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Beta Safe Than Sorry!
Beta Blocker & Calcium Channel Blocker Toxicity Review

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Just another day in the ED…

"Could I have your help with this patient?"

EM Physician

EM Pharmacist

Icons: Microsoft 365 icon library

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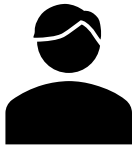

Patient M.C.

55 YO M

BP 105/72
HR 52

BG 278

QTc 545

Patient holding emesis bag

Icons: Microsoft 365 icon library

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"Patient is vomiting but QTc is 545, what can I give him?"

EM Physician

"Oh no! What else is going on? What brought him in?"

Icons: Microsoft 365 icon library

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About 1 hour PTA, patient took entire bottle of amlodipine 10 mg tablets

Rx bottle at bedside: filled 3 days ago for 30 day supply

Patient is vomiting, complains of dizziness

A&Ox3 and following commands

HR trending down: 55 → 52 → 48

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Learning Objectives

1. Describe the mechanism of toxicity of calcium channel blockers (CCB) and beta blockers (BB)
2. Review treatment options that have been studied in CCB and BB toxicity and briefly describe the quality of evidence for each
3. Predict & mitigate complications of high-dose euglycemic insulin therapy
4. Describe the management of specific toxicity profiles seen with overdoses of propranolol and sotalol

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Calcium Channel Blockers

	Dihydropyridine (DHP)	**Non-DHP** (phenylalkylamine)	**Non-DHP** (benzothiaprine)
Agents	Amlodipine Nifedipine Nicardipine	Verapamil	Diltiazem
Physiologic Properties	Selective affinity for vascular smooth muscle	Strong affinity for myocardium & vascular smooth muscle	Strong affinity for myocardium, less for vascular smooth muscle
Cardiac Effects	SVR = ↓↓	SVR = ↔ Inotropy = ↓↓↓ Chronotropy = ↓↓↓	SVR = ↔ Inotropy = ↓↓ Chronotropy = ↓↓

SVR = Systemic vascular resistance

Lange (2018), McGraw Hill (2019)
https://www.ncbi.nlm.nih.gov/books/NBK537147/

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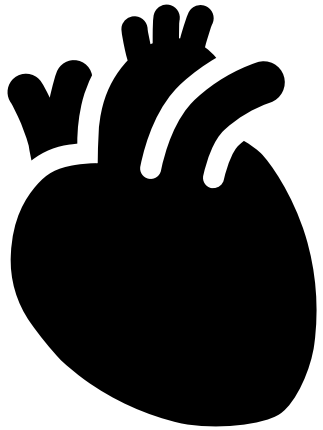
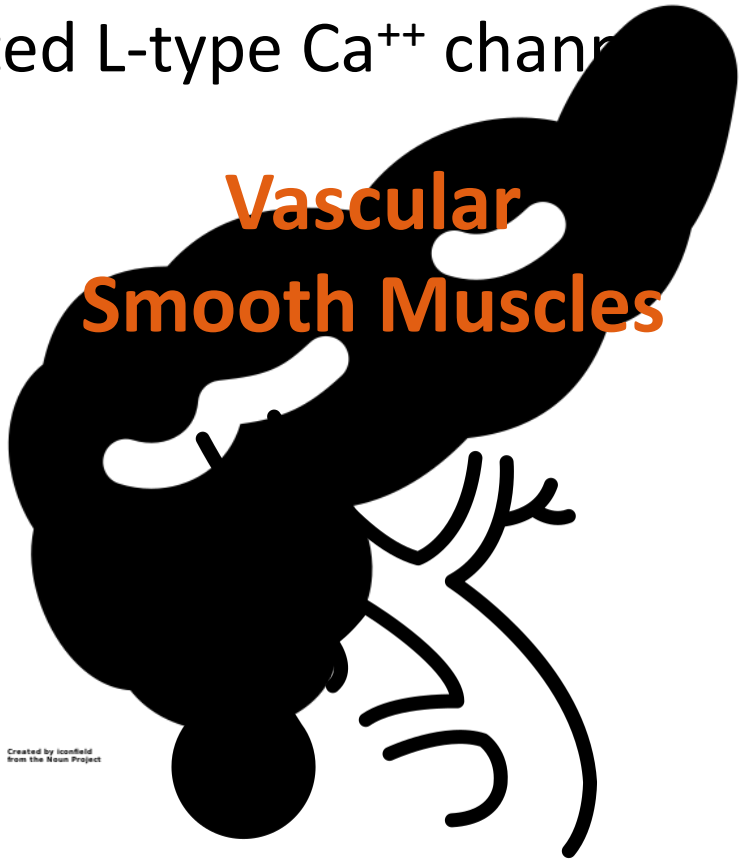
CCB Pharmacology

MOA: Block voltage-gated L-type Ca^{++} chann

Myocardium



Vascular Smooth Muscles



Pancreas

Icons: Microsoft 365 icon library & The Noun Project

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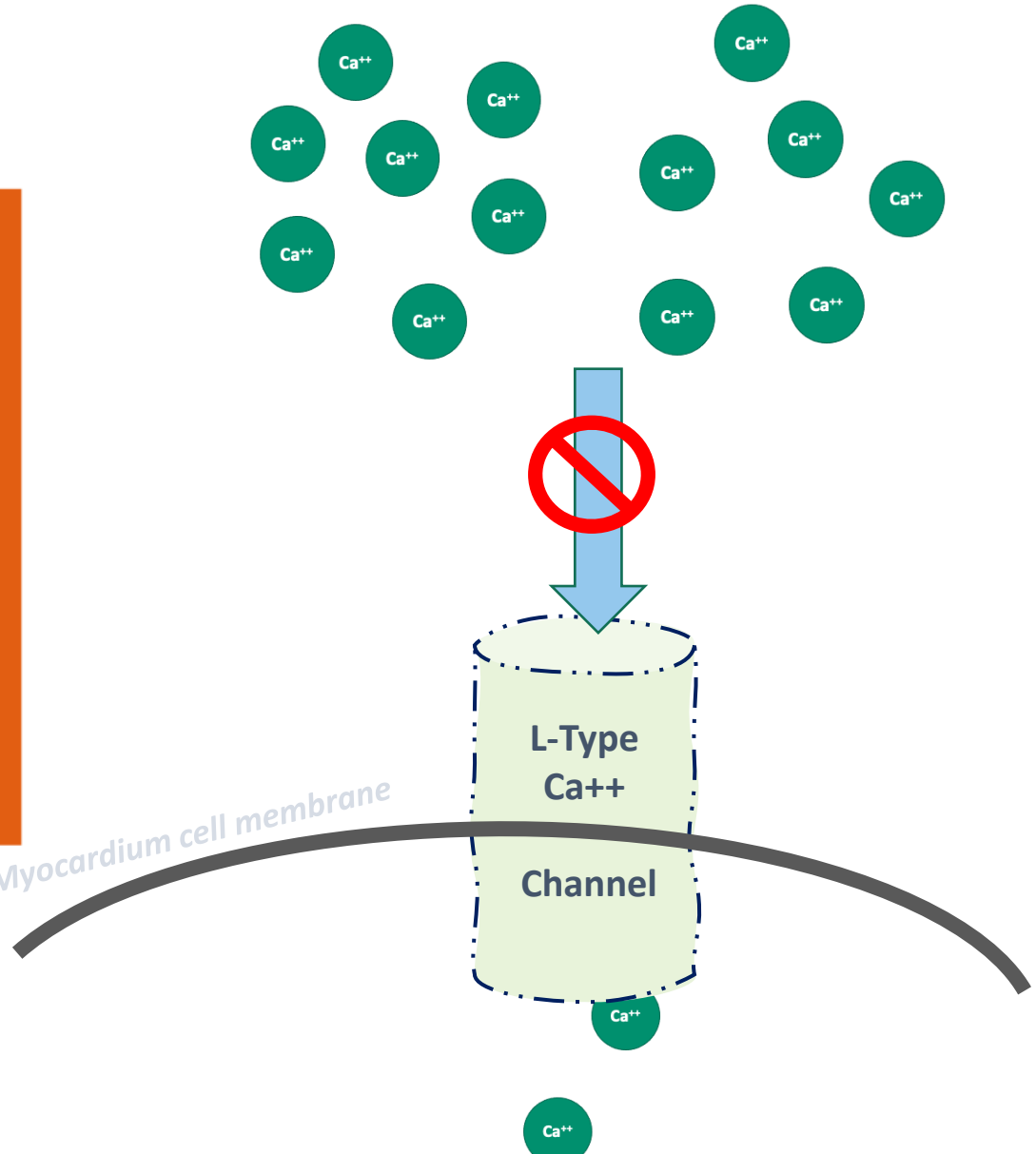
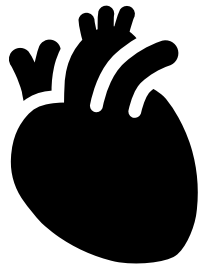


Myocytes, SA node, AV node



- Inhibition of Ca^{++} influx ↓ rate of pacemaker cell depolarization
  - Myocardial depression
  - Bradycardia
- Non-DHP (verapamil >> diltiazem)

Lange (2018), McGraw Hill (2019)
Icons: Microsoft 365 icon library & The Noun Project

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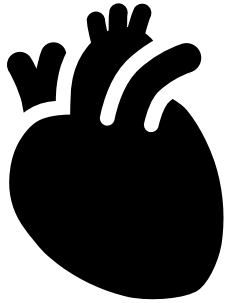

Resting Membrane Potential	
Myocardium	**Peripheral Vasculature**
- 90 mV	- 70 mV

Vascular Smooth Muscles

- Inhibition of Ca++ influx results in
  - Vasodilation = ↓ blood pressure
- DHP CCB (amlodipine, nifedipine)
  - **Preferentially bind** with peripheral vascular smooth muscles
- In overdose, selectivity is lost

Lange (2018), McGraw Hill (2019)
Icons: Microsoft 365 icon library & The Noun Project

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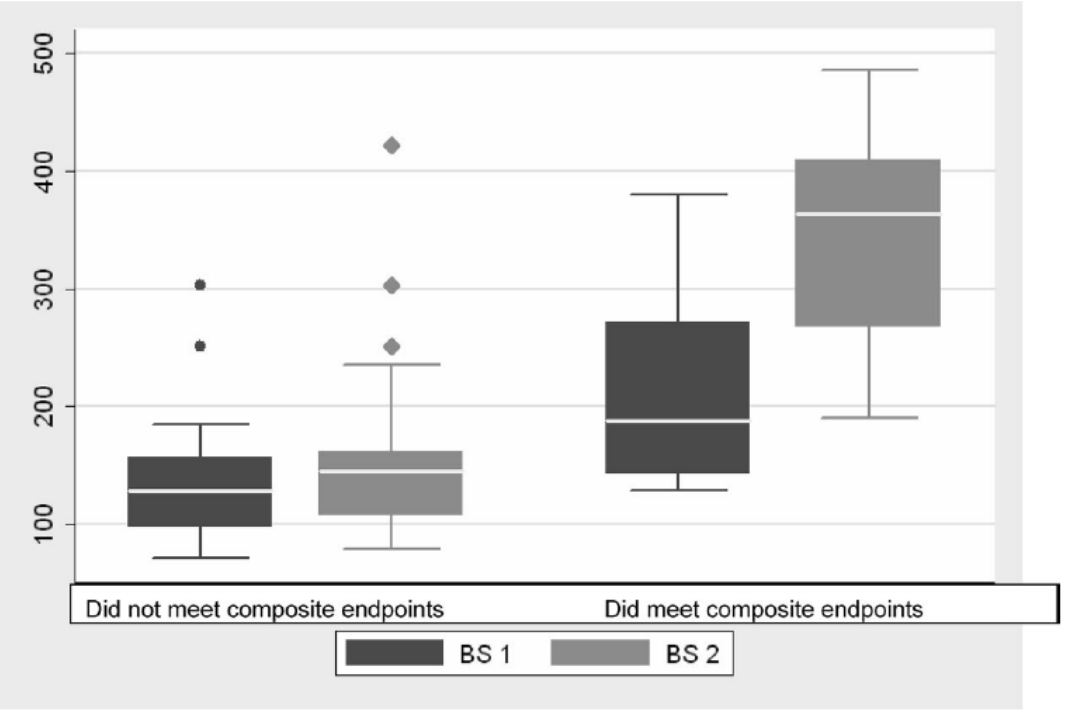
Assessment of hyperglycemia after calcium channel blocker overdoses involving diltiazem and verapamil

Levine et al (2007)

Retrospective case series (n=40)

Composite Endpoint =



Bottom Line

Serum glucose concentrations may correlate with the severity of CCB toxicity and overall prognosis.

PMID 17855820

Pancreatic β Islet Cells

- Inhibition of Ca++ influx results in
  - Impaired insulin release
  - Hyperglycemia
- Hypoinsulinemia ↓ cardiac myocyte glucose uptake

Lange (2018), McGraw Hill (2019)

Icons: Microsoft 365 icon library & The Noun Project

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Vitals

42 BPM

"We need atropine, STAT!"

EM Physician

EM Pharmacist

Images: Microsoft 365 stock images library

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Overview of Treatment Options

- Calcium
- Atropine
- Vasopressors
- Glucagon
- High-dose insulin euglycemic therapy (HIET)
- Intralipid emulsion
- Enhanced elimination strategies
- Emerging therapies

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Initial Management

Decontamination

- Activated charcoal if feasible and timing is appropriate
- Gastric lavage, whole bowel irrigation

Fluids

- Conservative, response-based approach
- Caution – Fluid overload, pulmonary edema

Atropine

- Dose = 1 mg IVP; may repeat Q3-5 min
- Symptomatic bradycardia or conduction disturbances

Lange (2018), McGraw Hill (2019)

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IV Calcium

Mechanism

- ↑ extracellular Ca^{++} to flood any available L-type Ca^{++} channels

Evidence

- Majority of animal studies reduced mortality, improved hemodynamics
- **SCCM (2017)** 1st line therapy to increase contractility and blood pressure (1D)

PMID 27749343

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Calcium: Dosing

	Calcium gluconate	Calcium chloride
Bolus dose	3 – 6 g	1 – 2 g
Frequency	Q 10-20 min	Q 10-20 min
Infusion	0.6-1.2 mL/kg/h	0.2-0.4 mL/kg/h

Lange (2018)
PMID 27749343

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Calcium: Practical Considerations

IV access:

- Vesicant!
- Central line preferred
  - Especially for $CaCl_2$ bolus and any continuous infusion

Preparation/Administration:

- Initial bolus: consider CaGluc 3g in 50 mL NS/D5 via peripheral line
- Max rate 200 mg/min (3g over 15 min)

Monitoring:

- Calcium level q1-2h
- IV site
  - In case of extravasation → hyaluronidase[1]

1. PMID 24420913

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Glucagon

Not included in the SCCM consensus guideline…

"The workgroup suggests not to use glucagon because case series reported variable effects. Vomiting and hyperglycemia have been reported in several case reports, and more effective interventions for the treatment of CCB poisoning are available"

PMID 27749343

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Vasopressors and Inotropes

SCCM consensus guideline recommendations

- Norepinephrine (1D) – increase blood pressure
- Epinephrine (1D) – increase contractility and heart rate
- Dopamine or vasopressin (as single vasoactive agent) – recommend against
- Phenylephrine – no recommendation

Inotropes

- Dobutamine (2D) – increase contractility if cardiogenic shock
- Milrinone (2D) – Alternative when dobutamine may not be effective (ex: concomitant beta blockade)

PMID 27749343

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High-dose Insulin Euglycemic Therapy (HIET)

Cardiac physiology:

- Energy → Free fatty acid vs carbohydrates
- CCB inhibit insulin release
- Insulin resistance

Mechanism

- Inotropy
- Improves intracellular glucose utilization
- Vasodilation → ↑ cardiac output

Lange (2018), McGraw Hill (2019)

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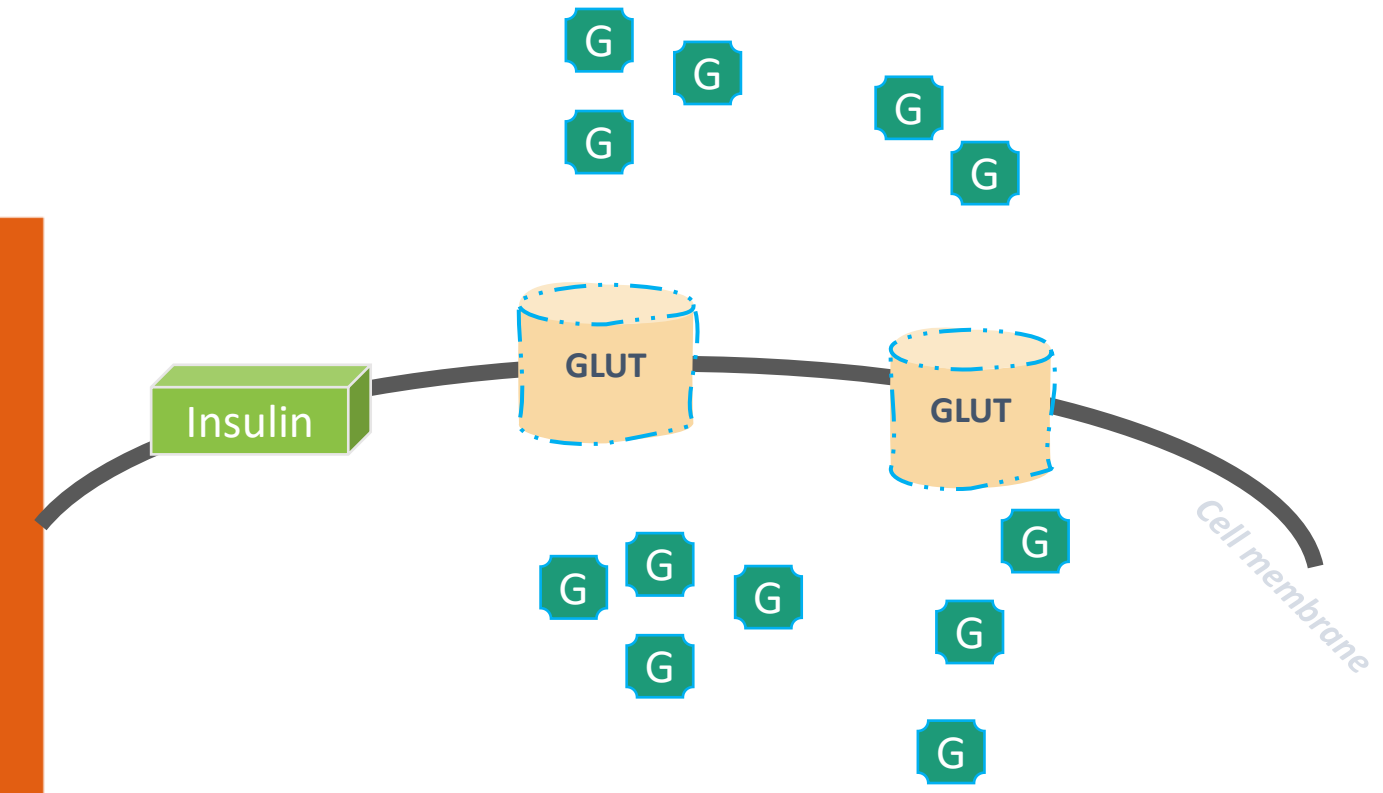

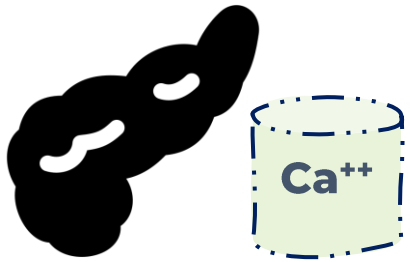

Cardiac Physiology

- Cardiac fuel
  - Non-stressed → free fatty acid
  - Stressed → carbohydrates
- Insulin release mediated via Ca^{++} channel in pancreas
- CCB toxicity ↓ insulin release leading to ineffective glucose utilization

Lange (2018), McGraw Hill (2019)

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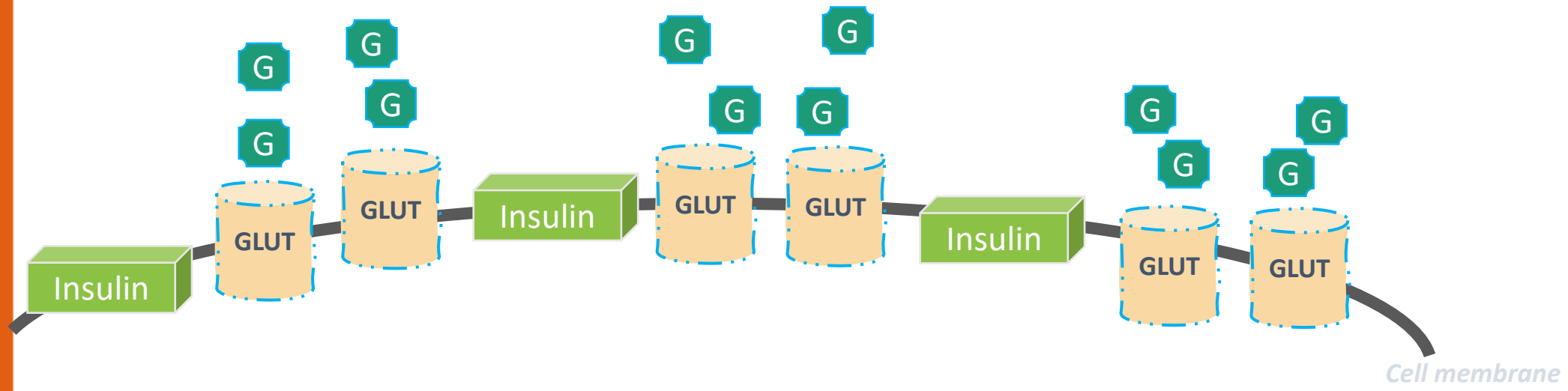
High-dose Insulin Euglycemic Therapy

- Mechanism
  1. ↑ intracellular glucose transport
  2. ↑ Inotropy
  3. Vasodilation to ↑ cardiac output



Lange (2018), McGraw Hill (2019)

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HIET: Evidence

Holger et al (2011)

- Consecutive case series (n=12) in BB/CCB/mixed agent overdoses
  - HIET was sole inotropic therapy
  - 7 patients on vasopressors → tapered off after HIET initiation
  - Mean max insulin infusion rate = 8.35 unit/kg/h (range: 0.5 – 21)
- 11 out of 12 survived to hospital discharge
  - 7 out of 11 had hypoglycemic events
  - 8 out of 11 experienced hypokalemia
- **Conclusion**: 1 – 10 unit/kg/h effective for toxin-induced cardiogenic shock

PMID 21819291

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HIET: Evidence

Page et al (2018)

- Retrospective chart review from two Australian toxicology units
- Beta blocker (n=12), calcium channel blocker (n=6), mixed (n=3)
  - Median loading dose = 80 unit (range: 50 – 125 units)
  - Median max infusion rate = 150 unit/h (range: 38 – 1,500 units/h)
- Safety
  - 73% developed hypoglycemia despite median dextrose 37.5g/hr
    - Persisted 18h after d/c of insulin drip
  - 82% developed hypokalemia (K < 3.5 mEq/L)
  - No complications from hypoglycemia or hypokalemia noted

PMID 29069937

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Cole et al (2018)

- Regional Poison Center (MN)

- BB (44%), CCB (33%), or both (23%) overdose who received HIET (n=199)
  - Median bolus = 1 unit/kg
  - Median peak infusion = 8 unit/kg/h (range: 0.5 – 18)
  - Median # of days on HIET = 2 days (range: 1 – 7)
- Safety:
  - Hypokalemia 29%
  - Hypoglycemia rate of 50% if using D10 or below; 30% using D20 or higher

- Check baseline creatinine, glucose, and potassium. Replace potassium if hypokalemia is present.
- Administer 25-50 g of dextrose 50% (D50) IV if blood glucose < 200 mg/dL.
- Administer 1 U/kg of regular insulin IV push.
- Begin infusion of 1 U/kg/hr of regular insulin along with an infusion of dextrose; use D20 via a peripheral IV line until central access has been obtained, then start D50 at 25 g/hr. Initial effects of HDI take at least 5-10 minutes to manifest.
- Obtain central venous access for safe infusion of concentrated glucose.
- Concentrate all fluids to avoid pulmonary edema. Consider using stock D70 as the glucose infusion. The insulin infusion should be concentrated to 10 U/mL.
- Increase insulin infusion 1-2 U/kg/hr every 10-15 minutes to a maximum of 10 U/kg/hr until shock improves. Doses up to 22 U/kg/hr have been safely used.
- Monitor blood glucose every 10-15 minutes until stable, then every 1-2 hour after steady state is reached. For every hypoglycemic reading, give 25 g of D50 as a bolus and increase the dextrose infusion by 25 g/hr.
- Monitor serum potassium every hour during titration, then every 4-6 hours once steady state is reached.
- Regarding electrolytes, maintain serum potassium ≥ 2.8 mEq/L and calcium 1.5-2 times the upper limit of normal. Monitor magnesium and phosphorus every 4-6 hours and replace as needed. We recommend standard ICU magnesium and phosphorus replacement protocols.
- Once stable, wean vasopressors before HDI. Contact the Poison Center regarding weaning of HDI once stability has been reached.

PMID 29452919

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HIET: Evidence

SCCM consensus guideline (2017)	
↑ Cardiac contractility (1D) ↑ Blood pressure (2D)	Refractory to 1st line therapies Refractory shock Peri-arrest

PMID 27749343

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HIET: Monitoring

PRIOR TO INITIATION	Blood Glucose (BG)	Potassium (K^+)
	D50 if < 200 mg/dL	K+ > 3.3 mEq/L
	Mg, Ca^{++}, Phos, central access	

MONITORING		TARGET
BG	Q15min until stable; then Q1H	100 – 200 mg/dL
K+	Q1H while titrating insulin	Normokalemia

PMID 29452919

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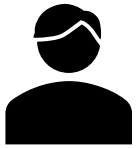

Patient M.C.

Labs/ Vitals

- K = 2.8 mg/dL
- BG = 278
- Weight = 68 kg

Treatment

- CaGluc 3g bolus is infusing
- 1 L LR
- Atropine 1 mg x2 & norepinephrine infusion started
- MD wants to start HIET

IV Access

- No central line yet
- 3 peripheral lines

Icons: Microsoft 365 icon library

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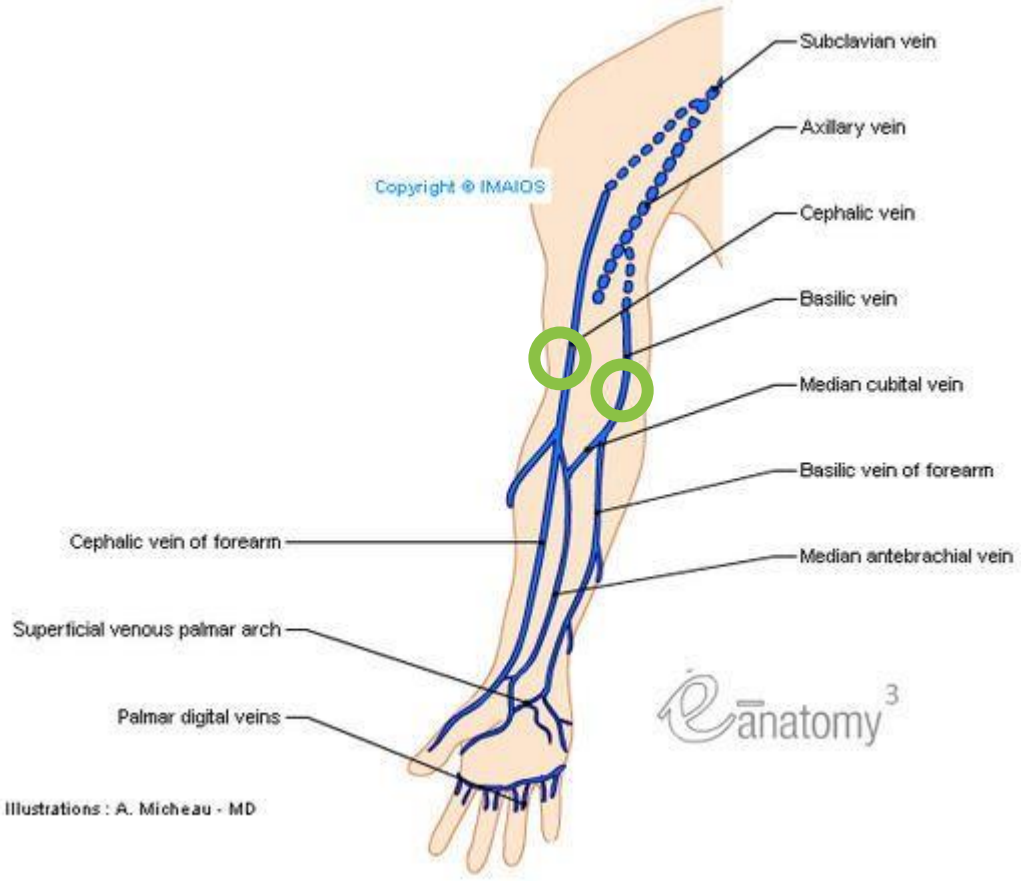
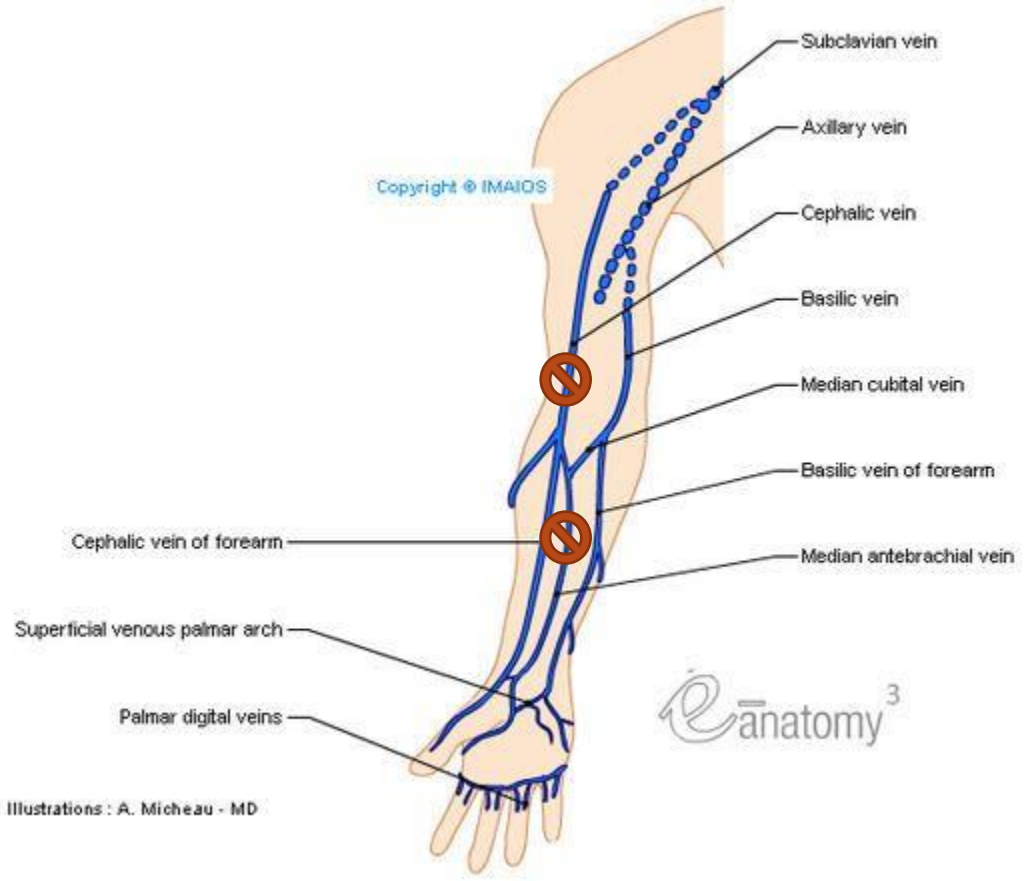
Infuse potassium at 10 mEq/hr into 2 peripheral IV lines simultaneously
(Avoid infusing in two veins that connect within periphery)





Illustrations: https://www.imaios.com/en/e-Anatomy/Upper-Limb/Upper-limb-Illustrations

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HIET: Insulin Dosing

HIET DOSING	**Bolus**	**= 1 unit/kg IV push**
	Infusion	**= Start: 1 unit/kg/h**
	Titration	**= 1 – 2 units/kg/h**
	Interval	**= Q 10 – 15 min**
	Max Dose	**= ~ 10 unit/kg/hr**

PMID 29452919

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HIET: Preventing hypoglycemia

DEXTROSE	Bolus	= 25-50 g initially if BG < 200
	Infusion	= Initial rate = 25 g/h
	Monitor BG	= Q 10 – 15 min until stable
	Hypoglycemia	= Bolus 25 g; then ↑ infusion by 25 g/h

PMID 29452919

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Assessment Question

After potassium has resulted within range, you are ready to begin HIET. BG is 278. Which of the following doses of dextrose and insulin are recommended for your 68 kg patient?

A) Insulin bolus 68 units x1, then 68 units/h + D5 @ 50 mL/h
B) Insulin bolus 34 units x1, then 34 units/h + D10 @ 50 mL/h
C) Insulin bolus 68 units x1, then 68 units/h + D20 @ 125 mL/h
D) Insulin bolus 34 units x1, then 34 units/h + D20 @ 125 mL/h

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Assessment Question

After potassium has resulted within range, you are ready to begin HIET. BG is 278. Which of the following doses of dextrose and insulin are recommended for your 68 kg patient?

A) Insulin bolus 68 units x1, then 68 units/h + D5W @ 50 mL/h
B) Insulin bolus 34 units x1, then 34 units/h + D10W @ 50 mL/h
C) **Insulin bolus 68 units x1, then 68 units/h + D20W @125 mL/h**
D) Insulin bolus 34 units x1, then 34 units/h + D20W @125 mL/h

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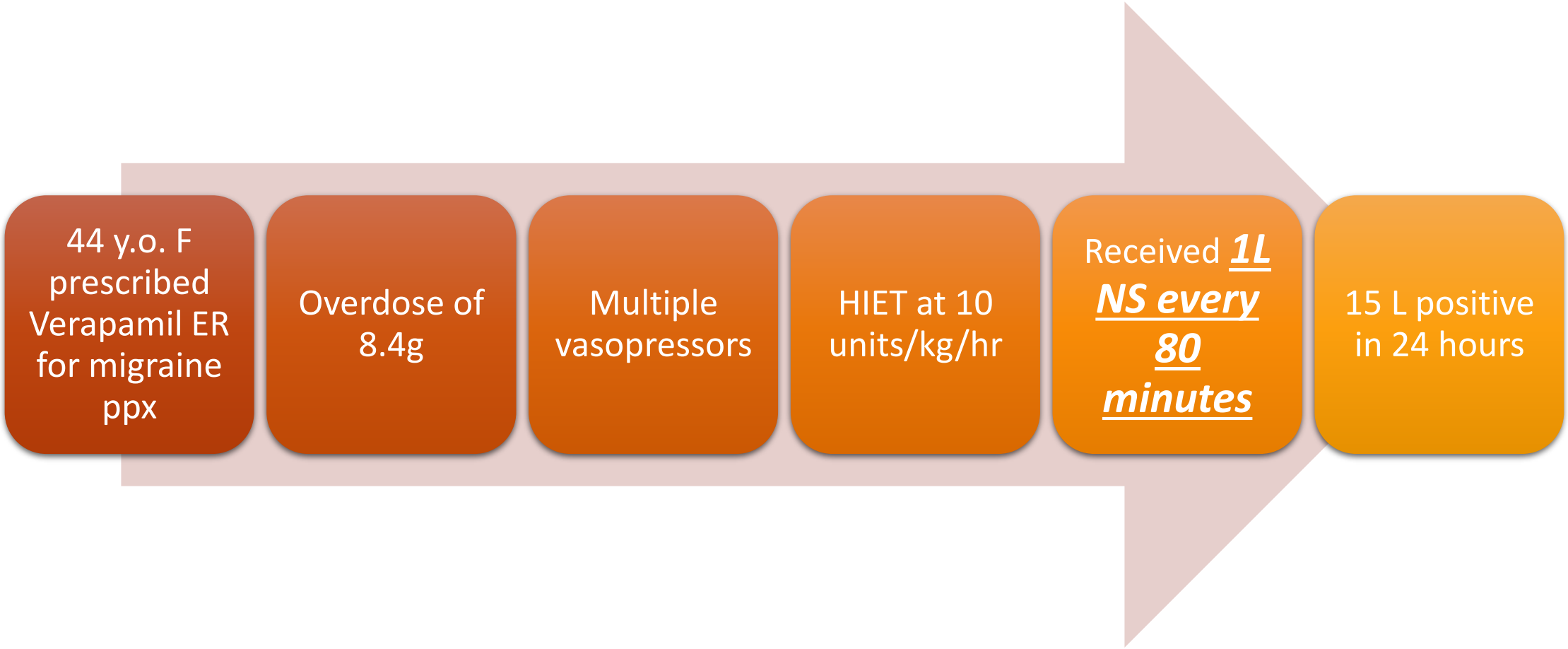
HIET: Clinical Considerations



PMID 30378442

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HIET: Clinical Considerations – Fluid Overload

Dextrose

- Use D20 via peripheral line; D50 or D70 when central access available
- Alternative: D50 boluses instead of infusion

Insulin

- Prepare concentrated insulin infusion
- Concentration – Up to 16 units/mL[1]
- Stability – 14 days at room and refrigerated temperature

Bottom Line

Conservative IV fluid approach, concentrate everything you can, monitor for pulmonary edema

1. PMID 27432286

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As the IV room pharmacist, you are attempting to concentrate the insulin regular infusion for a HIET patient on rate of 132 units/hr. Which of the following concentrations is the maximum concentration supported by literature?

A) Insulin 1 unit/mL
B) Insulin 5 units/mL
C) Insulin 16 units/mL
D) Insulin 100 units/mL

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As the IV room pharmacist, you are attempting to concentrate the insulin regular infusion for a HIET patient on rate of 132 units/hr. Which of the following concentrations is the maximum concentration supported by literature?

A) Insulin 1 unit/mL

B) Insulin 5 units/mL

C) Insulin 16 units/mL

D) Insulin 100 units/mL

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Intralipid Emulsion (ILE)

Proposed Mechanisms

- "Lipid Sink" theory
  - Sequesters lipid-soluble drugs within intravascular compartment
- Energy source
- Activation of L-type Ca^{++} channels = ↑ contractility

PMID 25534900, 25684131, 27608281
Image: https://serfinitymedical.com/products/baxter-healthcare-bag-iv-intravia-250ml-6package-8-pkca-2b8012-1258394 & https://www.fresenius-kabi.com/in/products/intralipid

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Intralipid Emulsion

Lipid Emulsion (20%)	**Bolus***	**= 1.5 mL/kg over 1 min**
	Infusion**	**= 0.25 to 0.5 mL/kg/min**
	Duration	**= 30 to 60 min**
	Max Total Dose	**Not established; ~10-12 mL/kg**

* Use LBW; may repeat bolus for persistent cardiovascular collapse

** Can double the infusion rate for persistent hemodynamic instability

PMID 25534900, 25684131, 27608281

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ILE: Clinical Considerations

Monitoring

- Adverse effects: Pulmonary toxicity, fat embolism, pancreatitis

Lipemia

- Laboratory derangements; delays in lab evaluation
- Potential issues involving concurrent use with extracorporeal assist devices
- Interference with other therapies that have evidence of benefit

PMID 27608281

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ILE: Evidence

Lipid Emulsion Workgroup (2016) Recommendations:

- **In life-threatening toxicity due to diltiazem, verapamil, or dihydropyridine calcium channel blockers, we suggest not using ILE as first-line therapy (2D).**

- **In cardiac arrest due to toxicity from calcium channel blockers, our recommendation is neutral regarding the use of ILE.**

SCCM consensus guideline (2017)
• Refractory to first line treatments (2D) • Refractory shock or peri-arrest (1D)

PMID 27608281, 27749343

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Enhanced Elimination, EXTRIP

EXTRIP Workgroup Systematic Review and Recommendations (2021)

"In patients severely poisoned with amlodipine, diltiazem or verapamil, we recommend against using ECTR in addition to standard care rather than standard care alone"

Strong recommendation, very low quality of the evidence

PMID 33555964

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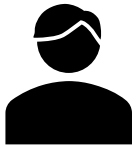

Patient M.C.

HIET
- Insulin 1 unit/kg bolus and 1 unit/kg/h → titrated to 2 units/kg/h
- BG checked q15min x4 then q1h → has been ~130-190 with intermittent D50
- 25g D50 ordered PRN BG < 100

Calcium
- Calcium chloride (undiluted) at 2 g/h infusing via central line

Pressors
- Norepinephrine infusing at 16 mcg/min

Lipids
- ILE started with 100 mL bolus and 20 mL/min infusion

HR begins to trend up!

Icons: Microsoft 365 icon library

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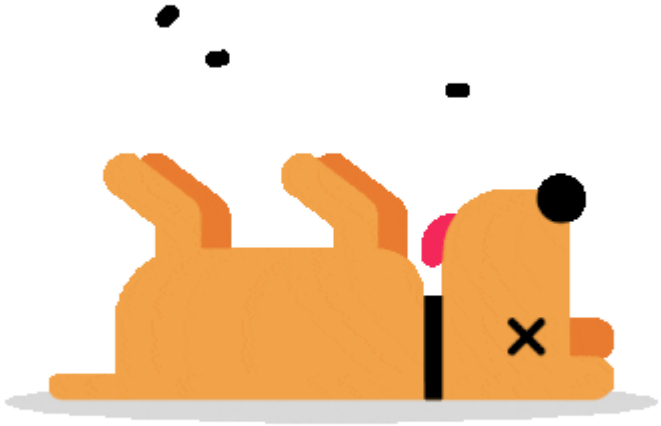
"MICU bed is ready! Report has been called. Let's roll!"

EM RN



EM Pharmacist

Images: Microsoft 365 stock images library

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CCB Toxicity - Summary

HIET & Calcium are the priority

- Safety considerations & monitoring will keep you busy!

Atropine, pressors, fluids can be helpful initially

Avoid glucagon

ILE for refractory cases

Concentrate drips as soon as you can

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Beta Blocker Toxicity

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Patient N.S.

- 23-year-old female presented with seizure
- Professional musician, prescribed propranolol 10 mg daily PRN for stage fright
- Has a very important competition next week
- In frustration over shakiness during rehearsal, took entire bottle of propranolol (qty 90)

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Beta Blockers

MOA: Competitive antagonism at cardiac β-adrenergic receptors

- Inverse agonism at both B2 and B3 receptors
- Membrane stabilizing effects
- Metabolic effects

Lange (2018), McGraw Hill (2019)

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Beta Blockers: Pharmacokinetics

	Receptor Selectivity	Physiologic Properties	Elimination
Atenolol	β_1		Renal
Carvedilol	β_1, β_2, α_1	MSA(+)[a], Vasodilation	Hepatic, Biliary
Labetalol	β_1, β_2, α_1	MSA(+)[a] Vasodilation (PO 1:3, IV 1:7)[b]	Hepatic
Metoprolol	β_1	MSA (±)[a]	Hepatic
Nebivolol	β_1	Vasodilation via nitric oxide release	Hepatic
Propranolol	β_1, β_2,	MSA (+++)[a]	Hepatic
Sotalol	β_1, β_2	Class II & III[c] antiarrhythmic effects	Renal

[a]Membrane stabilizing activity; low activity (+), high activity (+++)
[b]Ratio of α to β blockade
[c]Possesses both K^+ and Na^+ channel blocking properties

Lange (2018), McGraw Hill (2019)

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Membrane Stabilizing Activity (MSA)

Mechanism

- Na^+ channel blockade
- Class I antiarrhythmics characteristics

Propranolol >> Acebutolol

Carvedilol >> Labetalol

Clinical Manifestations of Toxicity

- Widened QRS
- Seizures
  - Most associated with propranolol (> 1.2 g)

Treatment Options	
Sodium Bicarbonate	**Benzodiazepines**
1-2 mEq/kg	Pick your favorite

Lange (2018), McGraw Hill (2019)

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Agents with Potassium Channel Blockade

Mechanism

- Block HERG K+ channels (repolarization)

Sotalol

Acebutolol

Clinical Manifestations of Toxicity

- Toxicity occurs with reduced renal clearance
- QT prolongation
- Ventricular dysrhythmias, Torsades de Pointes
  - Highest risk 4 – 15 h post ingestion
  - Prolonged toxicity – cases of >100 h

Treatment Options	
$MgSO_4$ (IV)	Pacing
Isoproterenol	

Lange (2018), McGraw Hill (2019)

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Initial Management

Similar to CCB overdose management:

- Decontamination
- Conservative with fluids
- Atropine
- IV Calcium
- Vasopressors

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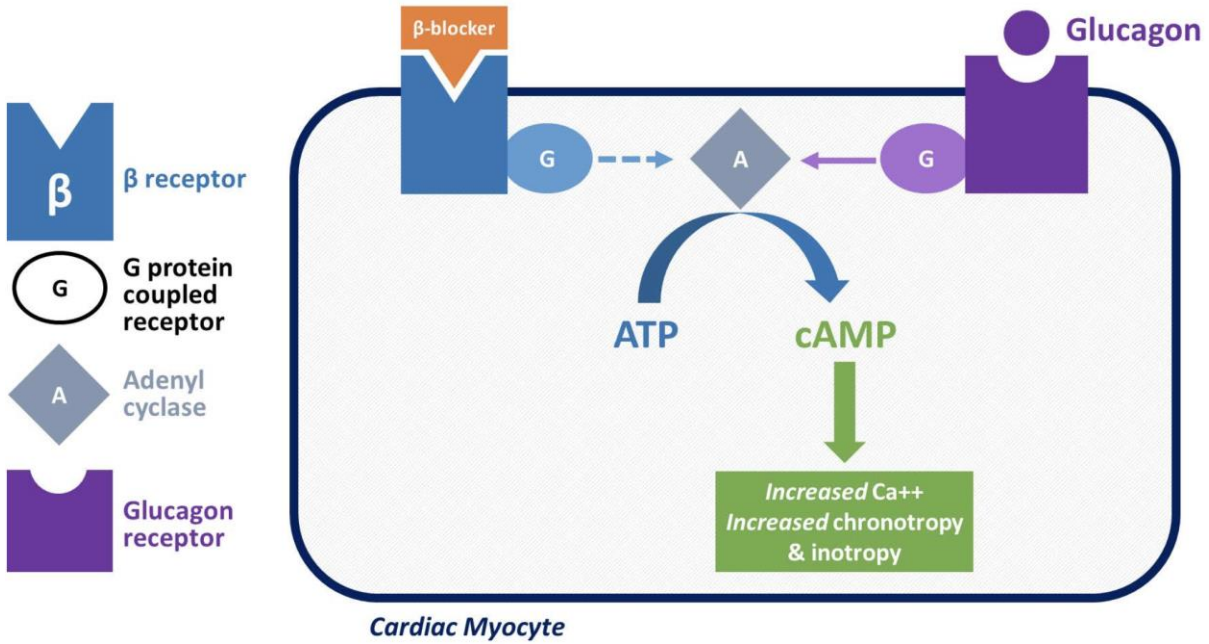
Beta Blockers



Glucagon

- ↑ adenylyl cyclase activity independent of β receptor activity
- Inhibits phosphodiesterase
  - ↓ cAMP breakdown
- Results in
  - ↑ Inotropy
  - ↑ Chronotropy

Lange (2018), McGraw Hill (2019)
Figure from: https://missouripoisoncenter.org/beta-blocker-overdose/

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Glucagon: Is there a role?

Evidence:

- Zero human trials of glucagon for beta blocker toxicity
- Animal studies

- **Rotella et al (2020) systematic review**
  - Minor improvements in hemodynamics primarily via ↑ HR
  - Limitations – Concurrent use of other therapies, variable results
  - Bottom Line = No difference in survival compared to HIET or ILE

PMID 4872564, 14514004, 32310006

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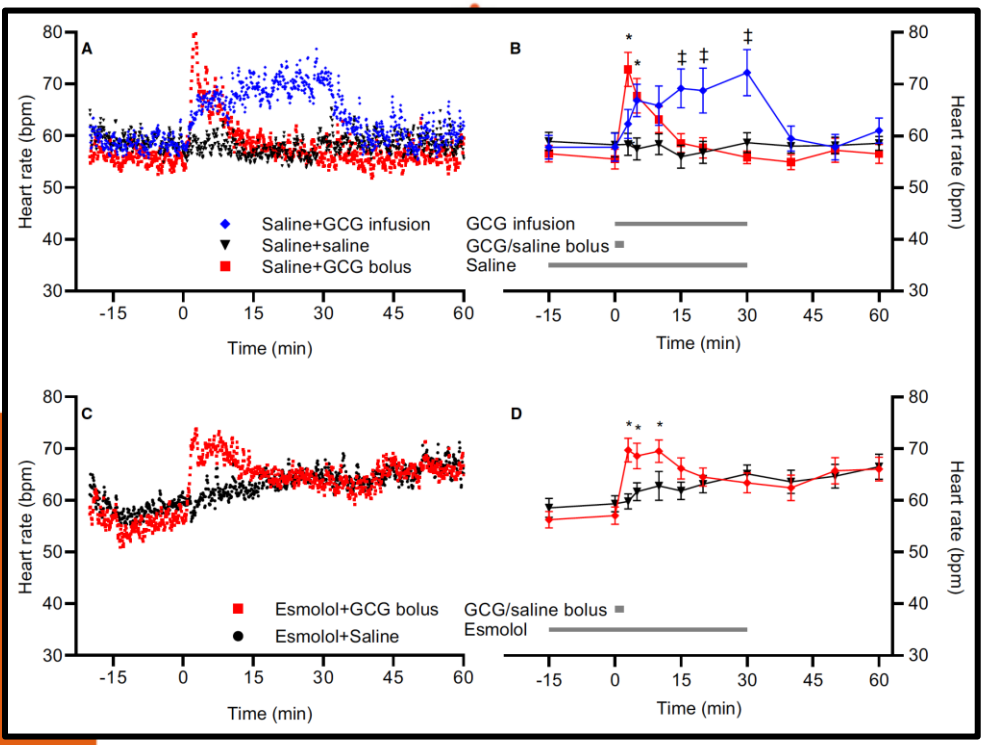
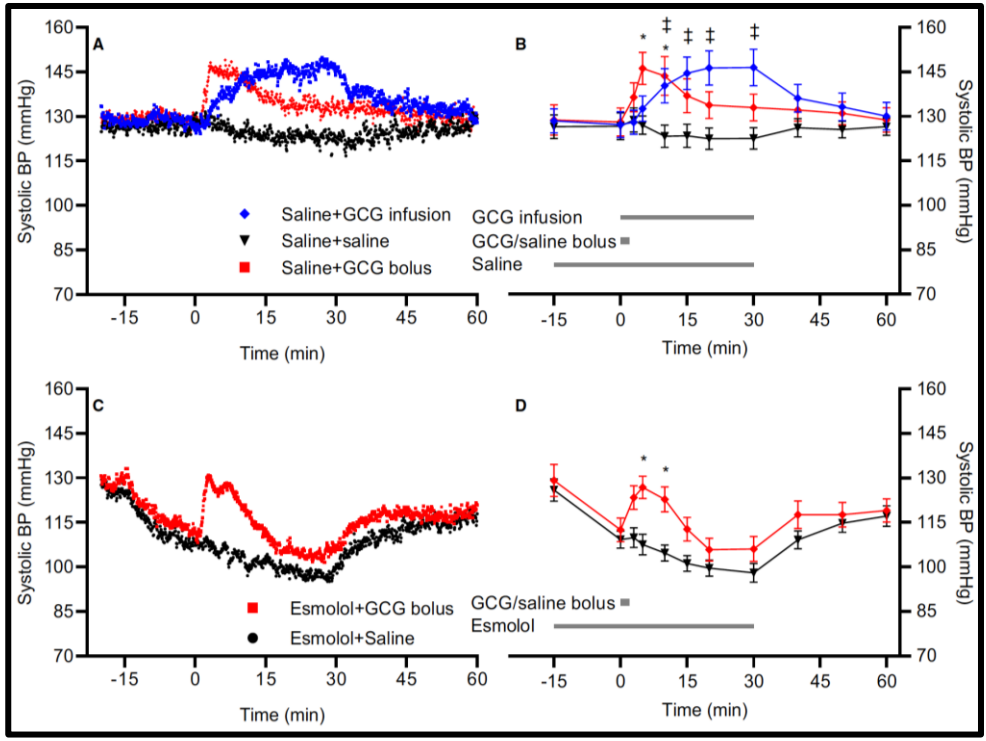
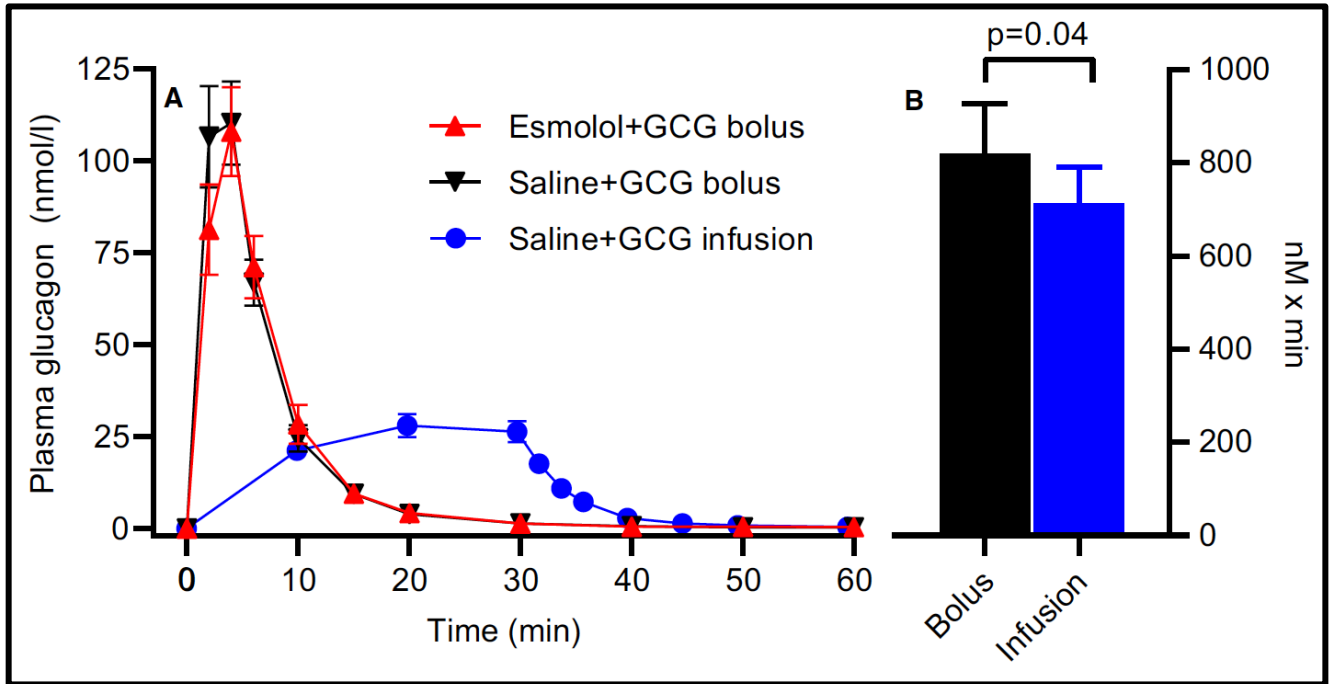
Glucagon: Evidence

Petersen et al (2020)					
Design	Randomized, crossover trial in (n=10) health adult males				
Allocation	Saline + saline	Esmolol + saline	Esmolol + glucagon bolus	Saline + glucagon (inf)	Saline + glucagon bolus
Goal	Investigate hemodynamic effects and safety of glucagon with or without beta blockade				

PMID 33103603







PMID 33103603

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Petersen et al (2020) – Findings

Glucagon ↑ BP/HR within 3-5 min of bolus (~15 min for infusion)

Comparable hemodynamic effects with glucagon infusion compared to bolus

- Longer lasting hemodynamic effects compared to bolus dosing strategy

High risk of ADEs –

- (n=2) participants unable to complete study due to vomiting
- Nausea occurred in 70-80% despite pretreatment with ondansetron 8 mg

PMID 33103603

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Glucagon

Glucagon Dosing	**Bolus***	= 50 – 150 mcg/kg or 3-10 mg (IV)
	Infusion	= 3 – 10 mg/h
	Titrate	**To hemodynamic response****
	Supply	**For 100 kg adult –** • 8 h supply = 90 mg • 24 h supply = 250 mg

*Administer slowly over at least 1 minute; may repeat if no clinical response

**Tachyphylaxis is common and will often occur

PMID 32310006

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Glucagon: Bottom Line

Who?

- Bradycardia, cardiogenic shock, cardiac pump failure

Things to consider prior to and throughout therapy –

- High risk aspiration, nausea/vomiting
- Vagal response → exacerbate hypotension and bradycardia
- Tachyphylaxis after 12– 24 h
- Pharmacy supply issue
- **When reconstituting –**
  - Supplied diluent contains glycerin → C/I in cardiac decompensation
  - Consider using sterile water or D5W to reconstitute!

Lange (2018), McGraw Hill (2019)

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Which of the following patients might be a candidate for IV glucagon?

A) Patient who received activated charcoal for a propranolol overdose and is currently vomiting

B) Patient receiving HIET for 2 hours with improvement in BP from 80/42 → 102/78

C) Patient who took double his verapamil dose for the past 3 days, with BP 108/73 and HR 60

D) Patient who ingested 30 tablets of atenolol 50 mg about 1 hour ago with BP 89/45 and HR 48, s/p 1 dose of atropine 1 mg

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ILE: Beta Blockers

Lipophilicity

- *High* = Propranolol
- *Moderate* = Carvedilol, labetalol, metoprolol
- *Low* = Atenolol, sotalol

Smolinske et al (2018)[1]

- 5 out of 102 (4.9%) overdoses obtained ROSC post-arrest

Lange (2018), McGraw Hill (2019)

1. PMID 30260247

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ILE: Beta Blockers

Cases w/ success[1]

- **Refractory to pressors, HIET, calcium**
- **In cardiac arrest**
- **Mixed OD including propranolol & other agents**

Cases w/ harm or fatality[2]

- **Mixed OD including CCB + BB → initial reversal of shock, death w/in 12 h**
- **Propranolol → fat embolism**

1. PMID 22002529 2. PMID 30260247

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EXTRIP Workgroup Systematic Review and Recommendations (2021)

	ECTR in addition to standard care vs standard care alone		Preferred ECTR modality
Atenolol	**YES**	Renal impairment + refractory bradycardia/hypotension	Intermittent HD
Propranolol	**NO**	Recommended against ECTR	N/A
Sotalol	**YES**	Renal impairment + refractory bradycardia/hypotension or torsade de Pointes	Intermittent HD
	NO	If ECTR used solely based on QT interval	

PMID 34112223

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Emerging Therapies

- Methylene Blue
- Levosimendan
- Cyclodextrins (e.g. Sugammadex)
- MARS: Molecular adsorbent recirculating system therapy

PMID 32310006, 27196698, 23724791, 23334490, 30598720, 30775633

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Patient N.S.

23-year-old female w/ seizure d/t propranolol OD

BP 102/72, HR 53
BG 54

A&O x 2, drowsy, confused

EKG shows QTc of 457, QRS of 115 msec

Icons: Microsoft 365 icon library

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Which of the following interventions would be appropriate for N.S.?

A) Discontinue propranolol
B) Sodium bicarbonate bolus 1 mEq/kg
C) Magnesium sulfate 2g IV over 20 minutes
D) Calcium gluconate 3g IV over 15 minutes

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BB Toxicity – Summary

HIET remains the priority

Calcium, atropine, pressors, fluids can be helpful initially

More evidence for glucagon vs. CCB

- Most human evidence limited to case reports

ILE

- Consider in cardiac arrest w/ lipophilic BBs
- Limited to case reports

MSA, lipophilicity, K channel blockade affect tx

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References

Book Publisher/Year/Ed.	Title
Lange (2018) 7th Ed.	Poisoning and Drug Overdose
StatPearls (2022)	Calcium Channel Blocker Toxicity (https://www.ncbi.nlm.nih.gov/books/NBK537147/)
McGraw Hill (2019) 11th Ed.	Goldfrank's Toxicologic Emergencies

PMID	Title
27749343	Experts Consensus Recommendations for the Management of Calcium Channel Blocker Poisoning in Adults
30378442	Risk of Fluid Overload From Failure to Concentrate High-Dose Insulin as an Intravenous Antidote
27432286	Stability of high-dose insulin in normal saline bags for treatment of calcium channel blocker and beta blocker overdose
25534900	Intravenous lipid emulsion in the emergency department: a systematic review of recent literature
25684131	Role of intravenous lipid emulsions in the management of calcium channel blocker and β-blocker overdose: 3 years experience of a university hospital
27608281	Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning
33555964	Extracorporeal treatment for calcium channel blocker poisoning: systematic review and recommendations from the EXTRIP workgroup
4872564	Cardiovascular effects of glucagon in man
14514004	Glucagon in beta-blocker and calcium channel blocker overdoses: a systematic review
32310006	Treatment for beta-blocker poisoning: a systematic review
33103603	High-Dose Glucagon Has Hemodynamic Effects Regardless of Cardiac Beta-Adrenoceptor Blockade: A Randomized Clinical Trial
27196698	A systematic analysis of methylene blue for drug-induced shock
23724791	Evaluation of the effectiveness of sugammadex for verapamil intoxication
30598720	Hemodynamic improvement using methylene blue after calcium channel blocker overdose
23334490	Methylene blue reverses recalcitrant shock in β-blocker and calcium channel blocker overdose

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References, cont'd

PMID	Title
30775633	Treatment of Severe Amlodipine Toxicity With Molecular Adsorbent Recirculating System
34112223	Extracorporeal treatment for poisoning to beta-adrenergic antagonists: systematic review and recommendations from the EXTRIP workgroup
24420913	Management of extravasation injuries: a focused evaluation of noncytotoxic medications
21819291	High-dose insulin: a consecutive case series in toxin-induced cardiogenic shock
29069937	The safety of high-dose insulin euglycaemia therapy in toxin-induced cardiac toxicity
29452919	High dose insulin for beta-blocker and calcium channel-blocker poisoning
30260247	Utilization of lipid emulsion therapy in fatal overdose cases: an observational study
22002529	Bet 2: intralipid/lipid emulsion in beta-blocker overdose
30260247	Utilization of lipid emulsion therapy in fatal overdose cases: an observational study

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Thank you!

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Beta Safe Than Sorry!
Beta Blocker & Calcium Channel Blocker Toxicity Review

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