# Medical Reference

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# 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 I will do my best to utilize appropriate clinical literature, but ultimately, these summaries are not peer-reviewed and medical decisions should not be made based upon this book.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

# Infectious Disease

# CHAPTER 1

# HIV

## 1.1 DIAGNOSIS

### 1.1.1 Initial Testing

- HIV Ig Testing
- CD4 Count
- Viral Load (Circulating HIV RNA)
- Hepatitis Testing
- Genotypic resitance testing
- Basic Labs

#### Drug Resistance Testing

- Therapy Naive Patients
- Entry to care
- Geontypic preferred to phenotypic
- Typically RT and PR genes, not INSTI genes unless concern for INSTI resistance
- Therapy Experienced Patients
- Virologic failure and RNA ¿ 1000 copies/mL
- RNA (500,1000), testing may be unsuccessfuly but should be considered
- Pts with suboptimal viral load reduction
- Failure of INSTI regimen
- Geontypic preferred to phenotypic
- Phenotypic can be added if complex resistance patterns expected

Consider adding Table 3: Timepoint or Frequency of Testing

### 1.1.2 Follow-Up Testing

- Viral load in 2-4 wks (no later than 8 wks) post intervention to determine viral response
- Viral load 4-8 wks after regimen changes
- Viral load Q3-4mo on stable regimens
- CD4 Q3-6mo

| Generic | Brand | Abbreviation |
|---|---|---|
| NRTI | | |

## 1.2 Drug Classes

## 1.3 Drug Therapy

### 1.3.1 Goals of Therapy

- Prevent OIs
- Maintain virologic suppression ($<$200 copies/mL $\implies$ not transmissible)

### 1.3.2 When to delay therapy

- Concern for IRIS (immune reconstitution inflammatory syndrome) in pts with cryptococcal or TB meningitis

### 1.3.3 Testing Prior to Drug Therapy

- Pregnancy test for all female pts of childbearing age
- HLA B*5701 if considering ABC-containing regimens

### 1.3.4 Guideline-Recommended Initial Therapies

- Bictegravir / TAF / Emtracitabine
- Dolutegravir / abacavir / lamivudine
- HLA-B*5701 (-) and no HBV
- Dolutegravir + (Emtricitabine or Lamivudine) + (TAF or TDF)
- Dolutegravir/Lamivudine
- CI w/ HBV, RNA ¿ 500k copies/mL, initiation before results of RT resistance testing are available
- Raltegravir + (Emtracitabine or Lamivudine) + (TAF or TDF)
- RAL containing regimens have lower barrier to resistance than others

### 1.3.5 Other Treatment Considerations

- INSTI regimens are the best tolerated
- PI regimens should have resistance testing conducted if possible, and DRV has the lowest rates of resistance
- NNRTIs have low barrier to resistance

## References

1. Centers for Disease Control and Prevention. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. 2019.
2. Centers for Disease Control and Prevention. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2019.

# Part II

# Critical Care

# CHAPTER 2

# Vasopressors

**Key Points**

**Abbreviations**

- NE: Norepinephrine
- EPI: Epinephrine
- DA: Dopamine
- PE: Phenylephrine
- DOB: Dobutamine
- AngII: Angiotensin II
- VP: Vasopressin
- MIL: Milrinone

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**Major Points**

- NE is almost always a good 1st choice vasopressor
- Make sure pt is not volume-down before initiating vasopressors

## 2.1 Receptor Pharmacology

- $\alpha_1$: Peripheral Vasoconstriction
- $\beta_1$: Chronotropy / Inotropy
- $\beta_2$: Bronchodilation, Vasodilation
- $V_1$: Vasoconstriction
- $V_2$: Renal fluid retention
- Ang-II: Vasoconstriction, activation of aldosterone
- PDE-3: Inotropy, vasodilation

Add pictures/graphs from favorite vasopressor article

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

## 2.2 Vasopressors

### 2.2.1 Vasoconstricters

- Phenylephrine

Table 2.1: Physiologic Effects of Various Vasopressors [1]

| Drug | HR | Contractility | Vasoconstriction | Vasodilation | Dopaminergic |
|---|---|---|---|---|---|
| NE | 1+ | 2+ | 4+ | 0 | 0 |
| EPI | 4+ | 4+ | 4+ | 3+ | 0 |
| LD DA | 1+ | 1+ | 0 | 1+ | 4+ |
| HD DA | 2+ | 2 – 3+ | 2 – 3+ | 0 | 2+ |
| PE | 0 | 0 | 3+ | 0 | 0 |
| VP | 0 | 0 | 4+ | 0 | 0 |
| DOB | 2+ | 3 – 4+ | 0 | 2+ | 0 |
| MIL | 1+ | 3+ | 0 | 2+ | 0 |

*LD: Low-Dose (<4 mcg/kg/min), HD: High-Dose*

Table 2.2: Adrenergic Receptor Specificity [2]

| Drug | $\alpha_1$ | $\beta_1$ | $\beta_2$ |
|---|---|---|---|
| PE | 4+ | 0 | 0 |
| NE | 4+ | 2+ | 1+ |
| EPI | 2+ – 4+ | 1+ | 1+ – 3+ |
| DA | 0 – 3+ | 0 – 3+ | 0 – 2+ |
| DOB | 1+ | 4+ | 2+ |

*Note: Scale from 0 - 4+*

- Norepinephrine
- Vasopressin
- Angiotensin II

### 2.2.2 Inopressors

- Epinephrine
- Dopamine

Sepsis trial comparing DA to EPI

### 2.2.3 Inodilators

- Dobutamine
- Milrinone

Finish table from lexi or AHA guidelines

## 2.3 Push-Dose Pressors [5]

### 2.3.1 Phenylephrine

- Final Concentration: 100 mcg/mL
- Dose: 0.5 – 2 mL (50 – 200 mcg) Q1-5min

Table 2.3: Milrinone Dosing [3]

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

Table 2.4: Vasopressor Dosing [2, 4]

| **Drug** | **Units** | **Initial** | **≈ Max** | **Titration** |
|---|---|---|---|---|
| **Vasopressors** | | | | |
| NE | mcg/min | 5 | 50 | 5 Q5min |
| PE | mcg/min | 20 | 200 | 20 Q10min |
| VP | Units/min | 0.03 | 0.03 | Fixed |
| Ang-II | ng/kg/min | 10 | 80 (<3hr); 40 (>3hr) | 5 Q5min |
| **Inopressors** | | | | |
| EPI | mcg/min | 5 | 30 | 5 Q5min |
| DA | mcg/kg/min | 5 | 50 | 2 Q5min |
| *Inodilators* | | | | |
| DOB | mcg/kg/min | 2.5 – 5 | 40 | 2.5 – 5 Q5min |
| MIL | mcg/kg/min | | See Table 2.3 | |

- Preparation
  - Add 10mg Phenylephrine (10 mg / 1 mL) to 100 mL NS
  - Final Concentration is 100 mcg/mL (10 mg / 100 mL)

### 2.3.2 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. Hollenberg SM. Vasoactive Drugs in Circulatory Shock. Am J Respir Crit Care Med 2011;183:847–55.
2. 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.
3. 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).
4. Overgaard CB and Džavík V. Inotropes and Vasopressors: Review of Physiology and Clinical Use in Cardiovascular Disease. Circulation 2008;118:1047–56.

5. Weingart S. Push-Dose Pressors for Immediate Blood Pressure Control. Clin Exp Emerg Med 2015;2:131–2.

# Part III

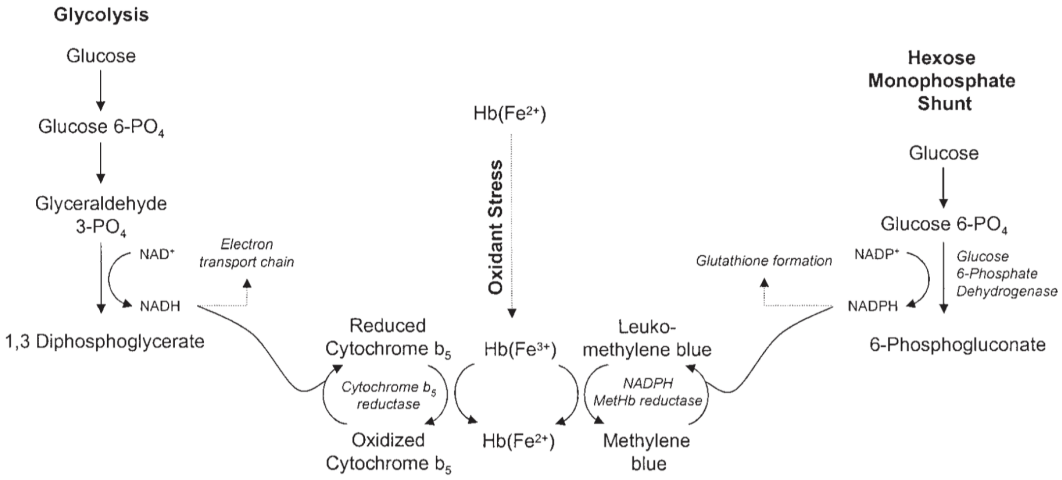
# Toxicology

# CHAPTER 3

# Methemoglobinemia

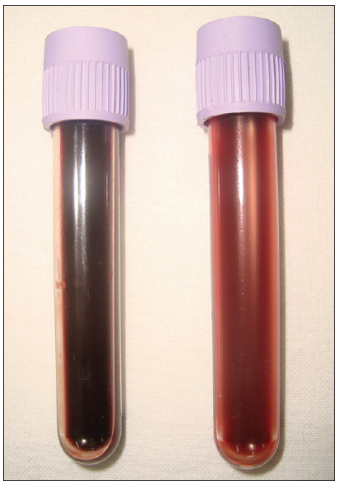
## 3.1 Pathophysiology

(a) Metabolism of Methemoglobin




*From Goldfrank's Toxicology (2007)*

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



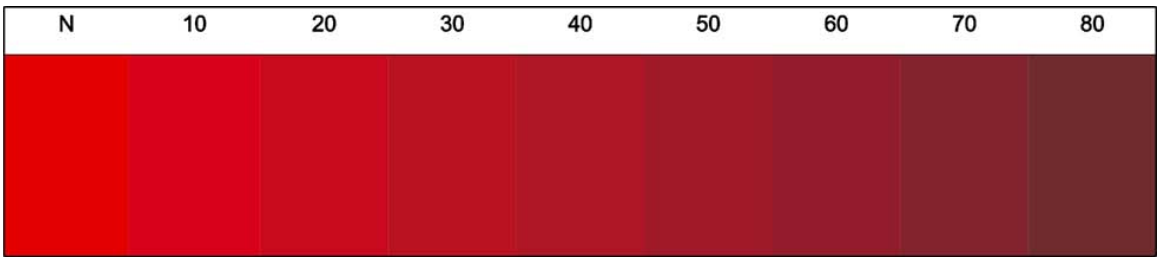
DOI: 10.4103/0019-5154.147895

- 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

### 3.1.1 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 3.2: **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*

## 3.2 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 3.1: Met-Hgb Symptoms

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

## 3.3 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 IV

# Miscellaneous

# CHAPTER 4

# Pharmacokinetics

## 4.1 Equations

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

$C =$ Concentration
$V_d =$ Volume of Distribution
$D =$ Dose
$F =$ Bioavailability

$\tau =$ Dosing Interval
$t_{\text{inf}} =$ Infusion Time
$\text{AUC}_{0-24} =$ Area Under Curve

$$CL = k \times V_d \tag{4.1}$$

$$C(t_2) = C(t_1)\mathrm{e}^{t_2 - t_1} \tag{4.2}$$

$$C_{max} = \frac{D\left(1 - \mathrm{e}^{-k\ t_{\text{inf}}}\right)}{V_d\ k\ t_{\text{inf}}\left(1 - \mathrm{e}^{-k\ \tau}\right)} \tag{4.3}$$

$$C_{min} = C_{max}\ \mathrm{e}^{-k\ (\tau - t_{\text{inf}})} \tag{4.4}$$

$$\text{AUC}_{0-24} = \frac{24}{\tau}\left(\frac{C_{max} + C_{min}}{2} t_{\text{inf}} + \frac{C_{max} - C_{min}}{k}\right) \tag{4.5}$$

## 4.2 Drug-Specific PK

### 4.2.1 Vancomycin

### 4.2.2 Aminoglycosides

### 4.2.3 Digoxin

### 4.2.4 Immunousppressants

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