O_2 & CO_2 transport in the blood

vaclav.hampl@lf2.cuni.cz

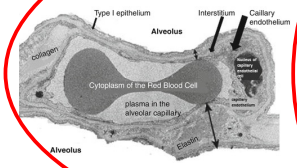
http://fyziologie.lf2.cuni.cz/en
http://vh.cuni.cz

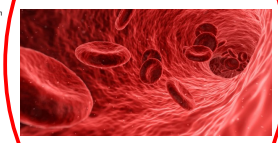
CHARLES UNIVERSITY
Second Faculty of Medicine

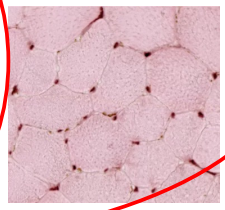
1

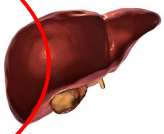
Transport of O_2 & CO_2 („blood gases“) in the body

convection ⇄ diffusion ⇄ convection ⇄ diffusion







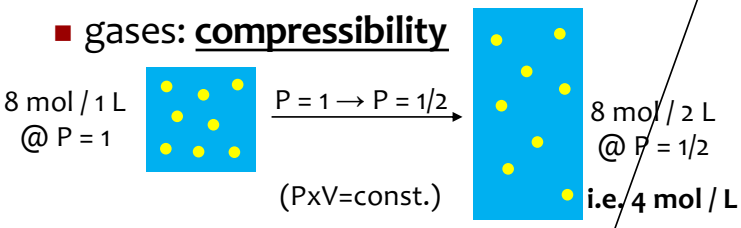


2

Diffusion in gases

Fick's first law (1855): $J = - \mathbf{D} / RT \times \mathbf{\Delta P} / \mathbf{\Delta x}$

- liquids: Δ concentration ($C_2 - C_1$)
- gases: **compressibility**



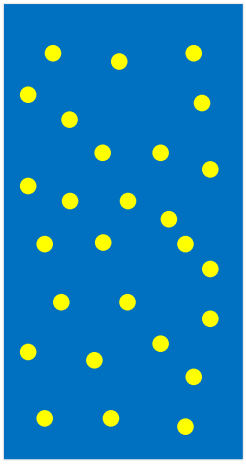
Adolf Eugen Fick
1829-1901

i.e. for gases, concentration without pressure info not very useful
→ hence partial pressure (C x P)

3

Concentration & partial pressure

O_2 molecules in air



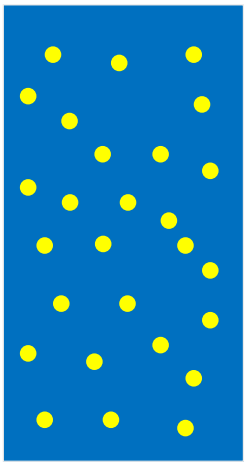
Dry air: 21% is O_2
F_{O2} = 0.21
$[O_2]$ = 210 ml/l

As P_B ~ 760 mmHg
P_{O2} = 0.21 x 760 mmHg
= 160 mmHg

4

Effect of water vapor

37°C

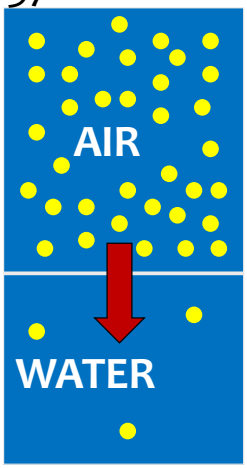


P_B ~ 760 mmHg
P_{H_2O} = 47 mmHg (at 37°C)
P_{DRY} = 713 mmHg
P_{O_2} = 0.21 x 713 mmHg
= 150 mmHg

5

O_2 in solution

37°C



37°C

After equilibration:
AIR: P_{O_2} = 150 mmHg
WATER: P_{O_2} = 150 mmHg

AIR: $[O_2]$ = 210 ml/l
WATER: $[O_2]$ = 4.5 ml/l

O_2 solubility
= 4.5 / 150 = 0.003 ml/(dl.mmHg)

6

O_2 transport in solution during exercise

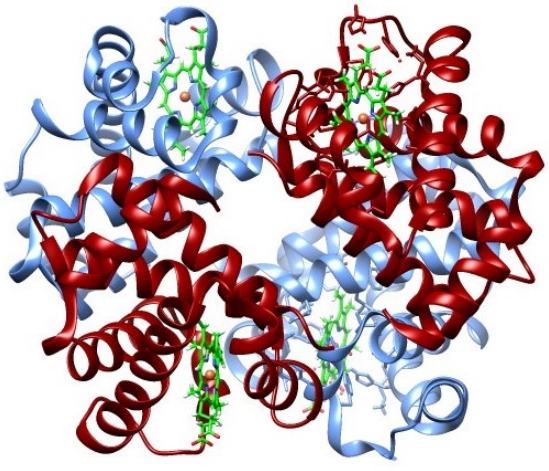
- solubility = 0.003 ml/(dl.mmHg)
- P_{O2} in arterial blood = 100 mmHg
- $[O_2]$ = 3 ml/l
- cardiac output = 30 l/min
- maximum O_2 available = 90 ml/min

But O_2 requirement is 3000 ml/min!

CO_2 similarly (solubility 0.067 ml/(dl.mmHg))

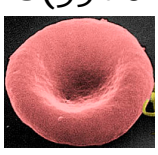
7

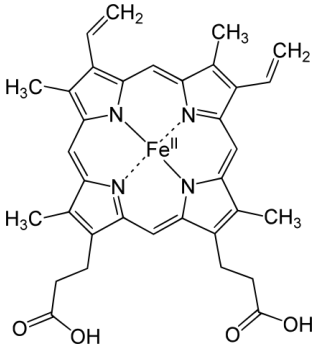
Hemoglobin (Hb)



oxyHb A: $\alpha_2\beta_2$

- both CO_2 & O_2 transport
  - NH_2 groups of N-terminal *val*
  - *heme* Fe^{2+}
- RBC (35% of it)





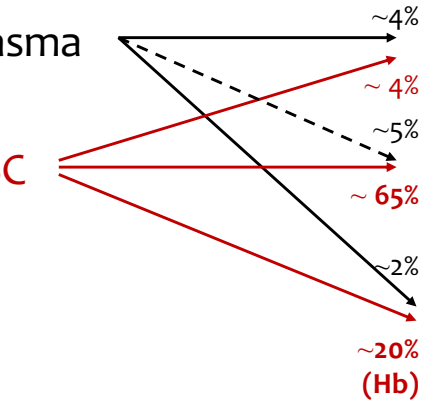
- 4 globins + 4 hemes (Fe^{2+} in porphyrine ring)

8

CO_2 transport in the blood

2 compartments:

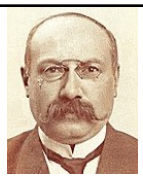
- plasma
- RBC



3 mechanisms:

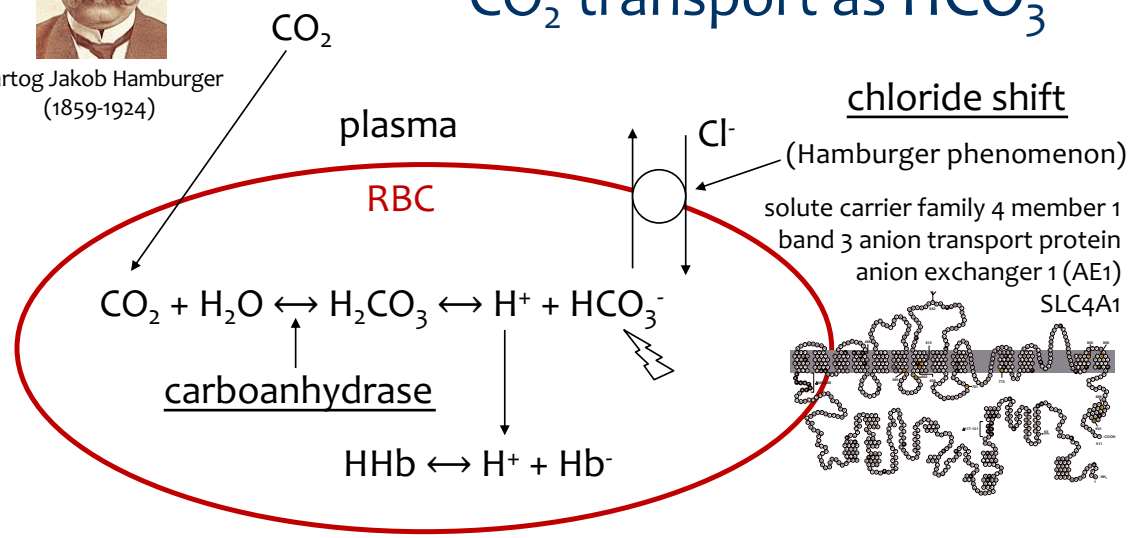
- dissolved (~8%)
  solubility > O_2 (22x)
- as HCO_3^- (~70%)
  carboanhydrase
- as carbamino protein complexes ($R\text{-}NH_2+CO_2$)

9



Hartog Jakob Hamburger
(1859-1924)

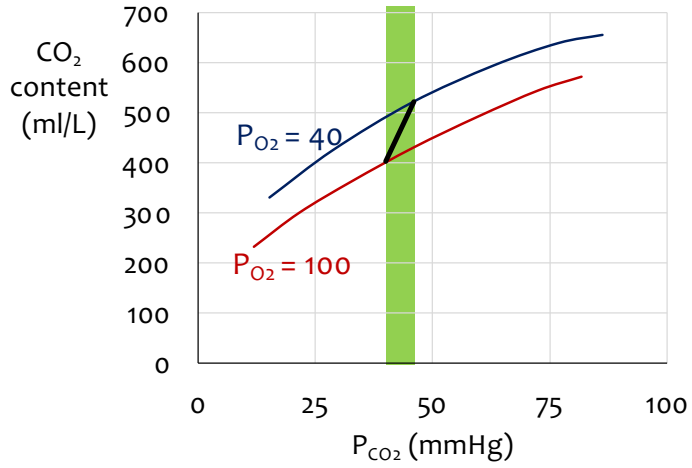
CO_2 transport as HCO_3^-



10

John Scott Haldane
(1860-1936)

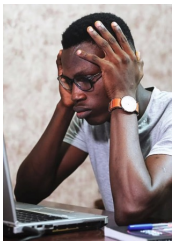
CO_2 transport as carbaminoHb: Haldane effect

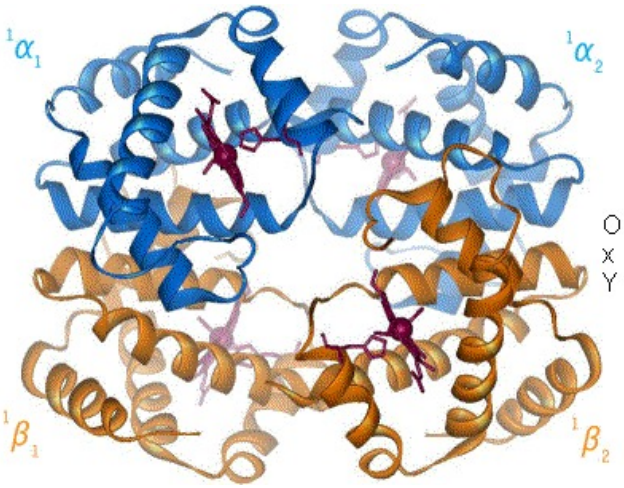


11

O_2 transport: 2 Hb conformation states

- **R** (relaxed):
  - at ↑O_2
  - high O_2 affinity
  - stabilized by ↑pH
- **T** (tense)
  - at ↓O_2
  - low O_2 affinity
  - stabilized by CO_2 & H^+

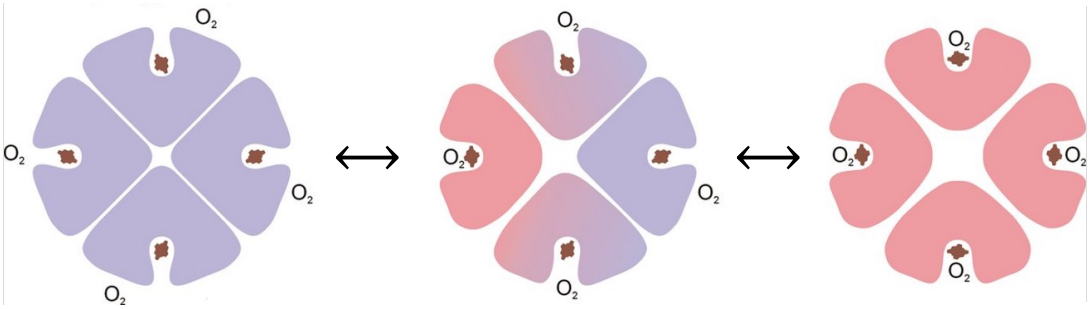




NH_3 groups protonation → + charge → ionic interactions with near COOH groups

12

T → R transition (Hb "breathing motions")

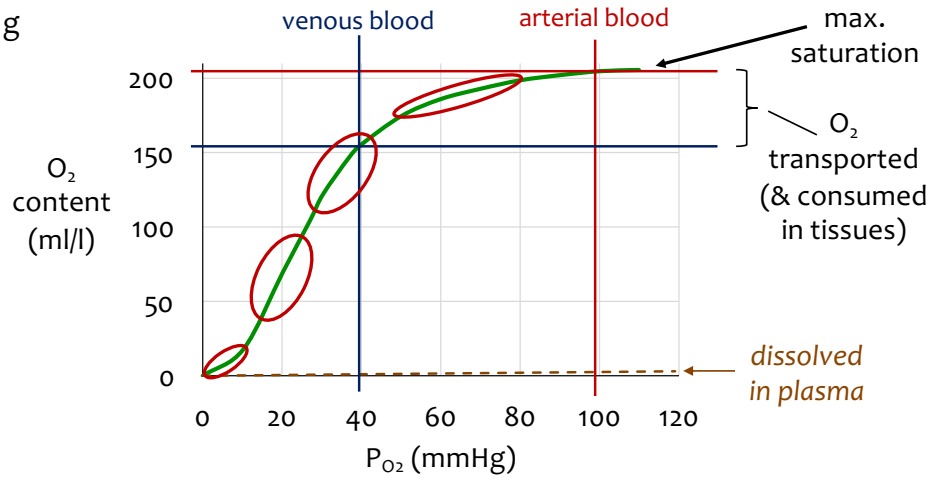


co-operative O_2 binding

13

O_2 transport in the blood: Hb-O_2 binding curve

co-operative O_2 binding



14

Pulse oxymetry

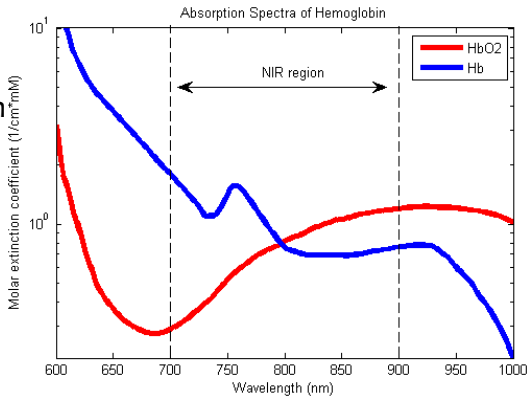
16

Pulse oxymetry (peripheral SO_2)

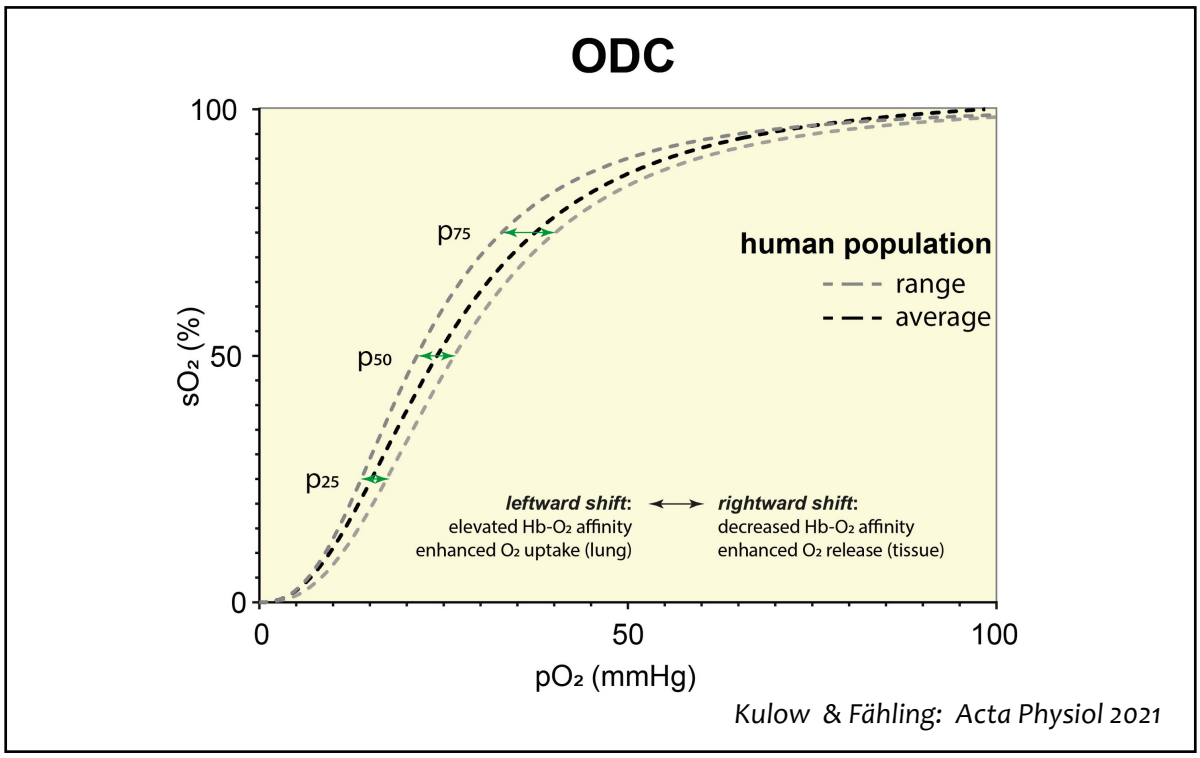
- safe, convenient, noninvasive, inexpensive, useful in ICU
- not always identical to arterial SaO_2
  - correlates pretty well
- 2 wavelengths of light through a thin body part to a photodetector
- measures the absorbance at each of the wavelengths
- pulsatile + non-pulsatile component
- ⇒ measures S_{O2}, not $[O_2]$ nor P_{O2}

  < 93% → !

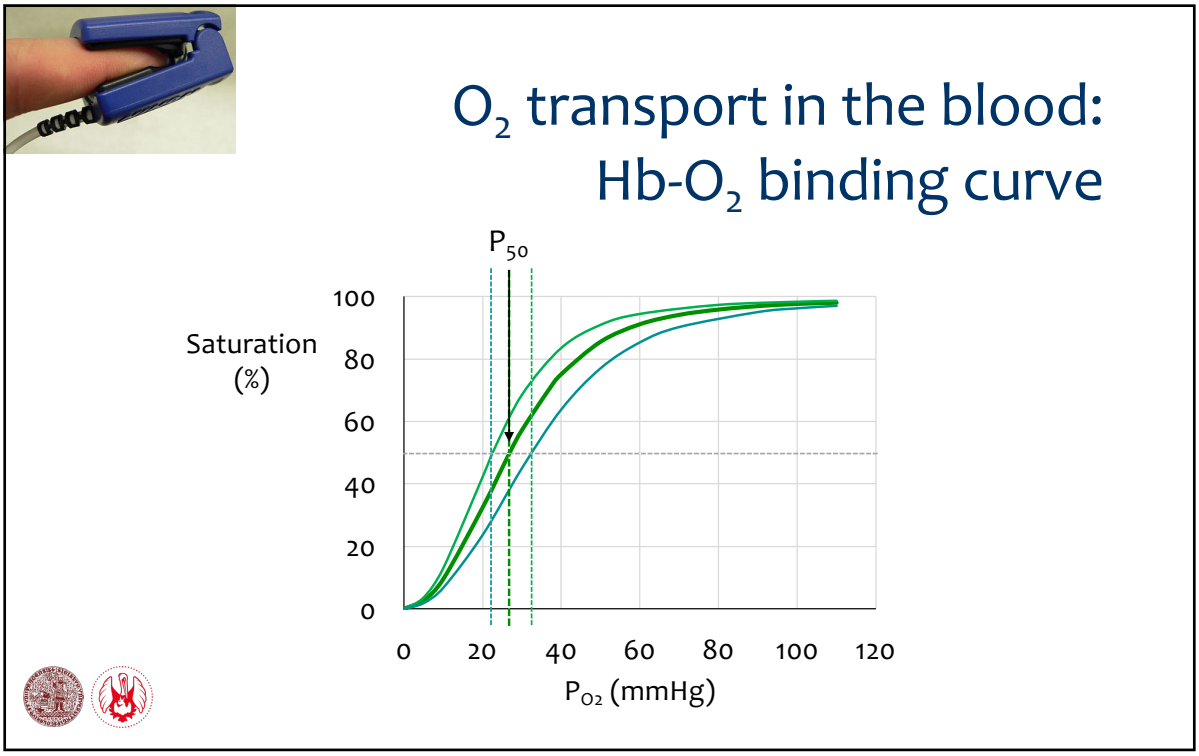
  < 90% → !!!



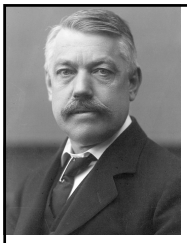
17


ODC
100
50
0
sO2 (%)
p75
p50
p25
human population
range
average
leftward shift:
elevated Hb-O2 affinity
enhanced O2 uptake (lung)
rightward shift:
decreased Hb-O2 affinity
enhanced O2 release (tissue)
0
50
100
pO2 (mmHg)
Kulow & Fähling: Acta Physiol 2021

18

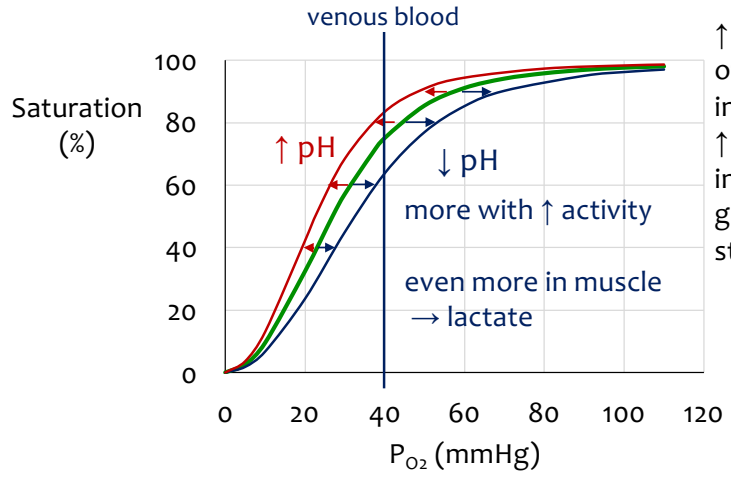

O2 transport in the blood:
Hb-O2 binding curve
P50
Saturation (%)
100
80
60
40
20
0
0
20
40
60
80
100
120
PO2 (mmHg)

19



Christian Bohr
1904

$H^+ \rightarrow \downarrow$ Hb-O_2 affinity: Bohr effect

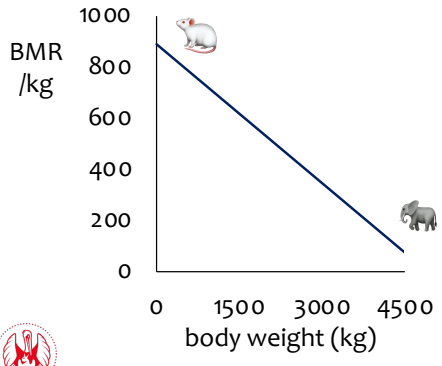


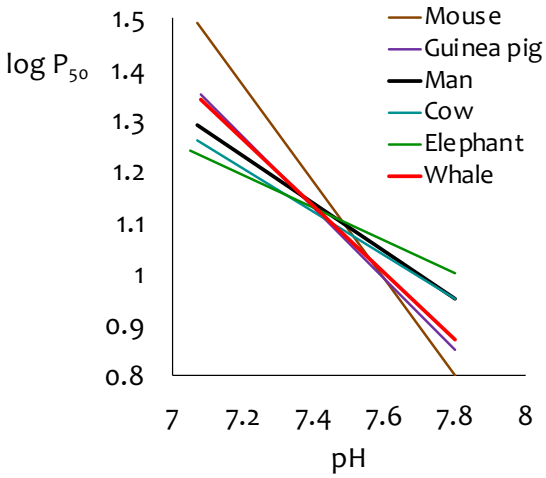
↑ $H^+ \rightarrow$ ↑ protonation of α & β chains in T state→
↑ + charge → ↑ ionic interactions w/ COOH groups nearby → stabilization of T state

CO_2 similar but smaller effect (via R-NH_2+CO_2) (~Haldane effect) + effect on pH

20

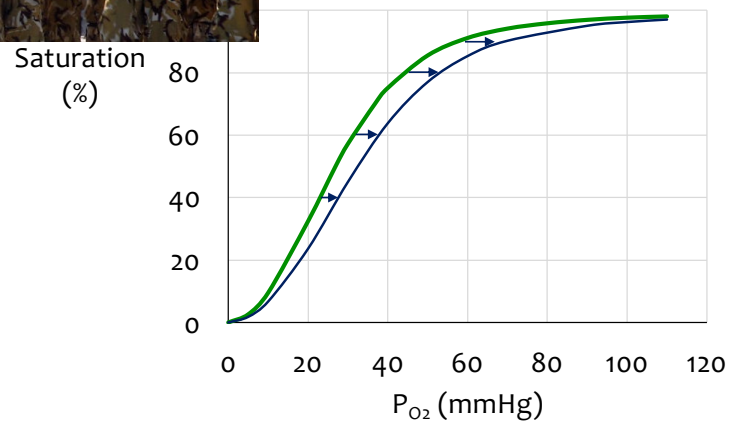
Bohr effect stronger in smaller mammals





21

CADETs – look right!

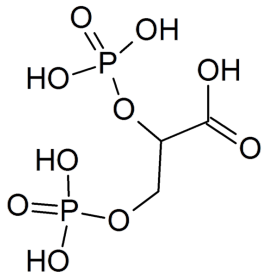


CO_2
Acidity
DPG (2,3-BPG)
Exercise
Temperature

supported by Cl^- shift: ↑[Cl^-] ⟶ ↑P50

22

2,3-bisphosphoglycerate (2,3-BPG) (2,3-diphosphoglycerate, 2,3-DPG)

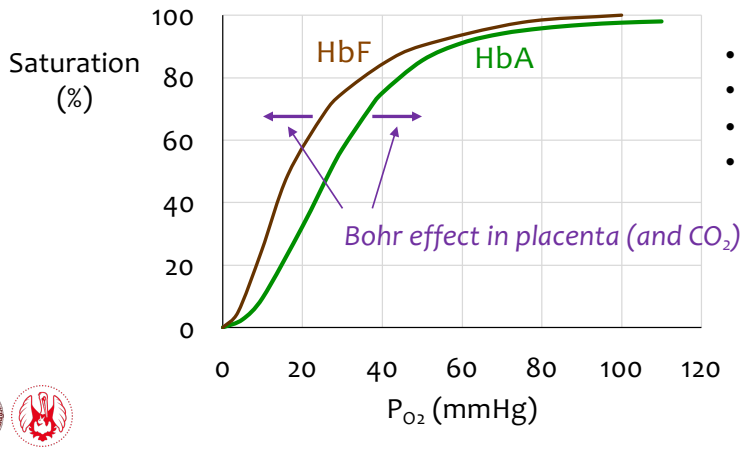


- intermediate of glycolysis in RBC (~ 5 mM)
- rapidly consumed at normal P_{O_2}, accumulates at ↓P_{O_2}
- binds preferentially to β chains
- at ~9 Å, it fits in the deoxyHb form (11 Å pocket), not in the oxyHb form (5 Å)

24

Fetal Hb (Hb F: $\alpha_2\gamma_2$)

- BPG binding: γ<α< β
- γ has less + charges that attract the - charges on BPG
- ↑ BPG formation in placenta

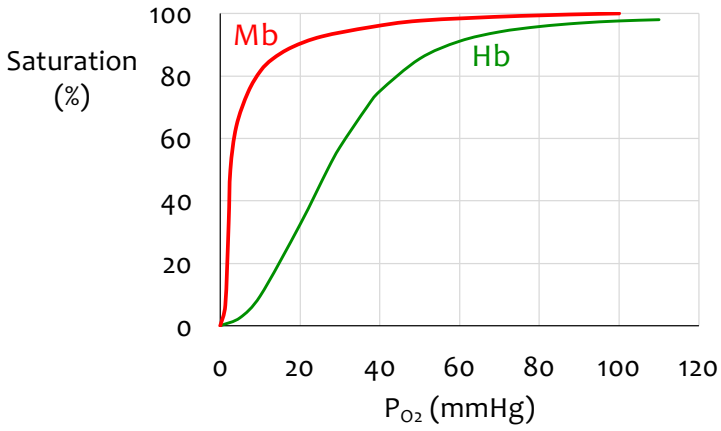


- from wk 6: embryonic Hb (incl. F)
- F dominates from 3rd mo
- A from wk 40
- at * 50-95% F
- A dominates from 6th mo

25

Myoglobin (Mb)

1 chain ⟶ no cooperative O_2 binding ("all or nothing")



26

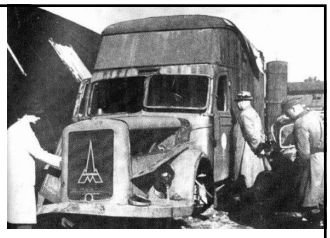
Dyshemoglobinemia

Hb forms that cannot transport O2: O_2:

1) **Competition with O_2 for Fe**: carboxy-Hb (carbonyl-Hb; CO-Hb)
   - Fe affinity for CO ~240x higher than for O_2
2) **Oxidation $Fe^{2+} \rightarrow Fe^{3+}$** : metHb
3) **Non-competitive blockade** of O_2 binding to Fe: sulf-Hb
   (S irreversibly binds the pyrrole nucleus of heme,
   interferes with O_2 binding) - H2S, sulfonamides, sumatriptan,...
4) **Hemoglobinopathies** - globin mutations affect O_2 binding (very rare; they mostly affect RBC viability and properties - thalassemia, sickle cell anemia) - $\uparrow P_{50}$ (Chesapeake) nebo $\downarrow P_{50}$ (Beth Israel)

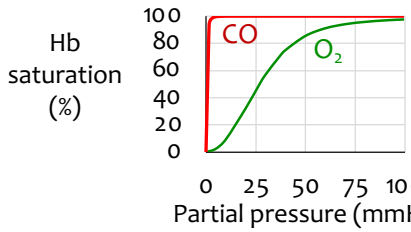
27

CO-Hb (CO poisoning)

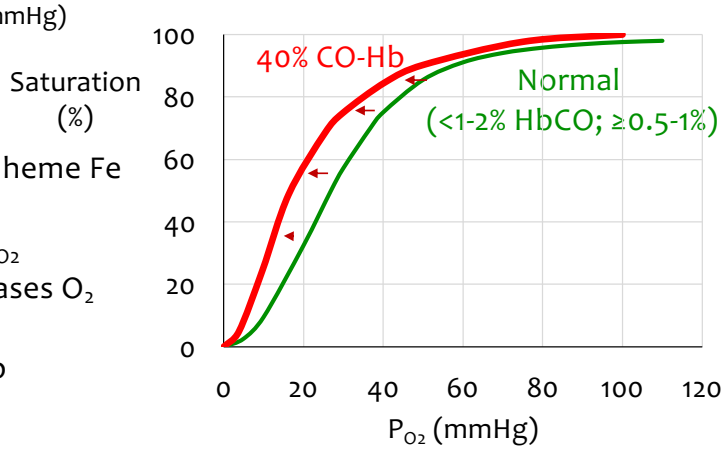


- fires, exhaust fumes, smoking, pollution, heating, volcanoes, ...
- endogenous - heme metabolism (mostly Hb): heme → biliverdin + Fe + CO (heme oxygenase)
- normally 0.5-2% of total Hb is CO-Hb (city ≤5%)
- smoking ≤10– max 15%, newborns ≤12%
- ≤2.5% OK, >15% problem, >30% life threatening
- 85% of CO bound to Hb (most abundant), the rest Mb, CytC oxidase (inhibition), NADPH reductase
- CO-Hb half-life normally ~5 hrs (~80-90 min at 100% O_2)

28



CO-Hb (CO poisoning)

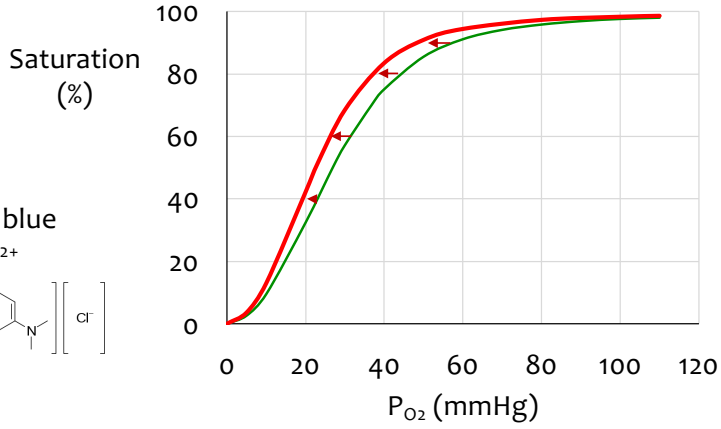


- 240x higher affinity to heme Fe
- + greater effect on cooperativity (when P_{O2} decreases, CO-Hb releases O_2 less readily- shift to L)
- prevents carbaminoHb formation → acidosis

29

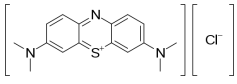
Methemoglobinemia

- Fe^{2+} in heme oxidized to Fe^{3+} (NO & its donors, C≡N)
- Fe^{3+} impairs Hb cooperativity → ↓ O_2 unloading in tissues (~Mb)



- normally 1-2%
- smokers more
- >5-7% hazard

Therapy:
metylene blue
$Fe^{3+} \rightarrow Fe^{2+}$

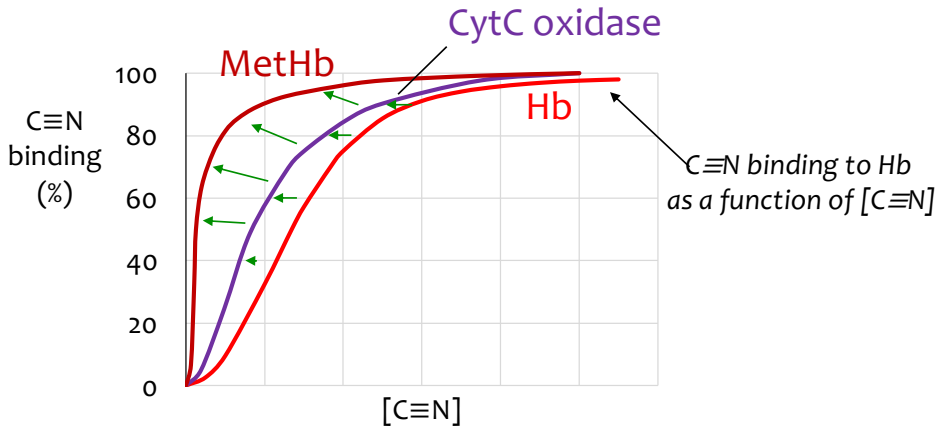


Correction:
NADH **metHb reductase** (cytochrome-b5 reductase)

31

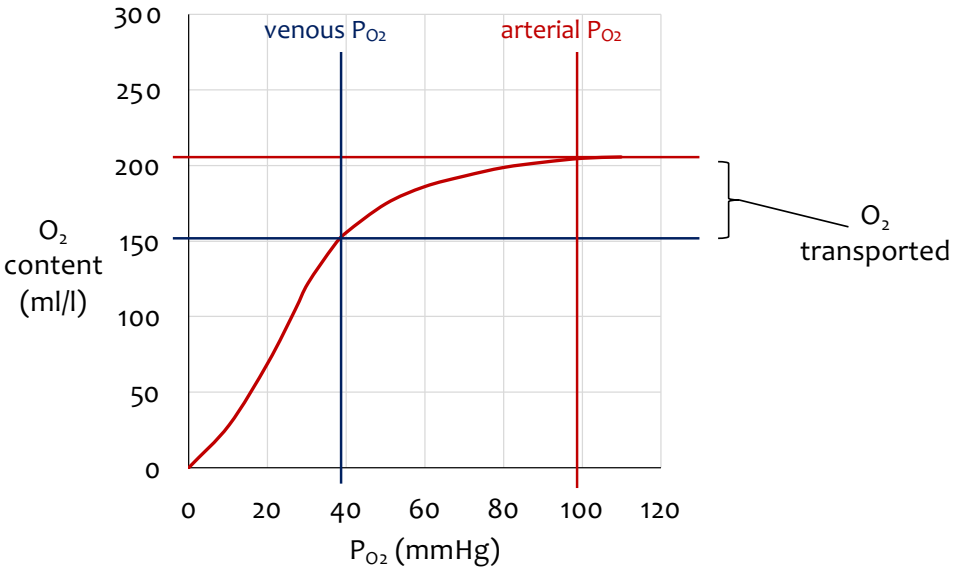
When is methemoglobinemia good?

Cyanide poisoning



32

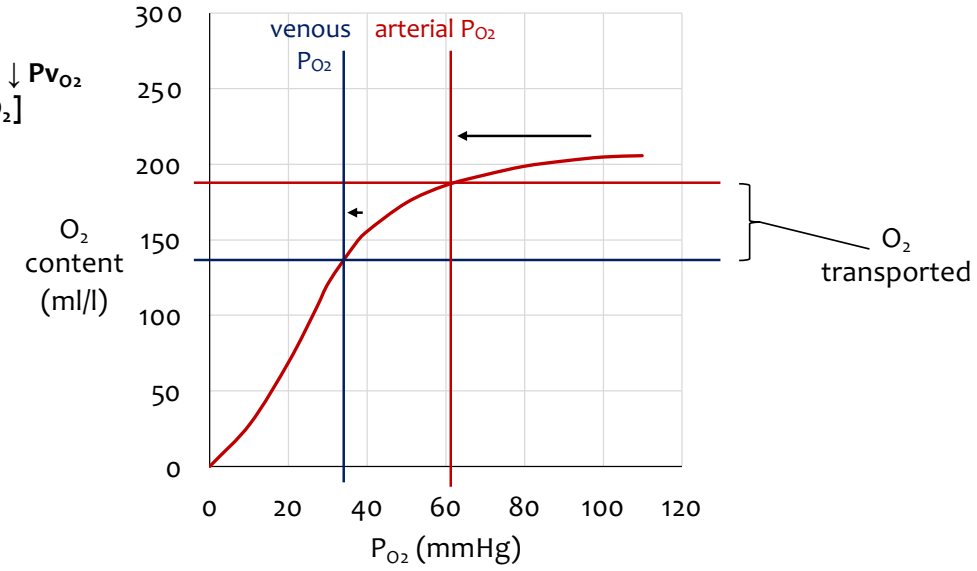
Types of hypoxia



33

Types of hypoxia: hypoxic

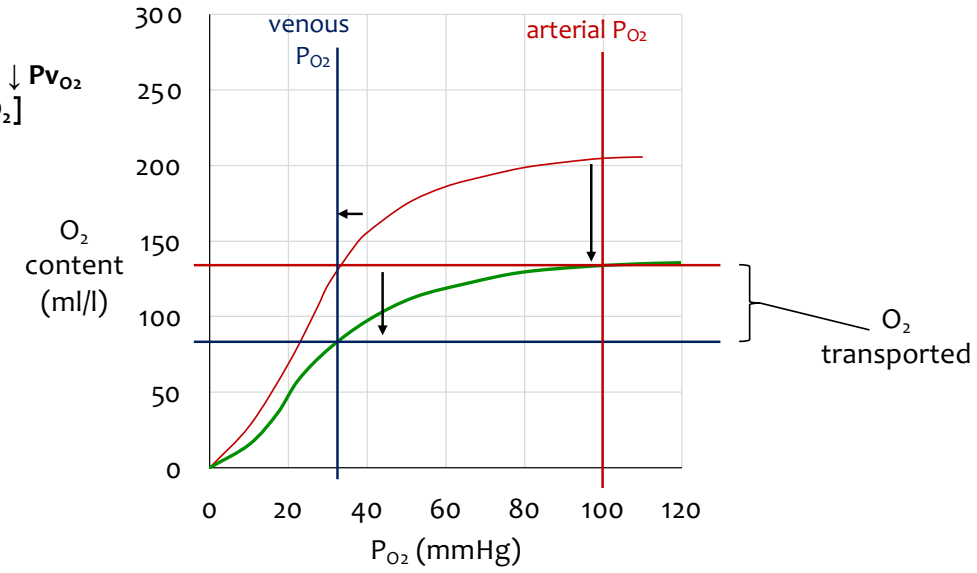
↓↓ Pa_{O_2} + ↓ Pv_{O_2}
= ΔA-V [O_2]



34

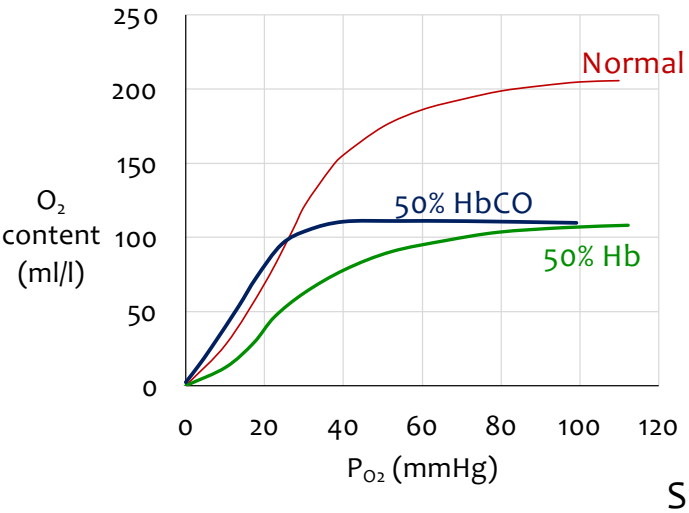
Types of hypoxia: anemic

= Pa_{O_2} + ↓↓ Pv_{O_2}
= ΔA-V [O_2]



35

CO poisoning

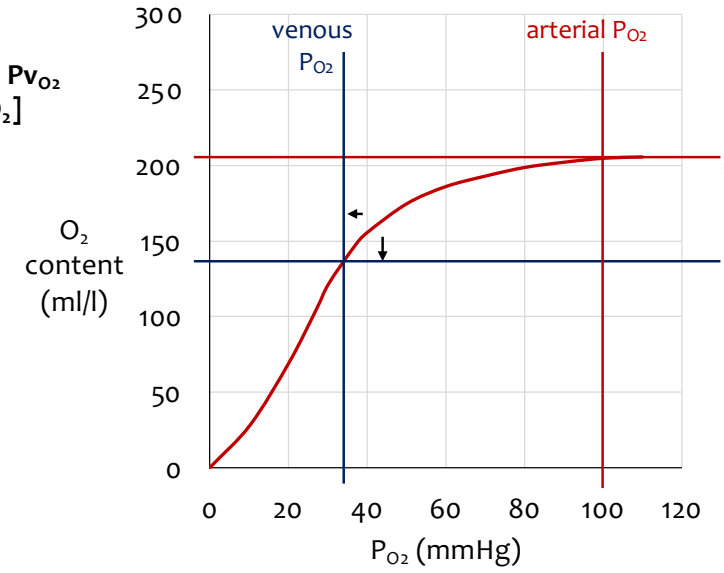


Similarly metHb

36

Types of hypoxia: ischemic (stagnant)

= Pa_{O_2} + ↓ Pv_{O_2}
↑ ΔA-V [O_2]

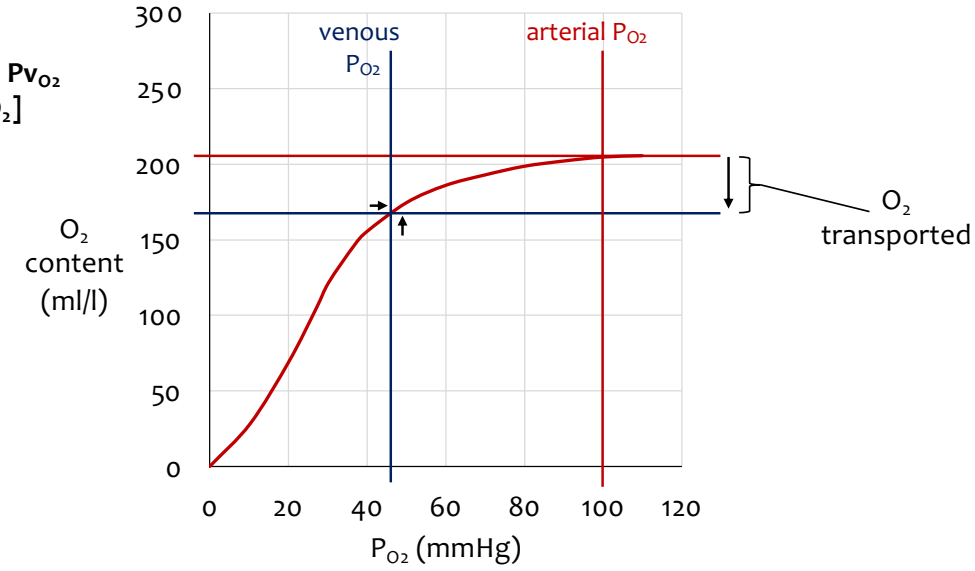


↓ ml/min of blood in tissues → they need to take up ↑ O_2 from each ml

37

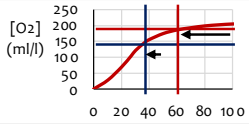
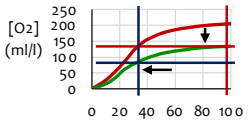
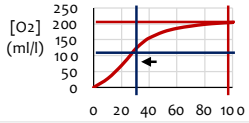
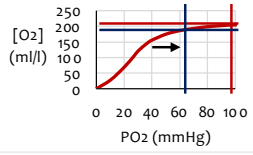
Types of hypoxia: histotoxic

= Pa_{O_2} + ↑ Pv_{O_2}
↓ ΔA-V [O_2]



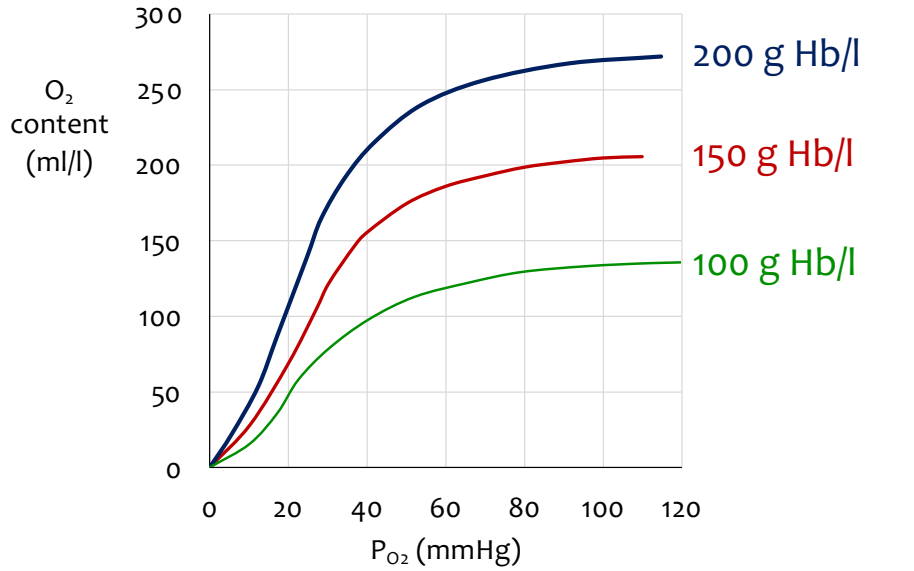
38

4 types of hypoxia

	Pa_{O_2}	ΔA-V [O_2]	Pv_{O_2}	
hypoxic	↓↓	=	↓	
anemic	=	=	↓↓	
ischemic	=	↑	↓	
histotoxic	=	↓	↑	

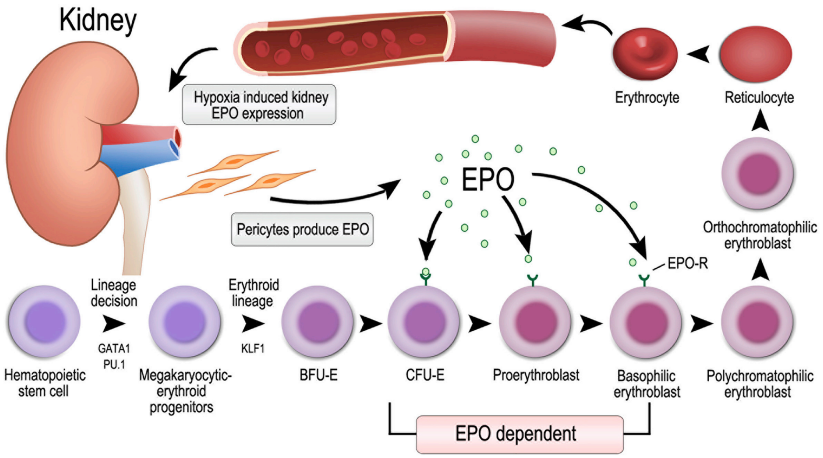
39

Compensation



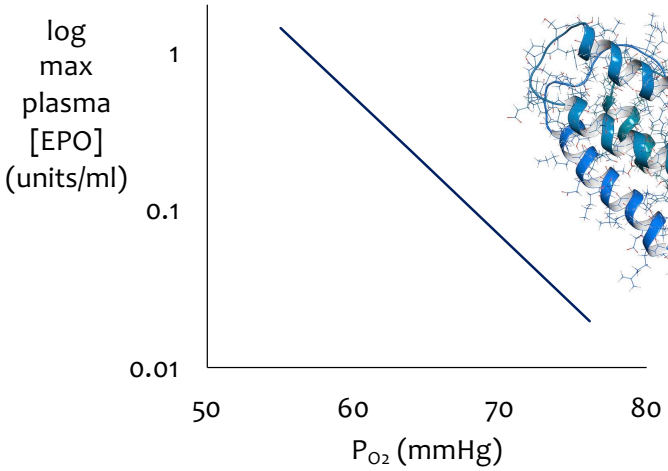
40

Erythropoietin controls RBC development



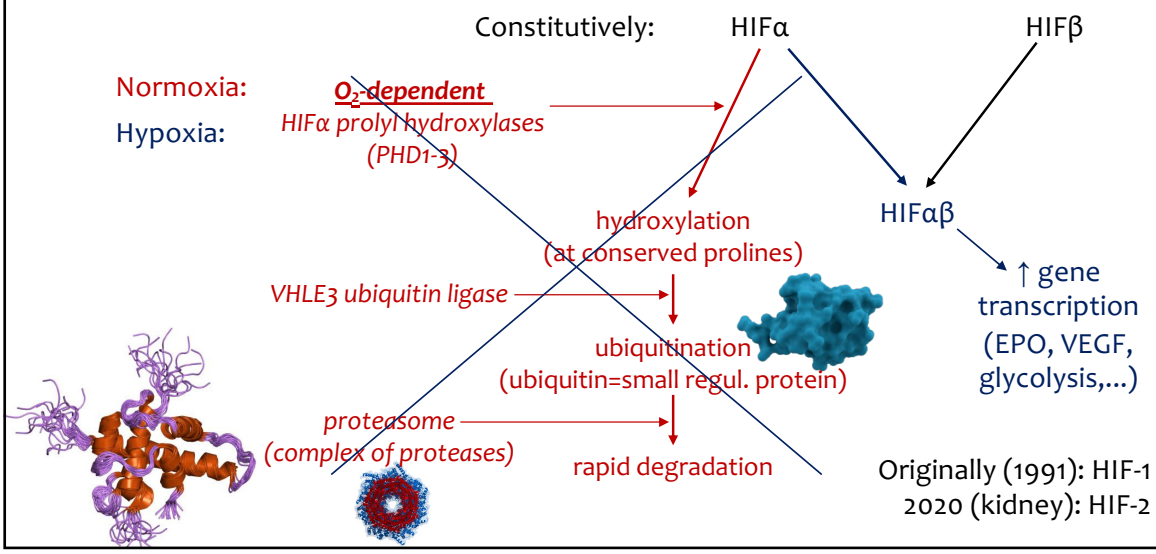
41

Erythropoietin release controlled by hypoxia



42

Hypoxia-inducible factors (HIF 1-3)



43

44