



UTAH SOCIETY OF  
HEALTH-SYSTEM PHARMACISTS

## Lipid Emulsion Therapy in Drug Overdose

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## Disclosure

- **Relevant Financial Conflicts of Interest**
  - CE Presenter, Joseph E. Lambson:
    - none
  - CE mentor(s), Amberly R. Johnson:
    - none
- **Off-Label Uses of Medications**
  - Lipid Emulsion Therapy



3

## Outlines

- Background
- Local Anesthetic Systemic Toxicity
- Non-local Anesthetic Drug Toxicity
- Pharmacy Considerations

## Learning Objectives – Pharmacists

- Describe the **mechanism of action** of lipid emulsion therapy
- Identify **adverse drug effects** and **laboratory abnormalities** of lipid emulsion therapy
- Demonstrate appropriate **dosing** and **administration** of lipid emulsion therapy
- Compare the **clinical presentation** of drug overdoses to determine the appropriateness of lipid emulsion therapy



4



5

## Learning Objectives – Technicians

- Identify appropriate **indications** for lipid emulsion therapy
- Identify the various **formulations** of lipid emulsion
- Demonstrate appropriate **storage and handling** of lipid emulsion



6



## BACKGROUND



7

## History of Lipid Emulsion



8

## Indication for Lipid Emulsion

### FDA-Approved

- Parenteral Nutrition
- Prevention of Essential Fatty Acid Deficiency

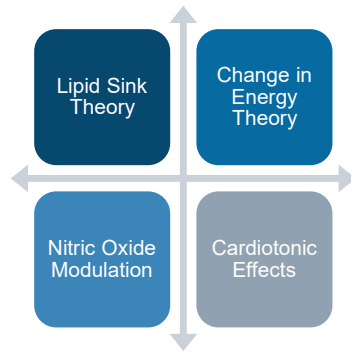
### Off-label

- Local Anesthetic Systemic Toxicity (LAST)
- Non-local Anesthetic Toxicity



9

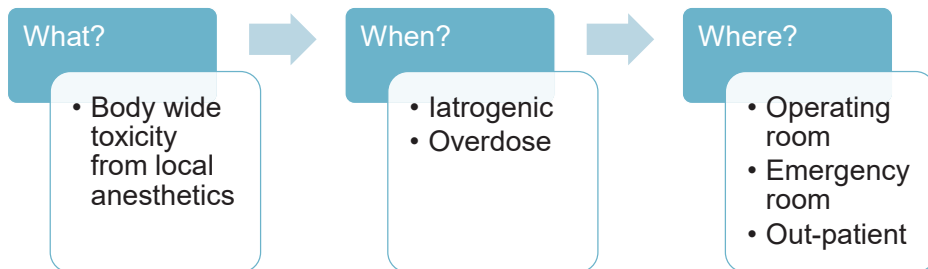
## Mechanism of Action



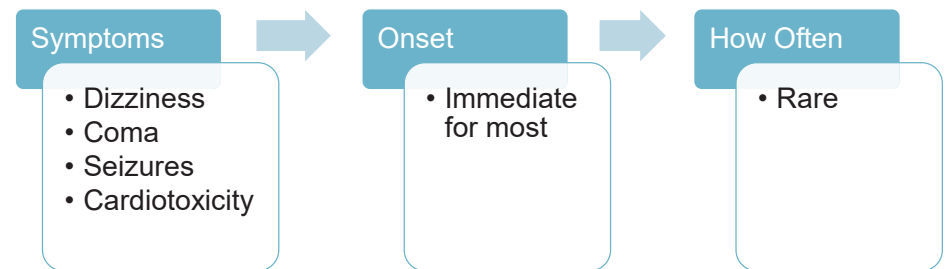
**LOCAL  
ANESTHETIC  
SYSTEMIC  
TOXICITY (LAST)**



## Background



## Background Continued



## Regional Anesthesia Guidelines

### 2010

“Administer Lipid Emulsion Therapy at the first sign of arrhythmia, prolonged seizure, or rapid clinical deterioration of the patient.”

### 2017

“...we now unequivocally recommend lipid emulsion therapy soon after airway management in **any LAST event** that is judged to **be potentially serious.**”



Neal JM et al. *Reg Anesth Pain Med.* 2018.

15

## Lipid Emulsion Therapy in LAST

- Airway Management
- Lipid Emulsion Therapy
- Supportive measures
  - Benzodiazepines for Seizures
  - Sodium Bicarbonate for QRS Widening
  - Low-dose Epinephrine for Cardiac Arrest



Neal JM et al. *Reg Anesth Pain Med.* 2018.

16

## Hoegberg et al (2016)

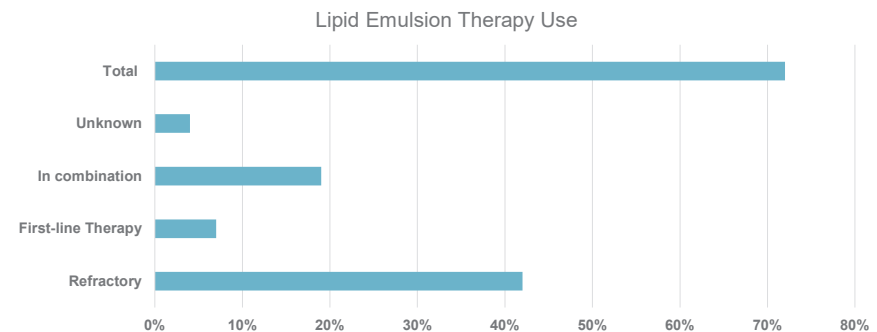
- **Population:** 83 patients (2 days – 91 years old)
- **Exposure:**
  - Nerve block (83%)
- **Clinical Effects:**
  - CNS depression/coma (54%)
  - Seizures (59%)
  - Hypotension/Hypertension/EKG Changes/Arrhythmias (47%)
  - Cardiac arrest (22%)
- **Outcomes:**
  - 98% survived (2 died)



Hoegberg LC et al. *Clin Toxicol (Phila).* 2016.

17

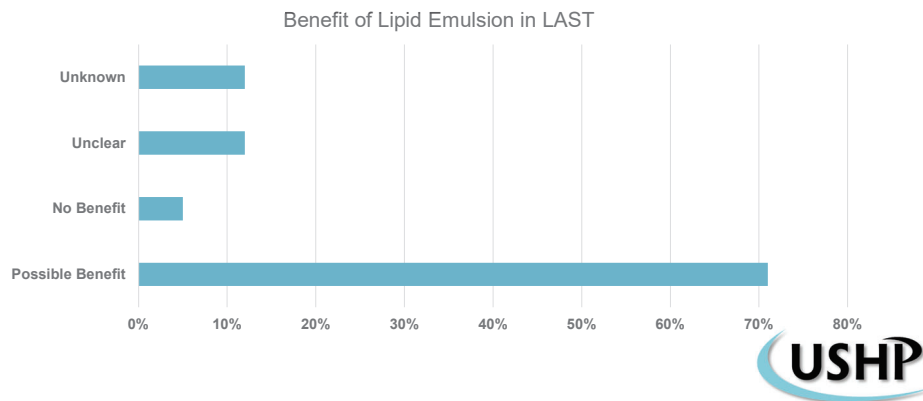
## Hoegberg et al (2016)



Hoegberg LC et al. *Clin Toxicol (Phila).* 2016.

18

## Hoegberg et al (2016)



Hoegberg LC et al. *Clin Toxicol (Phila)*. 2016.

19

## Take Home

- LAST is rare but life-threatening
- Though supported by limited evidence, lipid emulsion therapy is highly recommended by anesthesia guidelines for LAST
- Lipid emulsion therapy should be used early in LAST if potentially serious



22



## NON-LOCAL ANESTHETIC DRUG TOXICITY



23

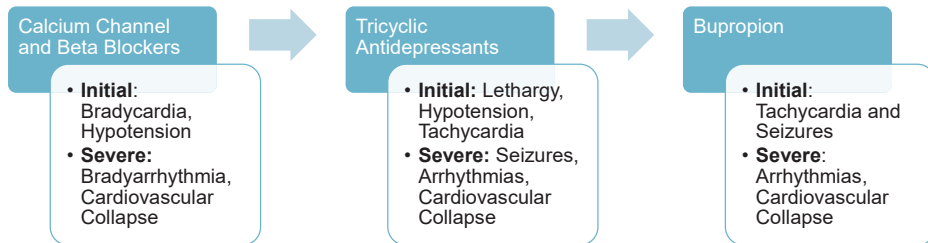
## Best Drug Candidates

- In Theory?
  - Lipophilic
  - Cause cardiovascular shock in severe overdose
- In Practice?
  - Lipophilicity highly variable



24

## Common Prescription Drugs



25

## Lipid Emulsion Therapy Workgroup Analysis

- 141 human studies/reports
- 3 RCTs
- 1 observational study
- Case reports and case series
- 61 animal studies
- Low and very low quality



Levine M et al. *Clin Toxicol (Phila)*. 2016.

26

## Workgroup Recommendations

Drug	Recommendation
Amitriptyline	<b>Cardiac Arrest:</b> Neutral <b>Life-threatening Toxicity:</b> Recommended if other therapies fail/in last resort <b>Non-life-threatening Toxicity:</b> Not recommended
Bupropion	<b>Cardiac Arrest:</b> Neutral <b>Life-threatening Toxicity:</b> Recommended if other therapies fail/in last resort <b>Non-life-threatening Toxicity:</b> Not recommended as first line therapy
Propranolol	<b>Cardiac Arrest:</b> Neutral <b>Life-threatening Toxicity:</b> Neutral <b>Non-life-threatening Toxicity:</b> Not recommended as first line therapy
Verapamil	<b>Cardiac Arrest:</b> Neutral <b>Life-threatening Toxicity:</b> Not recommended as first line therapy <b>Non-life-threatening Toxicity:</b> Not recommended as first line therapy



Levine M et al. *Clin Toxicol (Phila)*. 2016.

27

## Lipid Emulsion Therapy in Drug Toxicity

- IV Fluids
- Sodium Bicarbonate
- Vasopressors
- Glucagon and High Dose Insulin Therapy
- Lipid Emulsion Therapy
- CPR, Antiarrhythmics, ECMO

\*Consult your local poison center



28

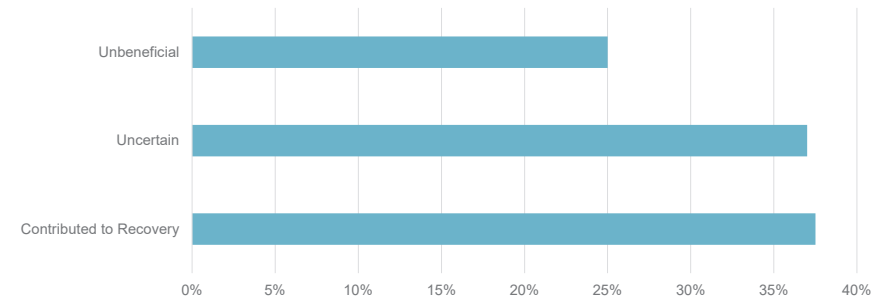
## Cave et al (2004)

- **Population:** 38 cases of non-local anesthetic toxicity
- **Exposure:** benzodiazepines (n=16), tricyclic antidepressants (n=15), other antidepressants (n=13), anticonvulsants (n=5), beta blockers (n=3), calcium channel blockers (n=3), other medications (n=17)
- **Clinical Effects:**
  - 30 patients received lipid emulsion therapy for isolated decreased consciousness
  - 8 patients for cardiovascular collapse.
- **Outcomes:** No deaths



## Cave et al (2004)

Benefit of Lipid Emulsion Therapy in Patients Treated for Cardiovascular Collapse



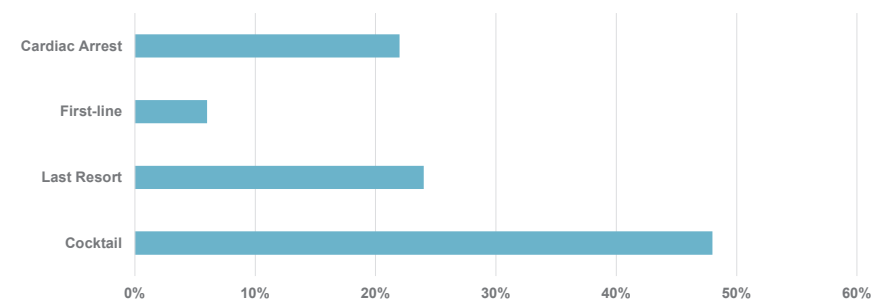
## Smolinske et al (2018)

- **Population:** 459 Fatalities reported to US Poison Centers
- **Exposure:**
  - Calcium channel blocker (39.9%)
  - Beta blocker (22.2%)
  - Bupropion (12%)
  - Tricyclic antidepressant (10%)
  - Others (15.9%)
    - Citalopram/Escitalopram, Quetiapine, Flecainide, Local Anesthetics
- **Outcome:** 100% death

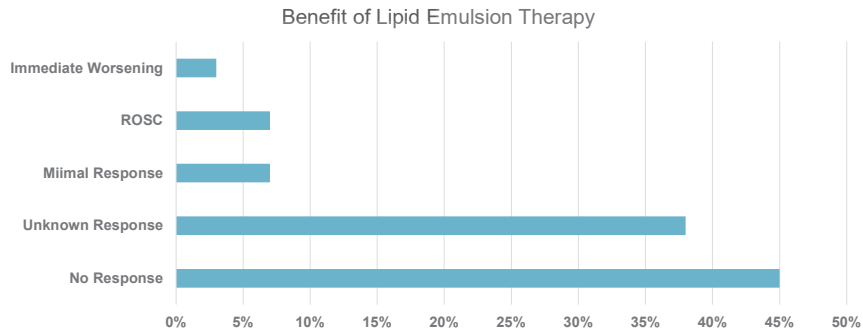


## Smolinske et al (2018)

Lipid Emulsion Therapy Use



## Smolinske et al (2018)



Smolinske S et al. *Clin Toxicol (Phila)*. 2019.

33

## Take Home

- Lipid emulsion therapy is typically indicated for drug overdoses that result in refractory cardiovascular shock
- Lipid emulsion therapy is **NOT** a fix all but may be beneficial
- Consult your local poison center when considering lipid emulsion therapy



37



## PHARMACY CONSIDERATIONS



38

## Lipid Emulsion Formulations

- **Brand Names:** Clinolipid, Intralipid, Nutrilipid, SMOFlipid
- **Strengths:** 10%, 20%, 30%
- **Volume:** 100mL, 250 mL, 500 mL, 1000mL
  
- **Most Studied:** Intralipid 20%



39



## Lipid Emulsion Storage and Handling

### Inpatient

- Onsite where local anesthetics are being used
- Emergency rooms/Central pharmacy

### Outpatient

- Rural locations where local anesthetics are being used



40

## Lipid Emulsion Therapy Dosing

- **Preferred Agent:** Intralipid 20%
- **Bolus:** 1.5 mL/kg (max 100 mL) infused intravenously over 1 minute
- **Repeat boluses:** Repeat boluses every 3-5 minutes to desired effect (NTE: 2 additional boluses)
- **Maintenance infusion:** 0.25-0.50 mL/kg/min for 30-60 minutes
- **Total maximum amount:** 12 mL/kg

\*Use actual body weight for dosing

\*\*No filter required for this indication



41

## Contraindications for Parenteral Nutrition

- Hypersensitivity to egg, soybean, peanut protein, or any component of the formulation
- Concomitant use of lipid-containing drugs
- Triglyceride level > 1,000 mg/dL



42

## Contraindications for Lipid Emulsion Therapy

- ~~• Hypersensitivity to egg, soybean, peanut protein, or any component of the formulation~~
- ~~• Concomitant use of lipid-containing drugs~~
- ~~• Triglyceride level >1,000 mg/dL~~
- **Benefit > Risk**



43

## Lipid Emulsion Therapy Adverse Drug Reactions

- **Fat Overload Syndrome**
  - Multi end-organ dysfunction due to inadequate clearance of lipids
- **Elevated Triglycerides and Pancreatitis**
  - Fat obstructs small vessels of pancreas causing ischemia and inflammation
- **Infection**
- **Pulmonary Toxicity**
  - Occludes pulmonary vasculature with microfat emboli



Levine M et al. *J Med Toxicol*. 2014.

44

## Lab Interference

- **Duration:** Up to hours after lipid emulsion therapy
- **Most Common Abnormalities:** Glucose, albumin, bilirubin, aminotransferase, creatinine, creatinine kinase, magnesium, and phosphate
- **Susceptible Methods:** Colorimetric > potentiometric
- **Mechanisms**
  - Light scattering
  - Electrolyte exclusion effect
  - Contaminants



Grunbaum AM et al. *Clin Toxicol (Phila)*. 2012.

45

## Lipid Emulsion Therapy and ECMO

- Fat emulsion deposition and clogging
- Cracking of stopcocks
- Malfunction of membrane oxygenator
- Increased blood clot formation



Bacon B et al. *J Cardiothorac Vasc Anesth*. 2019.

Lee HM et al. *Clin Toxicol (Phila)*. 2015.

46

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50

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