmias</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>CNS depression, coma, seizures, respiratory depression, decreased myocardial contractility, conduction delays (PR, QRS, QTc prolongation)</td>
</tr>
<tr>
<td>Typical and Atypical Antipsychotics</td>
<td>Seizures, delirium, coma, respiratory depression, hypotension, tachycardia, cardiac dysrhythmias (QTc prolongation)</td>
</tr>
<tr>
<td>Monoamine Oxidase Inhibitors</td>
<td>Anxiety, severe tachycardia, delirium, seizures, cardiovascular collapse, coma</td>
</tr>
</tbody>
</table>
IVFE – What Is It?

I. Composition
   a. 10 – 30% soybean oil as major lipid
   b. Egg yolk phospholipid and glycerin as minor source of lipids and phospholipids

II. IVFE Pharmacokinetics
   a. Distributed primarily to muscle and subcutaneous tissues
   b. Hydrolyzed into free fatty acids by lipoprotein lipase
   c. Excreted by the kidneys when very high dose administered
   d. 30 minute serum half-life of parent compound
   e. Parent drug cleared from serum within 80 minutes

II. FDA approved indications
   a. To provide free fatty acids for total parenteral nutrition and essential fatty acid deficiency
   b. Drug delivery vehicle for highly lipid soluble drugs (propofol, clevidipine, diazepam)

III. Off label use
   a. American Heart Association - local anesthetic toxicity
      i. Reasonable to consider 20% long-chain fatty acid emulsion for local anesthetic toxicity
      ii. Initial bolus of 1.5 mL/kg every 5 minutes until restoration of cardiovascular stability
      iii. Maintenance infusion of 0.25 mL/kg/min for at least 30 to 60 minutes
   b. American College of Medical Toxicology - cardiovascular collapse secondary to drug overdose/toxic ingestion
      i. Recommendation to consider IVFE for toxic ingestion of drugs with high degree of lipid solubility
   c. Decision to use IVFE and specific dosing recommendations based on clinical judgment

IV. Safety
   a. Black box warning – Deaths due to fat accumulation in the lungs of preterm infants due to poor rate of IVFE clearance
   b. Flushing, hypertriglyceridemia, nausea, vomiting, headache - common adverse events from use as parenteral nutrition
   c. Cholestasis, splenomegaly, thrombocytopenia, hepatomegaly, dyspnea, pulmonary fat embolism - serious adverse events from use as parenteral nutrition
**Mechanism of Action of IVFE**

I. Lipid Sink Theory
   a. Redistribution of lipid soluble drugs away from target tissues
   b. Ingested drug partitions into plasma-lipid phase
   c. Tissue drug concentration decreases

II. Metabolic effect
   a. Direct inotrope effect independent of drug redistribution via lipid sink
   b. Improve fatty acid metabolism to restore myocardial contractility

**IVFE In Animal Models**

I. Pre-treatment with IVFE increased dose of bupivacaine needed to induce asystole in rats

II. IVFE bolus dose 7.5 ml/kg, followed by 3 ml/kg/min infusion x 3 minutes

III. IVFE given after bolus doses of bupivacaine increased median lethal dose (LD₅₀) of bupivacaine from 12.5 mg/kg to 18.5 mg/kg

**Figure 4: Mortality from bolus doses of IV bupivacaine after resuscitation with either IV fat emulsion or saline**
## Predictors of IVFE Clinical Efficacy

I. **Partition coefficient**\(^{12,13}\)**
   a. Ratio of a substance in two immiscible phases/substances at equilibrium
   b. Determines degree of hydrophilicity and/or lipophilicity of a substance
   c. Able to assess which drugs may have higher affinity for IVFE

II. **Volume of distribution**\(^{14}\)**
   a. Proportionality factor describing apparent body space that can contain a drug
   b. Amount of drug in body compared to concentration of drug in plasma
   c. High volume of distribution – drug distributed to extravascular tissue
   d. Low volume of distribution – drug retained in vascular compartment

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<table>
<thead>
<tr>
<th>Purpose</th>
<th>To determine if specific drug properties correlate to clinical efficacy of IVFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td><em>In vitro</em> analysis of 11 drugs identified in IVFE toxicity reversal case reports</td>
</tr>
</tbody>
</table>
| Outcomes | • Primary: Amount of drug removed from human serum *in vitro* by IVFE  
• Secondary: Correlation of volume of distribution and partition coefficient to amount of drug removed by IVFE |
| Methods | • Drug added to human serum, followed by 20% IVFE (equal to 1.5 mL/kg in humans)  
• Sample vortexed, incubated, shaken, and centrifuged to separate serum from lipid  
• Amount of drug remaining in serum extracted and quantified using solid phase extraction and high performance liquid chromatography (HPLC) |
| Statistics | • Decrease in serum concentration expressed as percent decrease from baseline  
• Linear regression used to identify relationship between percent drug decrease, volume of distribution, and partition coefficient |
| Results | • Ability of IVFE largely dependent on drug’s lipid partition coefficient (*Appendix 1*)  
• Positive correlation between volume of distribution of drug and percent decrease in serum drug concentration after IVFE  
• Partition coefficient and volume of distribution account for 88% total efficacy of drug removal by IVFE  
• No correlation between percent protein binding, molecular weight, and percent drug ionized at pH 7.4 to percent decrease in serum drug concentration after IVFE |
Figure 5: Percent decrease in serum drug concentration vs. partition coefficient and volume of distribution after IVFE

- Predicted lipid extraction percent for specific drug best calculated using linear regression model (Appendix 2)

**Authors**

- IVFE has high likelihood of reversing cardiac toxicity caused by medications with high lipid partition coefficient and volume of distribution
- Amiodarone predicted to be most effectively sequestered by IVFE, followed by sertraline, TCA’s, fluoxetine, bupropion, and flecainide
- IVFE may also be useful to sequester haloperidol, calcium channel blockers, beta-blockers, and olanzapine

**Conclusion**

- Medications with high partition coefficient and volume of distribution are preferentially sequestered by IVFE
  - These drug properties should be taken into account when assessing efficacy of IVFE for toxic ingestion
- IVFE should be considered in toxic ingestion from medications with positive predicted lipid extraction percent
- In-vitro study – results have yet to be seen in humans

**Take Home Points**

**IVFE in Cardiac Arrest**

   a. Resuscitation from cardiac arrest after ingestion of 7.95 grams bupropion and 4 grams lamotrigine

II. Dean et al. *Anesthesiology* 2010;65:1149-501
   a. Resuscitation from cardiac arrest after ingestion of 7 grams propranolol

   a. Resuscitation from cardiac arrest after ingestion of 4.25 grams amitriptyline
### Patient History
- Unresponsive 17 year old, 55kg female
- Bottles of bupropion 150 mg and lamotrigine 100mg found at scene 5 hours after suicide text sent
  - Max ingestion 7.95 grams bupropion, 4 grams lamotrigine

### Presentation on Arrival (6 hours post ingestion)
- BP 123/77
- HR 116 beats/min
- RR 14 breaths/min
- SpO₂ 100% on non-rebreather mask on 100% oxygen
- GCS 6 (respond to painful stimuli)
- ECG sinus tachycardia, prolonged QRS-interval of 0.122 seconds, prolonged QTc of 0.485 seconds

### 0-10 hours post ingestion
- Supportive care management – 100% oxygen non-rebreather mask, nasopharyngeal airway, IV fluids

### 10 hours post ingestion
- Tonic clonic seizure
- Pulseless wide complex rhythm
- ACLS initiated
  - Chest compressions
  - Tracheal intubation
  - Pulseless ventricular tachycardia and ventricular fibrillation
  - Defibrillation x 11
  - Epinephrine 1 mg x 6
  - Amiodarone 300 mg x 1
  - Magnesium sulfate 1 gram x 1
  - Sodium bicarbonate 50 mEq x 1
  - 17 minutes later, return of spontaneous circulation

### 10 h, 28 min post ingestion
- PEA returned – wide complex rhythm
- ACLS resumed
  - Transcutaneous pacing
  - Epinephrine 1 mg x 12
  - Sodium bicarbonate 50 mEq x 2
  - Calcium chloride x 1 gram x 1
  - Norepinephrine and epinephrine infusions (high dose)

### 11 h, 20 min post ingestion
- 100 mL bolus 20% IVFE administered (1.8 mL/kg)

### 11 h, 21 min post ingestion
- Pulse detected

### 11 h, 45 min post ingestion
- QRS narrowed, sinus rhythm returned
- Vasopressor requirement reduced
- Sodium bicarbonate 100 mEq x 1
13 h, 15 min post ingestion
- Pulseless ventricular tachycardia developed
- Chest compressions + epinephrine 1 mg administered
- Ventricular tachycardia resolved

Toxicology Analysis
- Serial serum triglyceride, bupropion, and lamotrigine levels collected

<table>
<thead>
<tr>
<th>Time From Ingestion (hours)</th>
<th>Triglyceride (ng/dL)</th>
<th>Bupropion (ng/mL) (TR 50-100)</th>
<th>Lamotrigine (µg/mL) (TR 3-14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>103</td>
<td>180</td>
<td>26</td>
</tr>
<tr>
<td>10 (start of seizures/CV collapse)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>11.5 (IVFE infusion)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>12.75</td>
<td>681</td>
<td>880</td>
<td>24</td>
</tr>
<tr>
<td>18.25</td>
<td>81</td>
<td>390</td>
<td>21</td>
</tr>
<tr>
<td>28.75</td>
<td>33</td>
<td>62</td>
<td>18</td>
</tr>
</tbody>
</table>

*TR, therapeutic range; N/A, data not available

Hospital Course
- Significant acute lung injury
  - Inhaled nitric oxide x 5 days
  - Chest tube x 12 days
  - Mechanical ventilation x 17 days
  - Endotracheal surfactant
  - Antibiotics
- Vasopressors x 2 days
- Transferred from PICU to rehab at 24 days post ingestion
  - Conversant, talkative
  - Slight tremor
  - Mild memory deficits
  - Fine motor incoordination

Conclusion
- IVFE successful for reversal of cardiovascular collapse from bupropion and lamotrigine after 70 minutes of ACLS
- High likelihood that IVFE sequestered bupropion and lamotrigine away from target sites
  - Partition coefficient bupropion 3.2, lamotrigine 1.4<sup>12</sup>
  - Predicted % extracted bupropion 36%, lamotrigine 2%<sup>12</sup>
- Acute lung injury developed – not clear if due to IVFE, active resuscitation/chest compression, and/or high dose vasopressors
<table>
<thead>
<tr>
<th><strong>Patient Demographics</strong></th>
<th>Dean et al. <em>Anesthesia</em> 2010;65:1141-52(^\text{16})</th>
<th>Engels et al. <em>Resuscitation</em> 2010;81:1037-1039(^\text{17})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>27 year old female, weight unknown</td>
<td>27 year old male, 80 kg</td>
</tr>
<tr>
<td>Drug Ingested</td>
<td>7 grams propranolol</td>
<td>4.25 grams amitriptyline (50mg tabs x 85)</td>
</tr>
<tr>
<td>Presentation on Arrival</td>
<td>• BP 60/30 mmHg</td>
<td>• BP 67/40 mmHg</td>
</tr>
<tr>
<td></td>
<td>• HR 25 min(^{-1})</td>
<td>• HR 116 min(^{-1})</td>
</tr>
<tr>
<td></td>
<td>• RR 15 – 20 min(^{-1})</td>
<td>• RR 8 min(^{-1})</td>
</tr>
<tr>
<td></td>
<td>• Oropharyngeal airway</td>
<td>• Temp 35.4 °C</td>
</tr>
<tr>
<td></td>
<td>• GCS 3</td>
<td>• GCS 3</td>
</tr>
<tr>
<td></td>
<td>• Generalized tonic/clonic seizure</td>
<td>• Generalized tonic/clonic seizure x 2</td>
</tr>
<tr>
<td></td>
<td>• ECG severe wide complex bradycardia</td>
<td>• Wide complex tachycardia with prolonged QRS 240 ms</td>
</tr>
<tr>
<td>Treatment and course prior to IVFE</td>
<td>• IV fluids</td>
<td>• Midazolam(^*)</td>
</tr>
<tr>
<td></td>
<td>• 3 mg atropine x 1</td>
<td>• Sodium bicarbonate(^*)</td>
</tr>
<tr>
<td></td>
<td>• 5 mg glucagon x 3</td>
<td>• Pulseless ventricular tachycardia</td>
</tr>
<tr>
<td></td>
<td>• Glucagon infusion at 5 mg/hour</td>
<td>• ACLS x 18 minutes</td>
</tr>
<tr>
<td></td>
<td>• Insulin infusion at 70 units/hour</td>
<td>• Epinephrine (^*)</td>
</tr>
<tr>
<td></td>
<td>• Dextrose infusion(^*)</td>
<td>• Sodium bicarbonate(^*)</td>
</tr>
<tr>
<td></td>
<td>• 1 mg lorazepam x 8</td>
<td>• Pulseless ventricular tachycardia</td>
</tr>
<tr>
<td></td>
<td>• 1 g phenytoin x 1 , then 250 mg x 1</td>
<td>• ACLS x 4 minutes</td>
</tr>
<tr>
<td></td>
<td>• Isoproterenol infusion at 10 µg/min</td>
<td>• Epinephrine (^*)</td>
</tr>
<tr>
<td></td>
<td>• External pacing</td>
<td>• Sodium bicarbonate(^*)</td>
</tr>
<tr>
<td></td>
<td>• 100 µg Epinephrine boluses (number administered unknown)</td>
<td>• Epinephrine drip at 0.25 µg/kg/min</td>
</tr>
<tr>
<td></td>
<td>• Epinephrine drip at 66 µg/min</td>
<td>• Pulseless ventricular tachycardia</td>
</tr>
<tr>
<td></td>
<td>• ACLS x 2 cycles – pulse returned</td>
<td>• ACLS x 4 minutes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Epinephrine (^*)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sodium bicarbonate(^*)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Epinephrine drip at 0.25 µg/kg/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Norepinephrine drip at 1 µg/kg/min</td>
</tr>
<tr>
<td>Time from ingestion to IVFE</td>
<td>Unknown – presented to hospital one hour after ingestion</td>
<td>Unknown – IVFE administered 7.5 hours after hospital arrival</td>
</tr>
<tr>
<td>Dose of IVFE</td>
<td>100 ml 20% IVFE, then 400 ml over 5 minutes</td>
<td>100 ml 20% IVFE (1.25 ml/kg), then 400 ml (10 ml/kg/hour) over 30 minutes</td>
</tr>
<tr>
<td>Response</td>
<td>• 5 minutes after IVFE, epinephrine drip decreased to 13 µg/min</td>
<td>• 30 minutes after IVFE, norepinephrine and epinephrine requirement decreased(^*)</td>
</tr>
<tr>
<td></td>
<td>• Epinephrine &amp; glucagon drip discontinued 7 hours after IVFE</td>
<td>• Vasopressors discontinued 4.5 hours after bolus IVFE</td>
</tr>
<tr>
<td>Outcome</td>
<td>• Regained consciousness</td>
<td>• Extubated following morning</td>
</tr>
<tr>
<td></td>
<td>• Extubated 15 hours s/p arrival</td>
<td>• 2 days after admit, discharged from ICU with GCS 15</td>
</tr>
<tr>
<td></td>
<td>• No neurological deficits</td>
<td></td>
</tr>
</tbody>
</table>
E. VanWert

Partition coefficient of ingested drug $^{12}$

Predicted % of drug removed by IVFE $^{12}$

<table>
<thead>
<tr>
<th></th>
<th>3</th>
<th>5</th>
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<tbody>
<tr>
<td>Conclusion</td>
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</tbody>
</table>

- Treatment with IVFE led to successful resuscitation after standard resuscitation methods failed
- Success of IVFE with propranolol may be due to drug’s high partition coefficient
- Patient weight not reported – actual ml/kg dosing regimen of IVFE unknown

- Treatment with IVFE led to successful resuscitation after standard resuscitation methods failed
- Success of IVFE with amitriptyline may be due to drug’s high partition coefficient

*Specific doses not listed in study

**Methods for Administration of IVFE**

I. No studies comparing dosing regimens

II. The Association of Anesthetists of Great Britain & Ireland – Management of Severe Local Anesthetic Toxicity $^{18}$

   a. Developed by 7-member working group of experts in lipid rescue therapy
   b. Endorsed by Australian and New Zealand College of Anesthetists
   c. Authors note IVFE is NOT a standard of care – ultimate treatment plan to be made by physician and clinical scenario
   d. Management strategy
      i. Signs of severe toxicity
         1. Sudden change in mental status, severe agitation, loss of consciousness
         2. Tonic-clonic seizures
         3. Cardiovascular collapse
      ii. Circulatory arrest
         1. Begin CPR/ACLS, consider use of cardiopulmonary bypass
         2. Give IVFE
      iii. Without circulatory arrest
         1. Conventional therapies to treat hypotension, bradycardia, tachyarrhythmia
         2. **Consider** intravenous lipid emulsion
iv. Lipid emulsion algorithm

Immediately
• Give IV bolus of 20% lipid emulsion at 1.5 ml/kg over 1 minute
• Start IV infusion of 20% lipid emulsion at 15 ml/kg/hour

After 5 minutes
• Give maximum of two boluses (same dose) in the presence of cardiovascular instability or deterioration of circulation (5 minutes between boluses)
• AND continue IV infusion at rate of 30 ml/kg/hour in the presence of cardiovascular instability or deterioration of circulation 5 minutes after final bolus

Notes
• Continue CPR throughout infusion of lipid emulsion
• Recovery from local anesthetic toxicity may take > 1 hour
• Do not use lidocaine as an anti-arrhythmic agent
• Max cumulative dose of lipid emulsion: 12 ml/kg
III. American Society of Regional Anesthesia and Pain Medicine – Guideline for Managing Local Anesthetic Systemic Toxicity (2012)\(^\text{19}\)

a. No standard method for lipid emulsion therapy
b. Must be used in conjunction with high quality BLS/ACLS
c. Initial Focus
   i. Airway management
   ii. Benzodiazepines to suppress seizures
   iii. BLS/ACLS – may require prolonged effort
d. Lipid emulsion algorithm (20\% IVFE)

![Initial Dosing]

- Bolus 1.5 mL/kg over one minute (lean body mass)
- Continuous infusion at 0.25 mL/kg/min (equal to 15 mL/kg/hour)

![Repeat if Necessary]

- May repeat bolus once or twice for cardiovascular collapse
- May double infusion rate to 0.5 mL/kg/min if blood pressure remains low

![Notes]

- Continue infusion for at least 10 minutes after stable circulation achieved
- Upper limit recommendation: 10 – 12 mL/kg over first 30 minutes

e. Avoid use of the following agents
   i. Vasopressin, calcium channel blockers, beta blockers, local anesthetics
   ii. Propofol with cardiovascular instability
   iii. Individual high dose epinephrine (prefer doses < 1 mcg/kg)
      1. In animal studies epinephrine resulted in worse outcomes compared lipid emulsion for bupivacaine-induced asystole\(^\text{20}\)
      2. No studies demonstrating that combined epinephrine and lipid therapy led to worse outcomes
f. Consider cardiopulmonary bypass if lipid and vasopressor therapy fail
g. Report/post events
   i. Post events to lipidrescue.org and use of IVFE to lipidregistry.org

IV. Human dose based on FDA-approved conversion factor\(^\text{21}\)

a. Converts mg/kg dose in animal species to mg/kg dose in humans
b. Animals used in studies were rats
c. Conversion used for human dose selection
   i. Mg/kg dose [rats] divided by 6
I. Acute lung injury
   a. 13 year old female developed ARDS after amitriptyline-induced cardiac arrest treated with IVFE\textsuperscript{22}
      i. Progressed to bilateral pleural effusions
      ii. Unclear if ARDS due to IVFE or prolonged cardiac arrest, ACLS, and/or fluids
   b. 17 year old female developed acute lung injury after lamotrigine and bupropion-induced cardiac arrest treated with IVFE\textsuperscript{15}
      i. Required chest tube insertion and inhaled nitric oxide
      ii. Unclear if due to IVFE, active resuscitation/chest compressions, and/or high dose vasopressors

II. Pancreatitis
   a. 32 year old male developed hyperamylasemia after IVFE for bupivacaine-induced cardiac arrest\textsuperscript{23}
      i. Serum amylase measured at 608 IU/L upon admission to ICU
      ii. No clinical signs or symptoms of pancreatitis noted
      iii. Patient discharged 4 days after cardiac arrest
      iv. Clinical significance of hyperamylasemia in this patient unclear
   b. 13 year old female developed pancreatitis 5 days after IVFE\textsuperscript{22}
      i. Triglyceride level peaked 18 hours post IVFE at 8611 mg/dL
      ii. Lipase peaked 5 days post IVFE at 1849 IU/L
      iii. Subjective symptoms not available – patient sedated and intubated
         1. Once extubated, patient complained of epigastric pain after eating
      iv. Authors state peak lipase represented true pancreatitis

III. Interference with laboratory studies
   a. Unknown which laboratory values are affected
   b. May be instrument and/or assay specific\textsuperscript{24,25}
   c. Case reports
      i. “Standard” laboratory values could not be interpreted for 3 hours after IVFE due to profound lipemia in amitriptyline overdose\textsuperscript{22}
      ii. Lipemia interfered with laboratory values for unknown time in a patient who received 2 liters of IVFE due to protocol error\textsuperscript{26}

IV. Decreased efficacy of additional medications
   a. Medications commonly used in ACLS may be sequestered by IVFE
   b. No reports assessing decreased efficacy
   c. Practitioners must be aware of potential for decreased efficacy of antiarrhythmics, beta blockers, and calcium channel blockers
Conclusion

I. IVFE should be used for cardiovascular collapse from drugs with partition coefficients > 1 and/or positive percent predicted lipid extraction
   a. Administer if pulseless after >3 cycles ACLS

II. IVFE MUST be used in combination with ACLS
    a. Dosing of ACLS medications MUST follow recommended doses in ACLS guidelines

III. Dosing protocol for IVFE should follow American Society of Regional Anesthesia and Pain Medicine’s Guideline for Managing Local Anesthetic Systemic Toxicity

IV. Do not use IVFE for altered mental status induced by toxic ingestion
    a. Range and frequency of adverse events are unknown
    b. Adverse events reported from IVFE are not benign
Proposed Algorithm

Does patient have cardiovascular collapse from possible toxic ingestion?

No

Do not use IVFE

Yes

Is patient an infant?

Yes

Utilize antidote*

No

Do not use IVFE

Does the medication ingested have an antidote?

Yes

Do not use IVFE

No

Is the medication ingested a tricyclic antidepressant, local anesthetic, antiepileptic, amiodarone, or flecainide?

Yes

Did return of spontaneous circulation occur with 2-3 cycles of high quality BLS and ACLS?

No

Use IVFE

*If antidote does not cause return of spontaneous circulation for ingestion of calcium channel blocker or beta blocker, use IVFE


### Appendix 1: Serum Drug Concentration Decrease After IVFE Relative to Partition Coefficient & Volume of Distribution (French et al. *Clin Toxicol* 2011;49:801-809)\(^\text{12}\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percent Decrease in Serum Drug Concentration</th>
<th>Partition Coefficient ((P_{oil:water}))</th>
<th>Volume of Distribution ((L/kg))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine</td>
<td>1</td>
<td>1.4</td>
<td>2</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>12</td>
<td>1.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>13</td>
<td>2.1</td>
<td>9</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>18</td>
<td>2.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>7</td>
<td>2.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Bupropion</td>
<td>46</td>
<td>3.2</td>
<td>40</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>27</td>
<td>3.2</td>
<td>24</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>18</td>
<td>3.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Verapamil</td>
<td>34</td>
<td>3.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Sertraline</td>
<td>46</td>
<td>4.8</td>
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<tr>
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</table>
Appendix 2: Predicted IVFE extraction efficiency calculated from volume of distribution and partition coefficient using linear regression model (French et al. *Clin Toxicol* 2011;49:801-809.)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Volume of Distribution (L/kg)</th>
<th>Partition Coefficient</th>
<th>Predicted Lipid Extraction Efficiency (%)</th>
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