

MEDICAL REFERENCE

Corbin Cox

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Contents

I Pulmonology	2
1 COPD	3
II Critical Care	6
2 Vasopressors	7
III Toxicology	11
3 Methemoglobinemia	12
IV Miscellaneous	15
4 Pharmacokinetics	16

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 I will do my best to utilize appropriate clinical literature, but ultimately, these summaries are not peer-reviewed and medical decisions should not be made based upon this book.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

Pulmonology

CHAPTER 1

COPD

1.1 DIAGNOSIS AND STAGING

- Dx Criteria: FEV1/FVC <70%

Table 1.1: GOLD Staging

GOLD Grade	Criteria
Grade 1	FEV1 \geq 80%
Grade 2	80% > FEV1 \geq 50%
Grade 3	50% > FEV1 \geq 30%
Grade 4	80% > FEV1 < 30%

Table 1.2: GOLD Classification

≥ 2 or 1 hospitalization	C	D
0-1 (no hospitalization)	A	B
	mMRC 0-1 CAT <10	mMRC ≥ 2 CAT ≥ 10

1.2 TREATMENT

1.2.1 Principles of Treatment

- ICS are relatively ineffective alone
 - More benefit is seen when used in combination
 - More benefit is seen with higher blood eosinophil counts

Table 1.3: mMRC Functional Scale

mMRC Grade	Description
Grade 0	Breathless with strenuous exercise
Grade 1	SOB when hurrying or walking uphill
Grade 2	Walk slower than others or have to stop for breath when walking
Grade 3	Stop for breath after 100m on level ground
Grade 4	Cannot leave house, breathless when dressing / undressing

- * <100 are unlikely to benefit
- * 100-300 is unclear
- * >300 are likely to benefit

– Consider use with high BEC, Hx of asthma, or exacerbations

- Methylxanthines have debatable efficacy and serious side effects, avoid if possible

1.2.2 Primary Therapies

Group A

1. SABA or SAMA or LABA or LAMA

Group B

1. LABA or LAMA
2. LABA + LAMA

Group C

1. LAMA
2. LABA + LAMA

Group D

1. LAMA or LAMA + LABA if severe symptoms
2. LABA + ICS or LABA + LAMA + ICS

Treatment Escalation

- Add additional class of inhaler for uncontrolled dyspnea, remove if not effective
- Consider adding roflumilast or azithromycin if eosinophil count <100
 - Azithromycin unlikely to be effective in **current** smokers
- Consider roflumilast if on triple therapy and FEV1 <50%

1.2.3 Supplemental Therapies

- Smoking cessation
- Decrease exposure to pollutants / toxins

- Supplemental O₂
 - PaO₂ <55 or SaO₂ <88%
 - Titrate to SaO₂ ≥ 90%
- Influenza vaccination
- Pneumococcal vaccination
 - Normal indication after 65, but also PPSV23 x1 if under 65
- Pulmonary rehab
- Non-invasive ventilation

1.3 EXACERBATIONS

1.3.1 Staging

- No respiratory failure
 - RR 20-30
 - No accessory muscle use
 - Hypoxemia improved with suppO₂
 - No increased PaCO₂
- ARF - Non-life-threatening
 - RR >30
 - Improved hypoxemia w/ suppO₂
 - Increased PaO₂
- ARF - Life-threatening
 - Above + ...
 - Persistent hypoxemia
 - AMS
 - Acidosis

1.3.2 Treatment

- Bronchodilators
- PO/IV GCs (5-7d)
 - Pred 40mg PO x5d
- Abx (5-7d)
 - Must have 2/3: increased sputum volume, increased sputum purulence, increased dyspnea
 - Pt's requiring NIPPV or intubation
- NIPPV

References

1. GOLD Science Committee. Global Initiative for Chronic Obstructive Lung Disease 2020. 2019. URL: www.goldcopd.org.

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

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

- 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 pictures/graphs from favorite vasopressor article

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

2.2 Vasopressors

2.2.1 Vasoconstrictors

- 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	α_1	β_1	β_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=%2F1co%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.

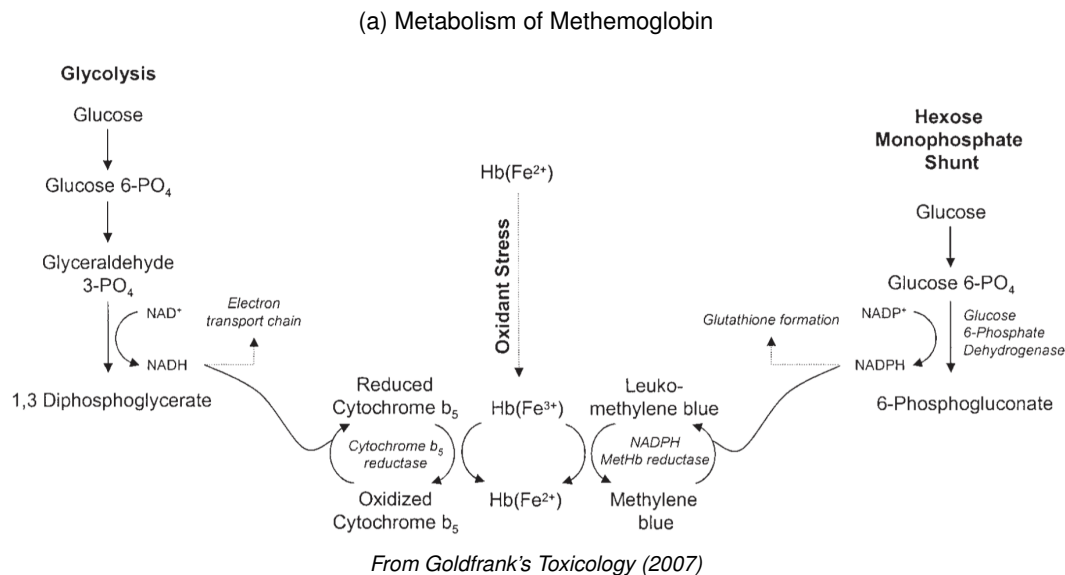
Part III

Toxicology

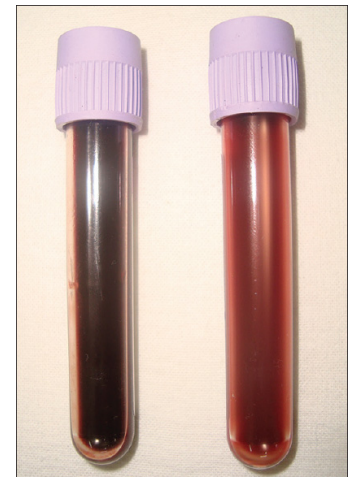
CHAPTER 3

Methemoglobinemia

3.1 Pathophysiology



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



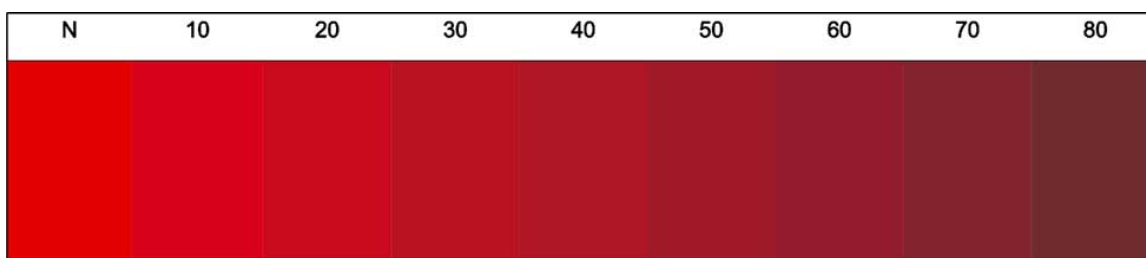
DOI: 10.4103/0019-5154.147895

- 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)
 - Aniline 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 $\pm 15\%$ 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 $\approx 50\%$, 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 $\approx 85\%$
 - 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 Headache Dizziness Fatigue
	Tachypnea
30-50%	Confusion Syncope
50-70%	Szs Coma 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 \Rightarrow serotonin syndrome
 - * Methemoglobinemia (doses >7 mg/kg/day)
- May not be as effective for aniline dye overdoses, aniline 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 hydroxylamine 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

τ = Dosing Interval

t_{inf} = Infusion Time

AUC_{0-24} = Area Under Curve

$$CL = k \times V_d \quad (4.1)$$

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

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

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

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

4.2 Drug-Specific PK

4.2.1 Vancomycin

4.2.2 Aminoglycosides

4.2.3 Digoxin

4.2.4 Immunosuppressants

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