WESTMEAD PRIMARY TEACHING

RESPIRATORY PHYSIOLOGY PART 2

RESPIRATORY PHYSIOLOGY

* Ventilation —> Pulmonary gas exchange —> Oxygen in blood —> Local tissue perfusion —> Diffusion at tissue level —> Tissue utilisation of oxygen

PULMONARY GAS EXCHANGE – OXYGEN AND THE BLOOD

- The amount of oxygen in the blood is expressed as a function of pressure of oxygen - the pressure of oxygen in a liquid is equal to the pressure of oxygen in the surrounding air.

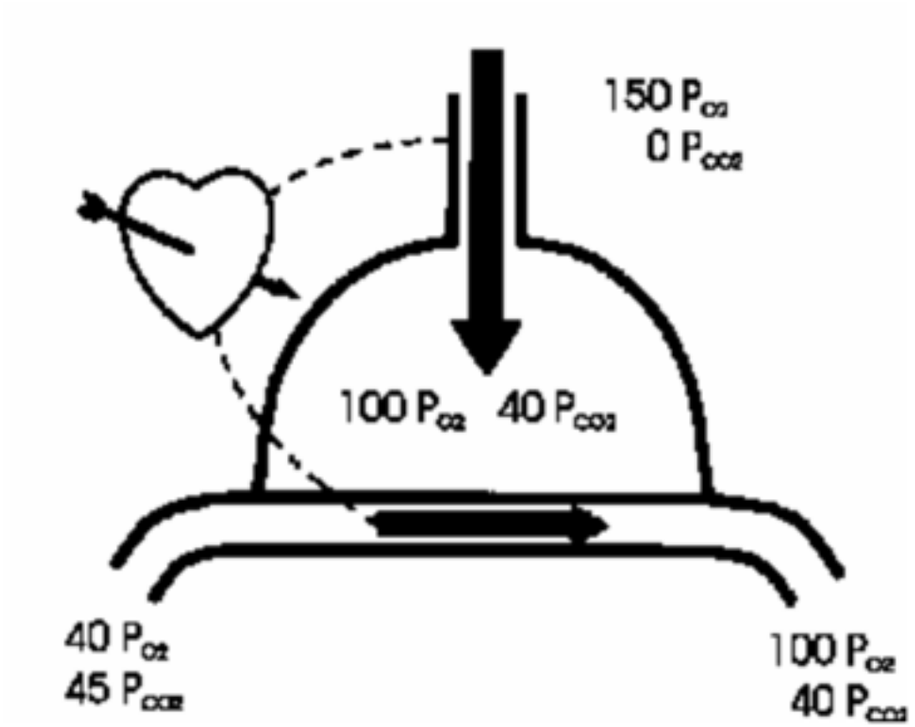


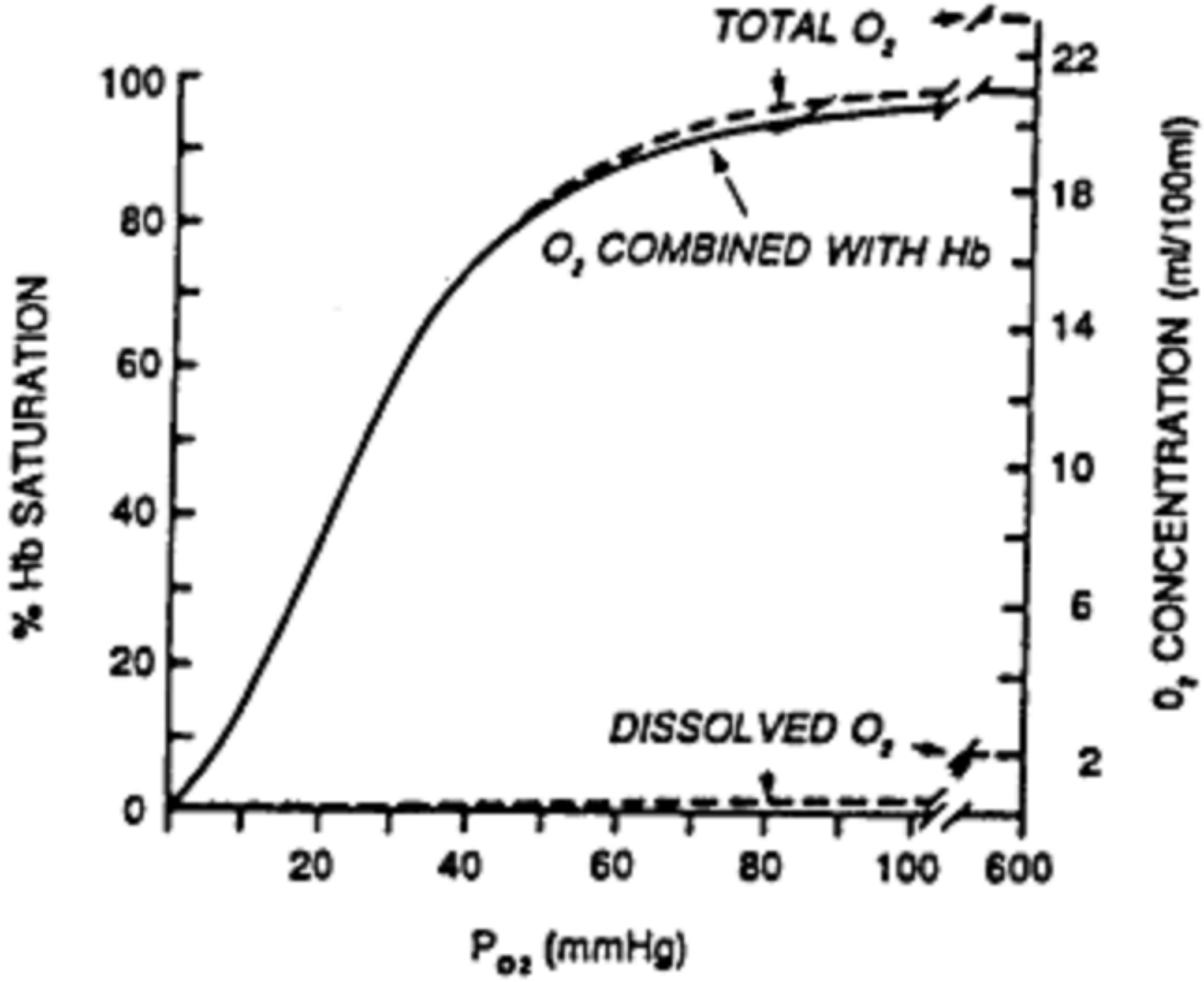
Figure 1

OXYGEN AND THE BLOOD

- Pressure and concentration are related as follows:
  - Concentration = Pressure x Solubility
  - Solubility of O2 in blood = 0.003mL/100mL/mmHg
  - 100mmHg x 0.003 mL O2/100ml blood
  - 0.3mL of O2 per 100mL of blood
    - The resting oxygen consumption of an adult is approximately 250 - 300 mL O2/minute
  - During exercise the oxygen demand can increase up to 4L/min
  - Clearly under these conditions physically dissolved oxygen in the blood cannot meet the metabolic demand for oxygen even at rest.

HAEMOGLOBIN – THE SOLUTION

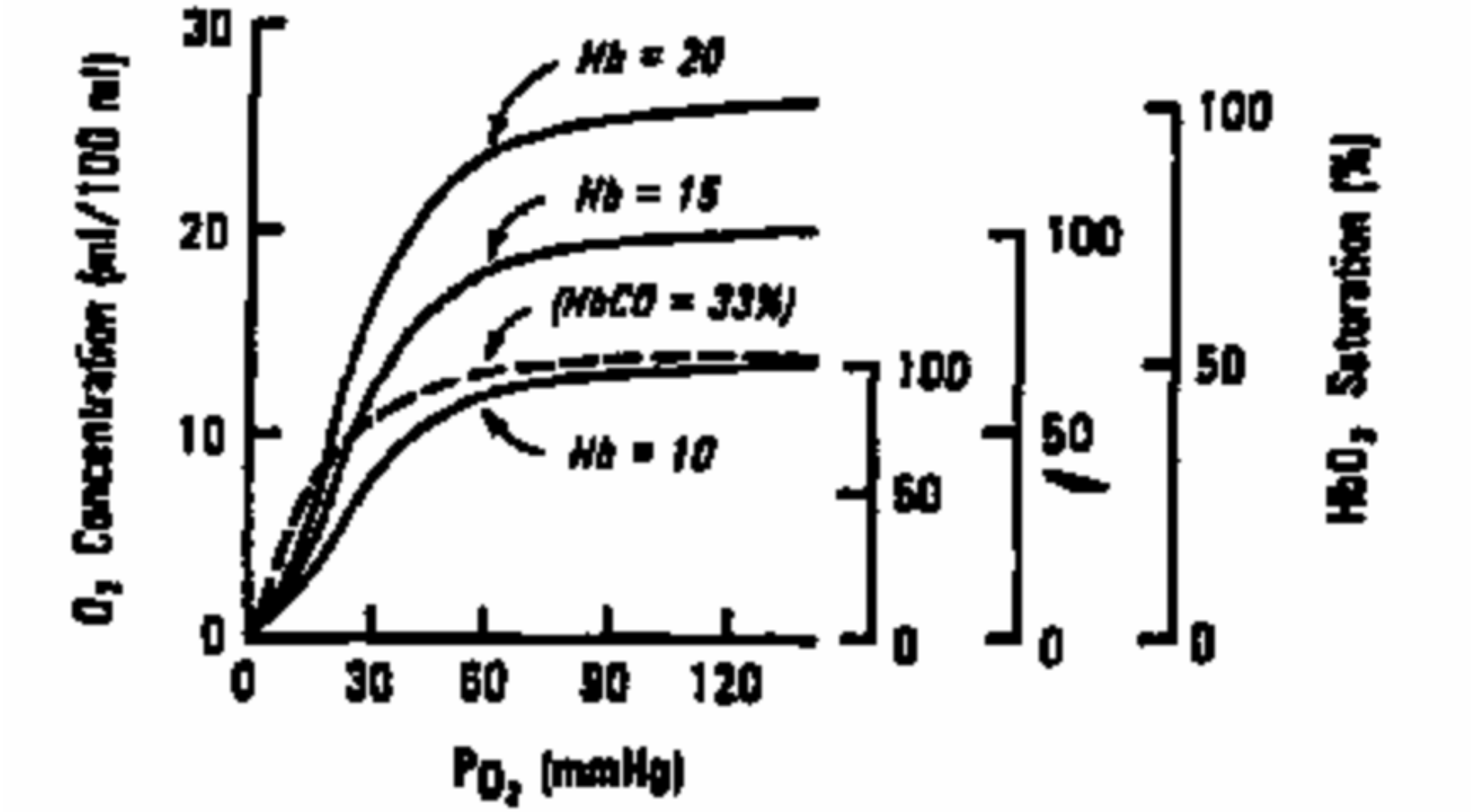
- Hb reverisbly binds oxygen
- Globular protein containing 4 sub units - each sub unit consists of a poly peptide chain binding an iron containing heme group
- Heme group binds O2, four molecules can bind each heme group
  - HbA is the adult haemoglobin consists of 2 alpha and 2 beta sub units
  - More than 120 variants of Hb genes discovered
  - Most common variant is HbS
- The oxygen capacity of Hb is defined as the maximum amount of O2 that can be combined with Hb
  - 1g of Hb can combine with 1.39 mL of O2
  - Since normal blood contains around 15g of Hb/100mL of blood the O2 carrying capacity of blood is around 20.8mL of O2/100mL of blood


TOTAL O_2
O_2 COMBINED WITH Hb
DISSOLVED O_2
% Hb SATURATION
O_2 CONCENTRATION (ml/100ml)
100
80
60
40
20
0
22
18
14
10
6
2
20
40
60
80
100
600
P_{O_2} (mmHg)

OXYGEN DISSASSOCIATION CURVE

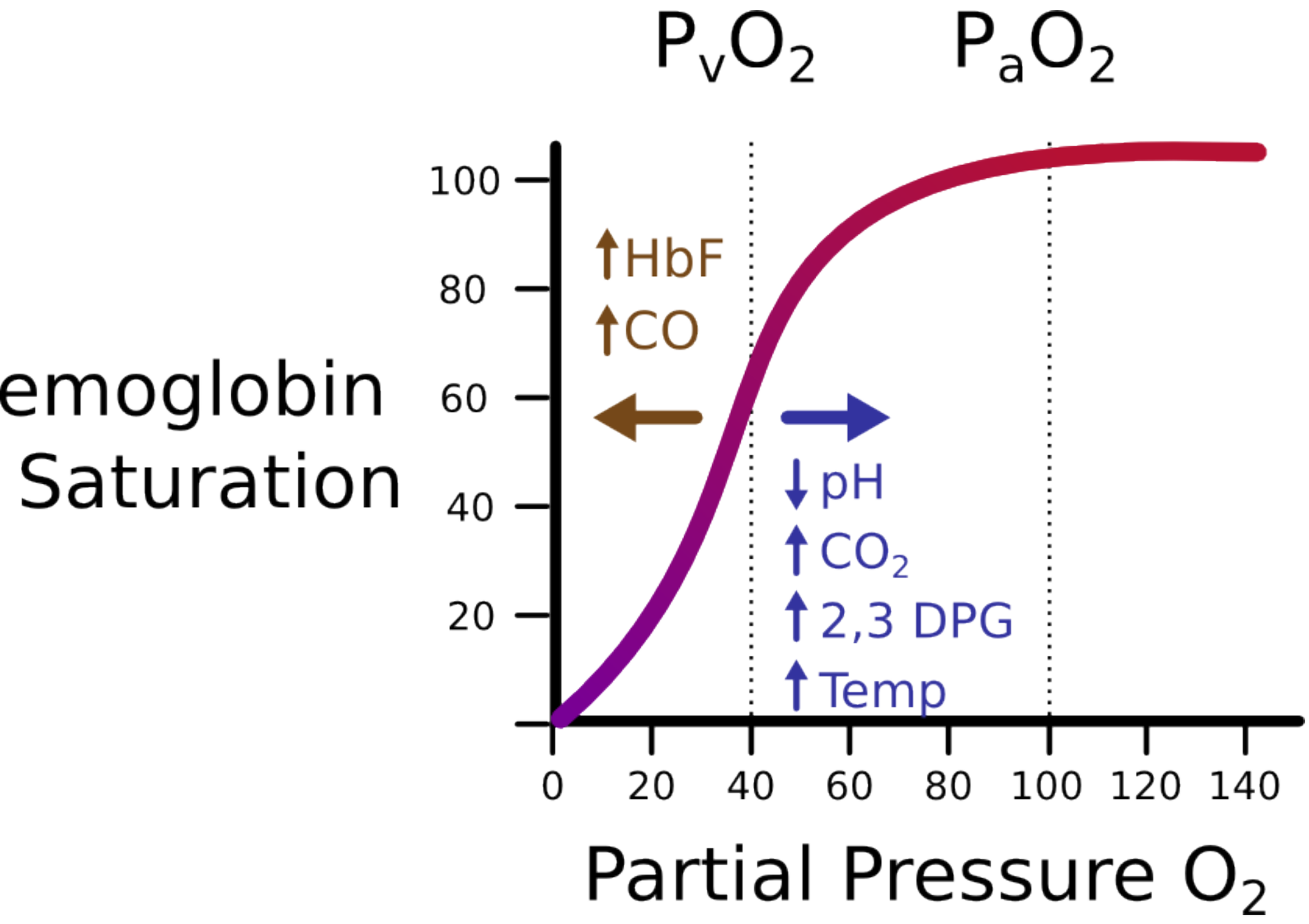
- The sigmoidal shape - a reflection that the affinity of Hb for O2 changes as more oxygen molecules combine
- The flat part of the curve - reflects a saturation of Hb binding sites
- The sigmoidal shape is advantageous because - it ensures that the PO2 found in peripheral tissues Hb will dissociate quite easily but at PO2 found in arterial blood - the Hb will be completely saturated
- Note that when the PO2 is above 70 the curve is nearly flat - meaning that there is only a small increase in the oxygen context of the blood between a PO2 of 70 and 100

TEXT


30
20
10
0
Hb = 20
Hb = 15
(HbCO = 33%)
Hb = 10
0
30
60
90
120
P_{O_2} (mmHg)
100
50
0
100
50
0
O_2 Concentration (ml/100 ml)
HbO_2 Saturation (%)

PATHOLOGICAL STATES AND THE CURVE

- Main point is that the oxygen carrying capacity of the blood is based on the concentration of Hb
- Carbon monoxide - binds to O2 binding sites on Hb and has an affinity 240 times greater than O2, therefore event small amounts can cause a drastic lowering of the oxygen carrying capacity of the blood
- Decreases O2 carrying capacity
- Shifts the curves to the left


P_vO_2
P_aO_2
100
80
60
40
20
0
20
40
60
80
100
120
140
↑HbF
↑CO
↓pH
↑CO_2
↑2,3 DPG
↑Temp
emoglobin
Saturation
Partial Pressure O_2

SHIFTS IN THE CURVE

- Low pH of high PCO2 shift the curve to the right and therefore reduce the affinity of Hb for O2 - therefore allowing for greater unloading of O2 at tissue sites
- Temperature also reduces the affinity - useful in high metabolic states such as fevers
- Concentration fo 2 - 3 DPG - an end product in RBC metabolism and increases during hypoxemia and this shift the curve to the right and increases peripheral oxygen delivery. Low levels (sepsis, old blood) will shift the curve to the left.
- Hb F - has a higher affinity for O2

TRANSPORT OF CO2

- Builds up in peripheral tissues and diffuses across the capillary wall back into blood, occurs via 3 pathways
  - Physically dissolved (5%)
  - With Hb (5%)
  - As bicarbonate

PHYSICALLY DISSOLVED CO2

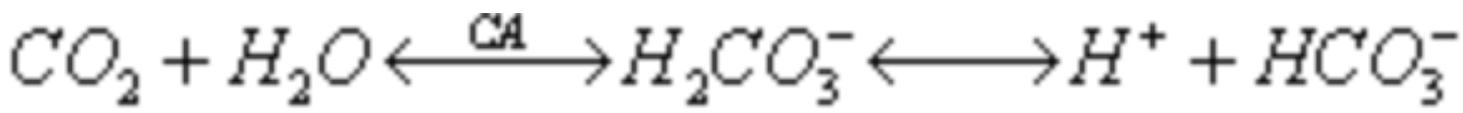
- About 20 times as soluble in plasma as O2
- Solubility coefficient is 0.06 ml CO2/100ml blood
- Concentration is around 2.4 mL/100ml

AS CARBAMINO COMPOUNDS

- Can combine with with amino groups of any portion in the blood and forms a carb-amino protein
- Occurs rapdily - no enzyme needed
- A hydorgen ion is liberated by this binding
- Because the major of blood protein is Hb, most of the CO2 transported this way is bound to portien and forms carb-amino-heamoglobin

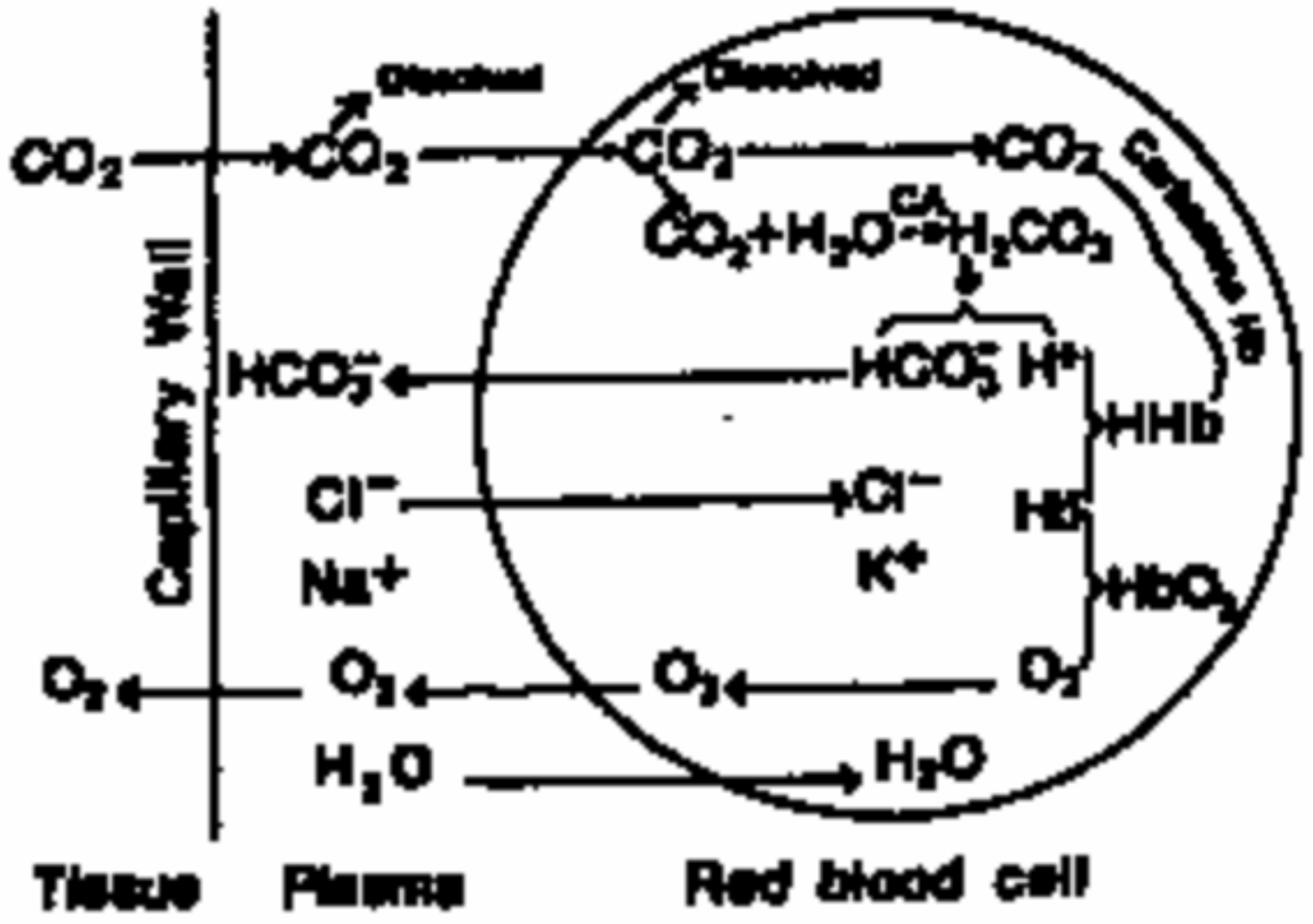
AS BICARBONATE

- Remaining 80 - 90% of CO2
- Formed within the RBC by



- This reaction occurs only in RBCs because of the required carbonic anhydrase enzyme
  - HCO3 diffuses out of the RBC in exchange for Cl ion (Chloride shift)
  - Hydrogen ions remain in the RBC where they are buffered by deoxyHb which is a better buffer for H+ than oxygenated Hb

IN PERIPHERAL TISSUES



IN THE LUNGS

- In the lungs all reactions occur in reverse:
  - Bicarb enters the cell in exchange for Cl and CO2 is diffused out in expiration via the alveoli

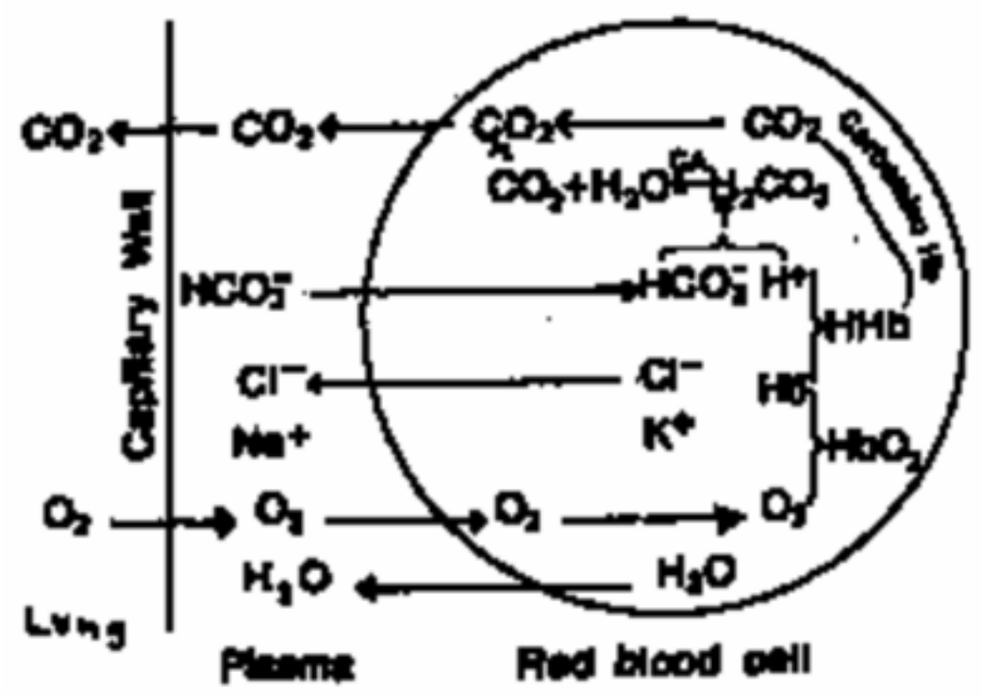
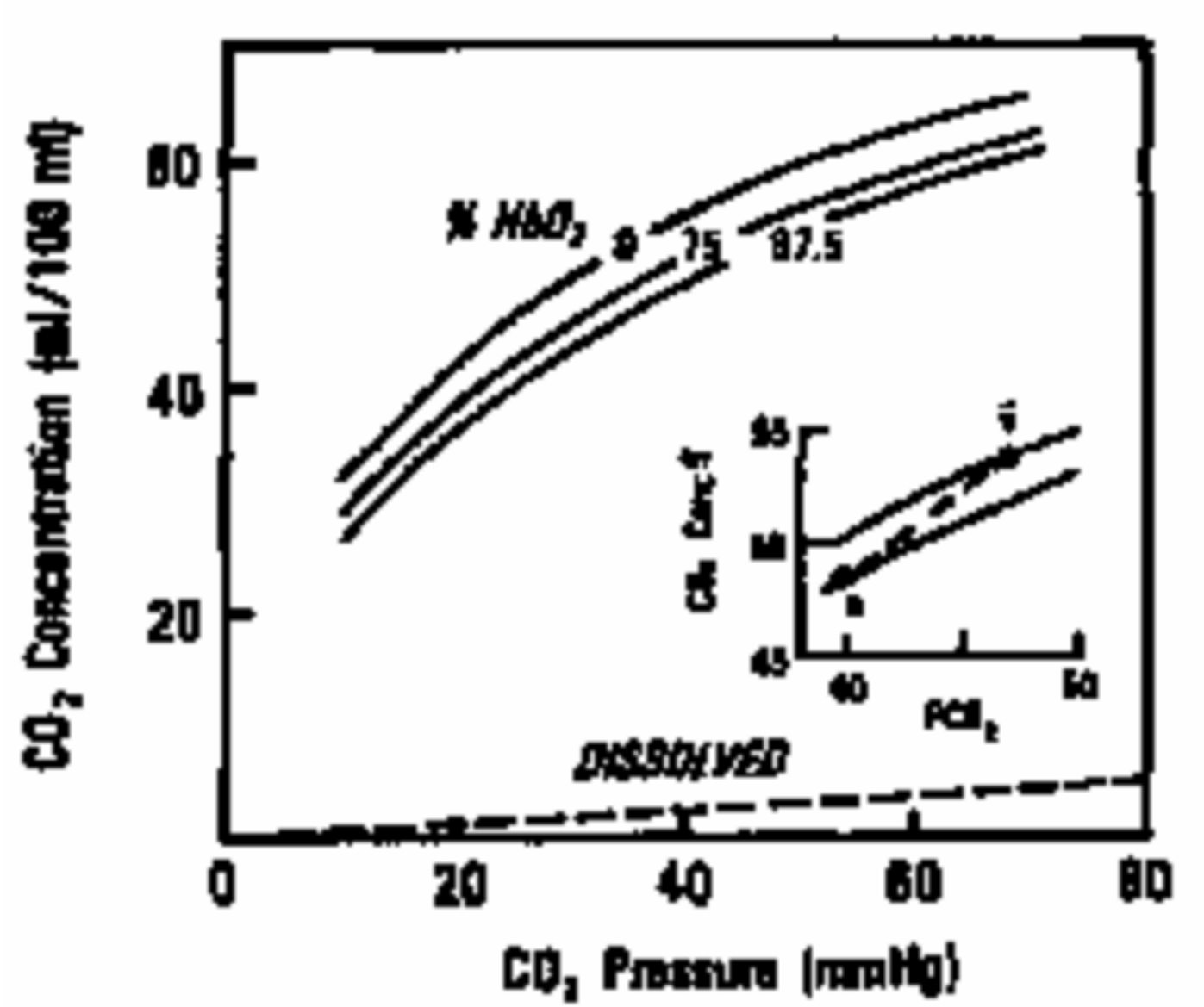


Figure 6

HB CO2 CURVE


80
40
20
0
20
40
60
80
% HbO2
75
87.5
DISSOLVED
Hb Conc'n
95
45
40
50
PCO2
CO2 Pressure (mmHg)

- When blood is oxygenated by the lung, Oxy Hb is formed.
- Hb O2 is a stronger acid than deoxygenated Hb and causes a fall in pH that shifts the CO2 curve to the right and this facilitates the unloading of CO2 in the lungs both from bicarbonate and from various carbo-amino compounds - this is called the Haldene effect
- Converse is true in peripheral tissues where the gradients and concentrations are reversed

ALVEOLAR GAS EQUATION AND A-A GRADIENT

- A - a gradient is PAO2 - PaO2
- PAO2 = FiO2 (Patm - pH2O) - (paCO2/RER)
  - Respiratory exchange ratio = 0.8
  - At sea level atmospheric pressure is 760 mmHg
  - Pressure of water at body temperature is 47mmHg
  - PAO2 = (FiO2 x 713mmHg) - (paCO2/0.8)
  - Aa gradient increases with age and varies with FiO2 (normal between 5 - 10)

GAS EXCHANGE IN PERIPHERAL TISSUES AND HYPOXEMIA

- The passage of oxygen is driven by the difference in oxygen concentration between the blood and the tissues
- Tissue hypoxia can be classified into 4 aetiologies
  - Derease arterial PaO2 (hypoxic hypoxia)
  - Decrease ability for blood to carry O2 (anemic hypoxia)
  - Reduction in blood flow (circulatory hypoxia)
  - Inability for tissue to utilise oxygen (histotoxic hypoxia)
  -

HYPOXIC HYPOXIA (HYPOXEMIA)

- 4 causes of hypoxemia include
  - Hypoventilation
  - Diffusion impairment
  - R to L shunt
  - Abnormal VQ ratio

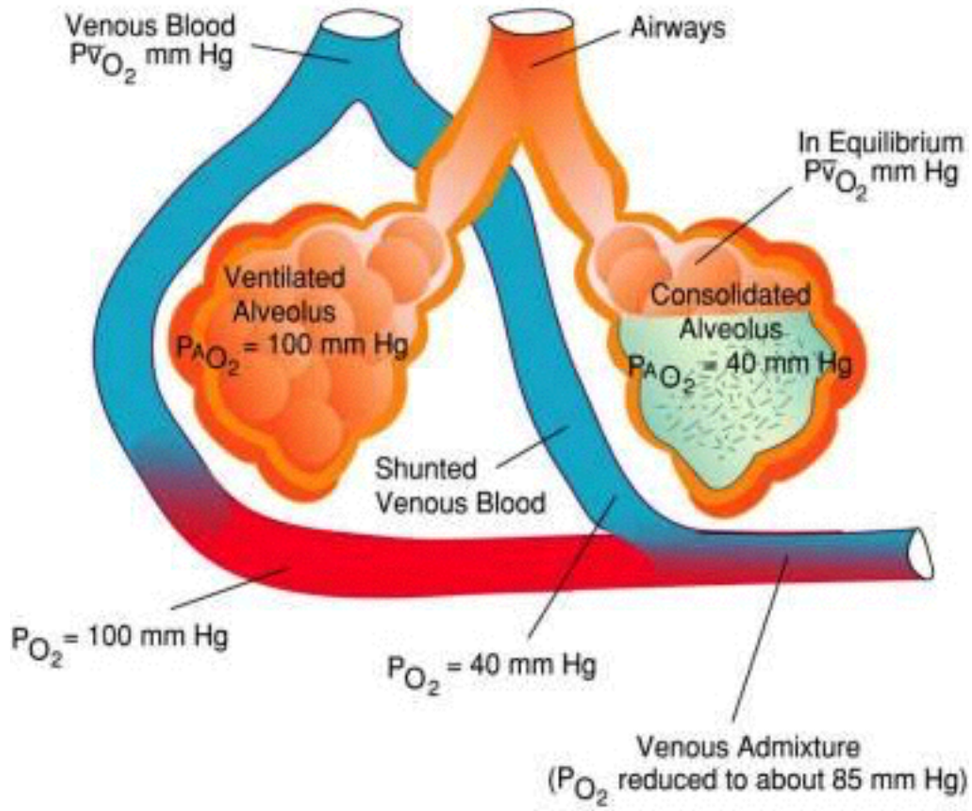
HYPOVENTILATION

- Caused by under-ventilated alveoli
- Clinical hallmark is elevated $PaCO_2$
- Most common cause is depression of the medullary respiratory centre by drugs
- Case example - a 50 yo M who presents with a BDz overdose, therefore his alveolar ventilation is halved whilst his CO_2 production remains unchanged
    - Blood gas on RA demonstartes PaO_2 of 50mmHg, $PaCO_2$ of 80mmHg,
- After giving 28% FiO_2 his RA saturations improved to 95% and PaO_2 increased to 100mmHg
    - $PaO_2 = PiO_2 - PaCO_2/R$
    - $PaCO_2 = VCO_2/Va$
        - Va = alveolar ventilation
        - VCO_2 = total produces CO_2
    - Decreasing alveolar ventilation raises $PaCO_2$, and raised $PaCO_2$ will decrease PaO_2
- Other things to note - PaO_2 is depressed around the same that $PaCO_2$ is elevated
- Even a 50% decrease is alveolar ventilation leaves a PaO_2 of 50mmHg which maintains saturations around 80%
- Hypoxemia caused by hypoventilation will be remedied by administering air that is only slightly enriched with O_2

SHUNTS

- Blood returning to the heart and entering the lungs through the pulmonary artery is called mixed venous blood
  - If blood bypasses functioning lung then arterial systemic blood will be a mixture of normally oxygenated and poorly oxygenated blood
    - 2 ways
      - Anatomical shunt (VSD)
      - Physiological shunt (APO, Pneumonia, Pneumothorax)
- Since shunted blood contacts no air, increasing the FiO2 will not improve oxygenation
- PaCO2 will be normal or low because of increased alveolar ventilation (increased RR) stimulated by hypoxia

DIAGRAM – SHUNT



VQ MISMATCH

- Most common cause of hypoxemia
- Under ventilated lung gets blood flow or no blood flow to ventilated lung units
- The relationship between PaO2 and PaCO2 in these cases of VQ mismatch is key to understand
- Hyperventilation of some units does not add enough oxygen to balance out the low oxygen content or the hypoventilated units - the result is a final oxygen concentration determined mainly by low VQ areas
- V/Q imbalance will also cause an increase in PCO2 in the poorly ventilated alveoli
  - but the systemic CO2 will remain normal because the hypoxemia stimulates increased ventilation in the rest of the lung
  - The reason increasing ventilation will not improve PaO2 has to do with the shape of the dissociation curves
  - The CO2 curve is nearly linear over the physiological range of PaCO2 and its slope is much steeper than the slope of the oxygen dissociation curve
  - Thus a reduction in alveolar PCO2 and corresponding increase in alveolar PO2 due to hyperventilation can cause a large decrease in CO2 but only a small increase in O2