Medical Reference

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Last Updated: 2019-11-26

Contents

Foreword

This is a collection of topic-discussion level summaries of a myriad of different disease states. The book will be organized into parts by primary organ system / topic, and each chapter will cover a single disease state.

References will be listed at the end of each chapter. I will do my best to utilize appropriate clinical literature, but ultimately, these summaries are not peer-reviewed and medical decisions should not be made based upon this book.

Links will be colored like this throughout the book.

Key Points

This will be the format for section summaries / key points at the start of each chapter. These **will not** be present in every chapter

Literature Deep Dive

This is the format for description / analysis of major primary literature associated with a given topic. These will be my own personal analysis, and may not be reflective of clinical practice everywhere. They will also be more frequent in topics related to critical care and emergency medicine, as those are my primary interests.

Part I

Critical Care

CHAPTER 1

Vasopressors

Key Points

Add pressor abbreviations

1.1 RECEPTOR PHARMACOLOGY

- α_1: Peripheral Vasoconstriction
- β_1: Chronotropy / Inotropy
- β_2: Bronchodilation, Vasodilation
- V_1: Vasoconstriction
- V_2: Renal fluid retention
- Ang-II: Vasoconstriction, activation of aldosterone
- PDE-3: Inotropy, vasodilation

Add table for physiologic effects of receptor stimulation from Vasoactive Drugs in Circulatory Shock, also add pictures/graphs from favorite vasopressor article

Table 1.1: Adrenergic Receptor Specificity[1]

Drug	α_1	β_1	β_2
Phenylephrine	4+	0	0
Norepinephrine	4+	2+	1+
Epinephrine	2+ – 4+	1+	1+ – 3+
Dopamine	0 – 3+	0 – 3+	0 – 2+
Dobutamine	1+	4+	2+

Note: Scale from 0 - 4+

Add basic description of each vasopressor and their general place in therapy

1.2 VASOPRESSORS

1.2.1 Vasoconstricters

- Phenylephrine
- Norepinephrine
- Vasopressin
- Angiotensin II

1.2.2 Inopressors

- Epinephrine
- Dopamine

Sepsis trial comparing DA to EPI

1.2.3 Inodilators

- Dobutamine
- Milrinone

Finish table from lexi or AHA guidelines

Table 1.2: Milrinone Dosing[2]

CrCL mL/min	**Initial** mcg/kg/min	**Max** mcg/kg/min	**Titration** mcg/kg/min
>50			
40			
30			
20			
10			
5			

Table 1.3: Vasopressor Dosing [1, 3]

Drug	**Units**	**Initial**	≈ **Max**	**Titration**
Vasopressors				
Norepinephrine	mcg/min	5	50	5 Q5min
Phenylephrine	mcg/min	20	200	20 Q10min
Vasopressin	Units/min	0.03	0.03	Fixed
Ang-II	ng/kg/min	10	80 (<3hr); 40 (>3hr)	5 Q5min
Inopressors				
Epinephrine	mcg/min	5	30	5 Q5min
Dopamine	mcg/kg/min	5	50	2 Q5min
Inodilators				
Dobutamine	mcg/kg/min	2.5 – 5	40	2.5 – 5 Q5min
Milrinone	mcg/kg/min		See Table 1.2	

1.3 Push-Dose Pressors[4]

1.3.1 Phenylephrine

- Final Concentration: 100 mcg/mL
- Dose: 0.5 – 2 mL (50 – 200 mcg) Q1-5min
- Preparation
  - Add 10mg Phenylephrine (10 mg / 1 mL) to 100 mL NS
  - Final Concentration is 100 mcg/mL (10 mg / 100 mL)

1.3.2 Epinephrine

- Final Concentration: 10 mcg/mL
- Dose: 0.5 – 2 mL (5 – 20 mcg) Q1-5min
- Preparation
  - 1 mL cardiac epinephrine (1 mg / 10 mL)
  - Dilute to 10 mL NS, final concentration 100 mcg / 10 mL (10 mcg/mL)
  - Can also use 0.1 mL anaphylaxis epinephrine (1 mg/mL)

References

1. Jentzer JC, Coons JC, Link CB, and Schmidhofer M. Pharmacotherapy Update on the Use of Vasopressors and Inotropes in the Intensive Care Unit. J Cardiovasc Pharmacol Ther 2015;20:249–60.
2. Lexi-Drugs. Milrinone. URL: http://online.lexi.com.ezproxy.lib.purdue.edu/lco/action/doc/retrieve/docid/patch_f/7300?cesid=40MoAG2VKHX&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dmilrinone%26t%3Dname%26va%3Dmilrinone (visited on 11/26/2019).
3. Overgaard CB and Džavík V. Inotropes and Vasopressors: Review of Physiology and Clinical Use in Cardiovascular Disease. Circulation 2008;118:1047–56.
4. Weingart S. Push-Dose Pressors for Immediate Blood Pressure Control. Clin Exp Emerg Med 2015;2:131–2.

Part II

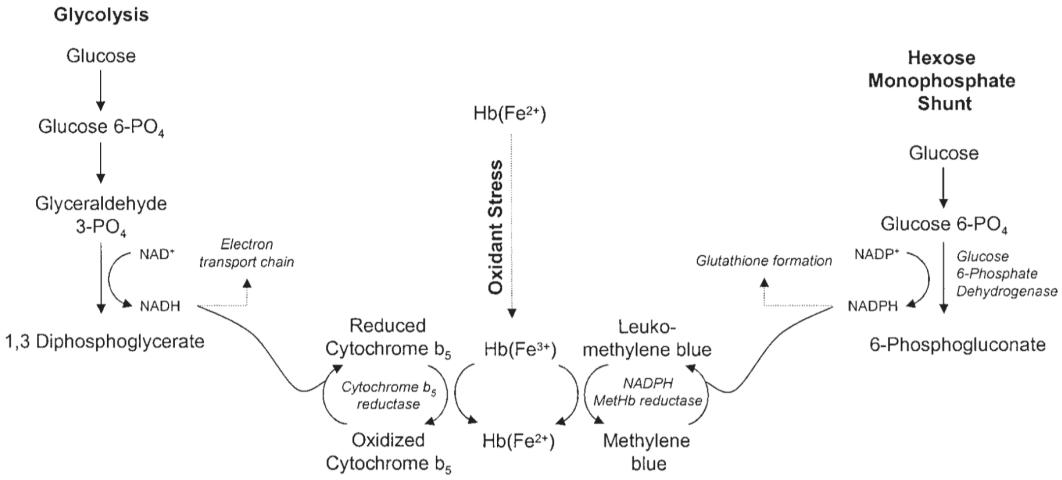
Toxicology

CHAPTER 2

Methemoglobinemia

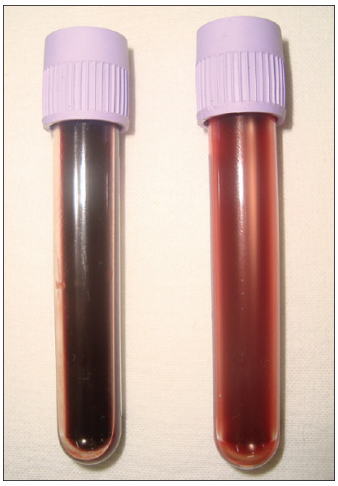
2.1 Pathophysiology

(a) Metabolism of Methemoglobin



From Goldfrank's Toxicology (2007)

(b) Met-Hgb (left), Normal (right)



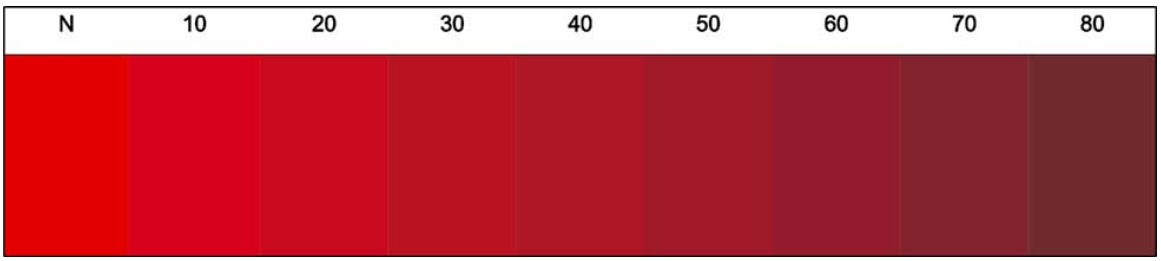
DOI: 10.4103/0019-5154.147895

- Oxidant stress converts hemoglobin iron from Fe^{2+} to Fe^{3+}
  - Still binds oxygen, but doesn't release it (shifts binding curve left)
- NADH (glycolosis) pathway detoxifies most methemoglobin (Met-Hgb) during normal situations
- NADPH is upregulated when needed, such as toxin-induced methemoglobinemia

2.1.1 Causes

- Conditions
  - Cytochrome b_5 reductase deficiency
  - Hemoglobin M
- Drugs
  - **Dapsone**
  - **Benzocaine** (and other local anesthetics)
  - Nitrite-containing compounds (NTG, nitroprusside, amyl nitrite)
  - Sulfonamides (sulfa antibiotics)
  - Analine dyes
  - Primaquine / chloroquine
  - Many others

Figure 2.2: **Methemoglobin %**



Shihana et al.

Place a drop of blood on white paper, allow it to dry, and compare with chart above. Chart Met-Hgb should be within ± 15% of lab value

2.2 Diagnosis

- **Be suspicious for methemoglobinemia in cyanotic patients with an SpO2 in the mid-80%'s which is unresponsive to supplemental oxygen, and in patients with chocolate-colored blood**
- Hypoxic cyanosis usually doesn't occur until SpO2 is ≈50%, this is a rare case of cyanosis with "high" SpO2
- **SaO2 - SpO2 >5%** is an indication that something is messing with pulse-ox reading, usually a deviant Hgb like Met-Hgb
  - High Met-Hgb will make SpO2 trend toward ≈ 85%
  - Supplemental O2 will drive up PaO2, and SaO2 on iStat ABGs will increase because it is calculated from PaO2
- Order methemoglobin from lab for confirmation, if symptomatic with high suspicion for methemoglobinemia, can treat empirically

Table 2.1: Met-Hgb Symptoms

Met-Hgb %	Symptoms
1-3%	Normal
10-20%	Cyanosis
20-30%	Anxiety Headache Dizziness Fatigue
30-50%	Tachypnea Confusion Syncope
50-70%	Szs Coma Metabolic Acidosis
>70%	Death

2.3 Treatment

- **Treat symptomatic patients or any patient with Met-Hgb >30%**
- Call Toxicology
- Methylene Blue 1-2 mg/kg IV over 5 min
  - Can repeat in 30-60min if needed
  - SpO2 may decrease significantly during infusion, caused by interference with pulse-ox, not hypoxia

  - Will discolor body fluids
  - Side effects
    * MAO inhibition $\Longrightarrow$ serotonin syndrome
    * Methemoglobinemia (doses $>$7 mg/kg/day)
  - May not be as effective for analine dye overdoses, analine metabolite inhibits entry of methylene blue into RBCs
- Methylene Blue continuous infusion
  - Limited evidence for dosing
    * One case series reported 2 mg/kg over 6hr (0.33 mg/kg/hr, daily dose 8 mg/kg)
    * Some self-reporting from toxicologist starting at 0.1 mg/kg/hr
    * Rates of 0.5-1 mg/kg/hr when used for vasoplegia, so higher doses *may* be safe
    * **Bottom line: Call tox if you have to start continuous methylene blue**
  - Usually not needed, consider if Met-Hgb induced by long-acting agent like dapsone, or if $>$2 bolus doses needed
- Cimetidine for Dapsone induced Met-Hgb
  - Inhibits CYP450 metabolism of dapsone $\rightarrow$ hydroylamine dapsone, which produces more Met-Hgb than dapsone
- Other Therapies
  - High-Dose Vitamin C (takes a long time to work)
  - Riboflavin (takes a long time to work)
  - Hyperbaric oxygen
  - Red-cell exchange

References

1. Goldfrank LR and Hoffman RS, eds. Goldfrank's Manual of Toxicologic Emergencies. New York: McGraw-Hill Medical, 2007.
2. Ludlow JT, Wilkerson RG, and Nappe TM. Methemoglobinemia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, 2019. pmid: 30726002. URL: http://www.ncbi.nlm.nih.gov/books/NBK537317/ (visited on 11/09/2019).
3. Prasad R, Singh R, Mishra OP, and Pandey M. Dapsone Induced Methemoglobinemia: Intermittent vs Continuous Intravenous Methylene Blue Therapy. Indian J Pediatr 2008;75:245–7.
4. Shihana F, Dissanayake DM, Buckley NA, and Dawson AH. A Simple Quantitative Bedside Test to Determine Methemoglobin. Annals of Emergency Medicine 2010;55:184–9.
5. Skold A, Cosco DL, and Klein R. Methemoglobinemia: Pathogenesis, Diagnosis, and Management. Southern Medical Journal 2011;104:757–61.

Part III

Miscellaneous

CHAPTER 3

Pharmacokinetics

3.1 Equations

CL = Clearance
k = Rate Constant
$t_{1/2}$ = Half-life

C = Concentration
V_d = Volume of Distribution
D = Dose

F = Bioavailability
τ = Dosing Interval
t_{inf} = Infusion Time

$$\text{CL} = k \times V_d \tag{3.1}$$

$$C(t_2) = C(t_1)\mathrm{e}^{t_2 - t_1} \tag{3.2}$$

$$C_{max} = \frac{D\left(1 - \mathrm{e}^{-k\ t_{\text{inf}}}\right)}{V_d\ k\ t_{\text{inf}}\left(1 - \mathrm{e}^{-k\ \tau}\right)} \tag{3.3}$$

Complete equations, add description of PK, maybe some graphs, and PK/PD targets / parameters for specific drugs