PROTECTION OF RED CELLS FROM HAEMOLYSIS

By:

- Super oxide dismutant

  $O_2 + O_2 + 2+ \rightarrow H_2O_2 + O_2$

- Catalase:

  $H_2O_2 \rightarrow 2H_2O_2$

- Glutathione

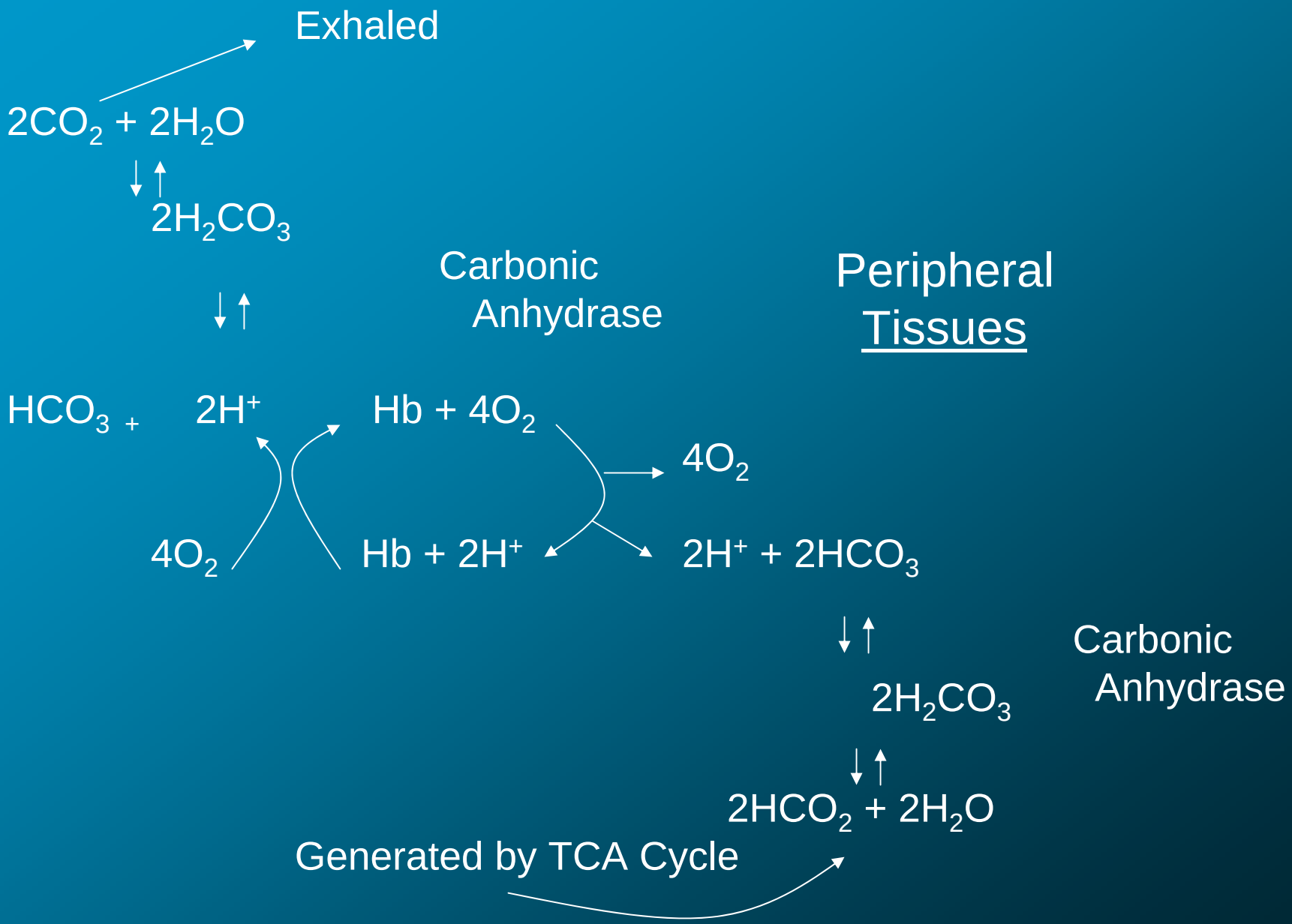
  $2GSH + RO - OH \rightarrow GSSG + H_2O + ROH$

PRODUCTION OF POWERFUL OXIDANT IN RED CELLS DURING METABOLISM

- During metabolism, there is production of:
  - Superoxides (O_2): $O_2 + e \rightarrow O_2$
  - Hydrogen peroxide (H_2O_2)

    $O_2 + O_2 + 2H \rightarrow H_2O_2 + O_2$
  - Peroxyl radicals (ROO)
  - Hydroxyl radicals (OH)
- These oxidizing radicals are highly reactive molecules and can meet with proteins, mucleic acids, lipids and other mol. to alter their structure and produce tissue damage.
- Red cell needs several reducing rections to keep it in reduced state and protect it from damage by oxidizing radicals.

THE BOHR EFFECT



BINDING OF 2,3 DIPHOSPHOGLYCERATE

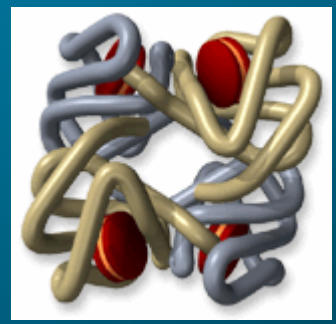
- 1 molecule of 2,3 DPG Hb molecules
- 2,3 DPG binds between 2 β-chains of HbA.
- It is formed from 1,3 DPG (a glycolytic intermediate).
- In peripheral tissues level of 2,3 DPG is high. It binds Hb and decreases affinity for O_2.
- HbF cannot bind 2,3 DPG and has higher affinity for O_2.
  - O_2 can be transported from mother to fetal blood

GLUCOSE TRANSPORTERS IN RED CELL MEMBRANE

- Glucose uptake by red cells is by facilitated diffusion.
- Proteins involved in facilitated diffusion of glucose are glucose transporters (~ 2% to membrane protein of RBC).
- Almost 7 different glucose transporters have been identified and in different tissue.
- Glucose transporters in red cells membrane are insulin-independent.

HAEMOGLOBIN IN THE RED CELLS

Haemoglobin



- Major solute in red cells.
- Globular protein
- Conjugated protein: globin + haem.
- Made of 4 subunits (Quarternary structure)

  4 globins + 4 haems $\rightarrow$ haemoglobin.
- Binds O_2 to haem group to form oxyhaemoglobin

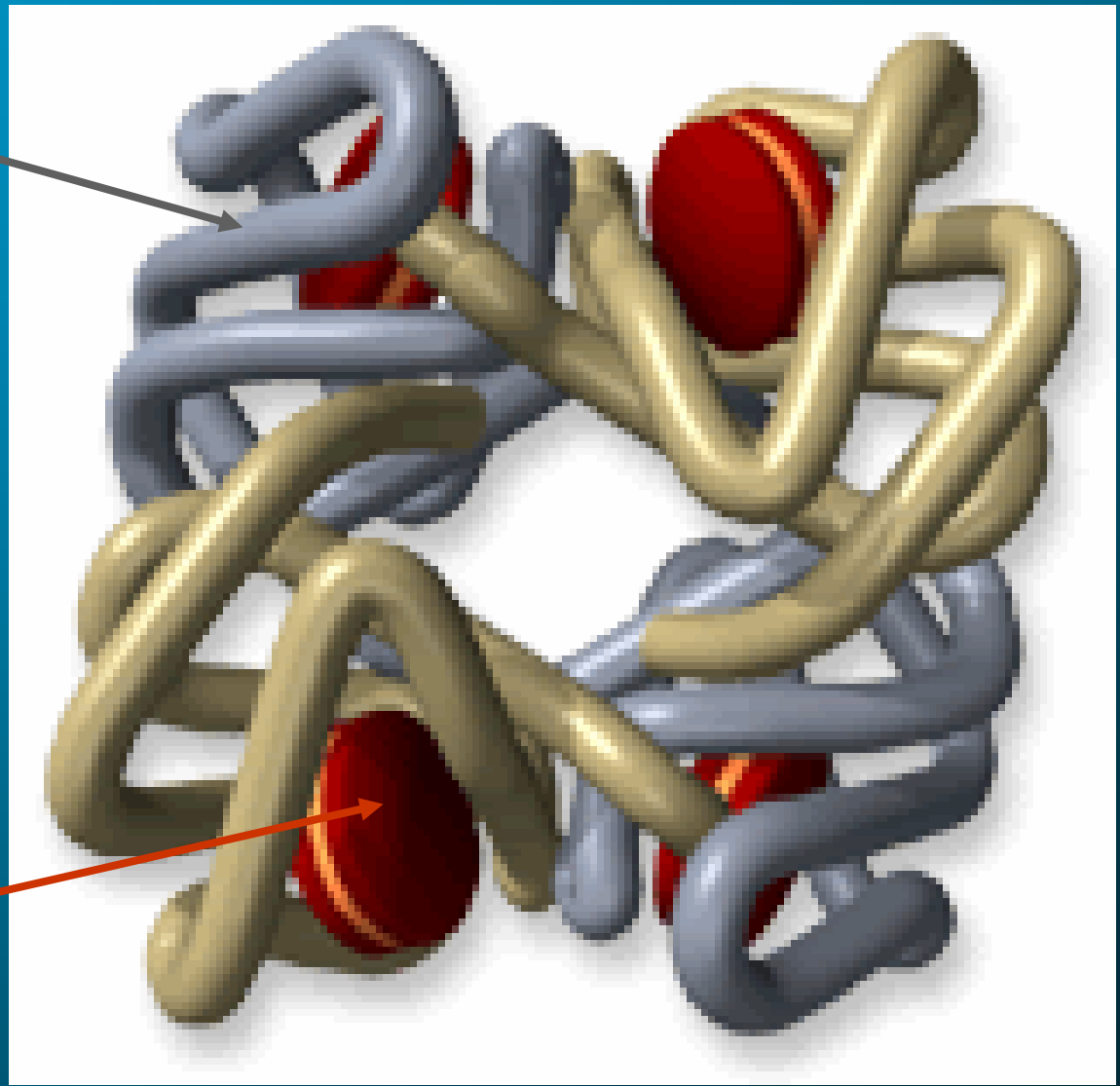
  Hb + 4 O_2 $\rightarrow$ Hb (O_2).

Contd…..

Haemoglobin

Globin Chains

Heam Group



HAEMOGLOBIN IN THE RED CELLS

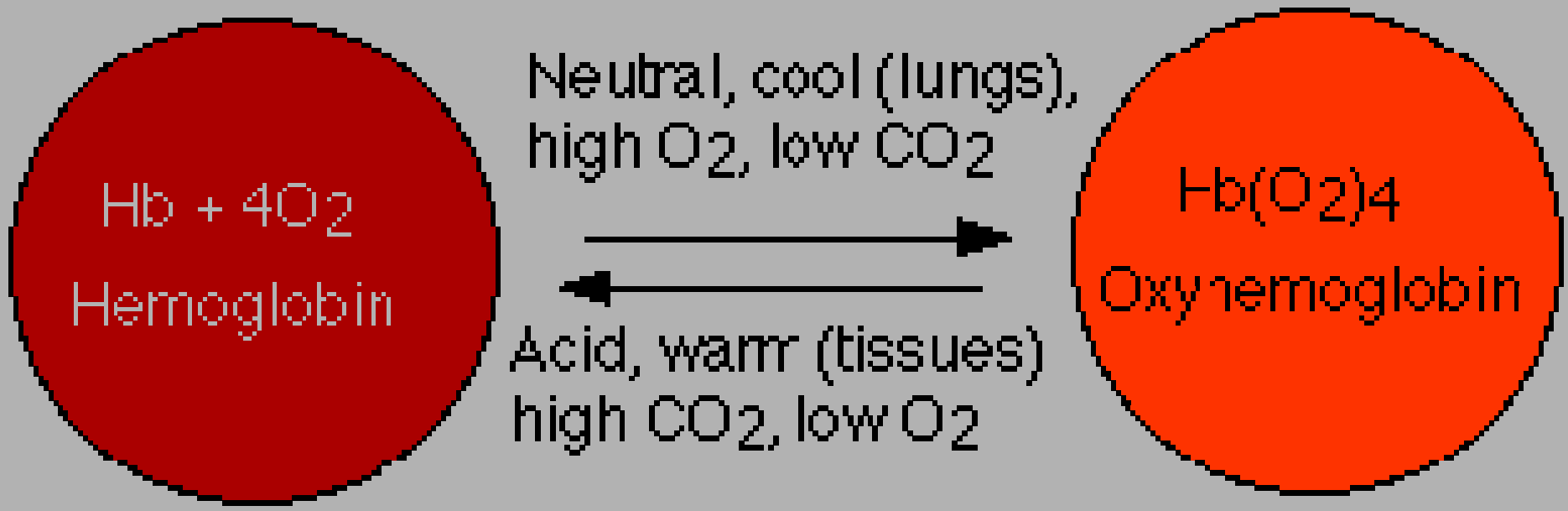
Haemoglobin…..Contd

- Affinity for O_2 depends on partial pressure of O_2, CO_2, and H+, 2,3 DPG level.
- Binds CO_2 to N-terminal of β-globin chain $\rightarrow$ to form crabamino Hb.

Carboxy Hb.

$Hb + 4CO \rightarrow Hb(Cl)_4$.

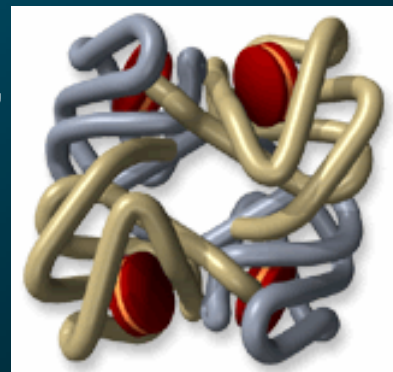
Has high affinity for CO


Hb + 4O2
Hemoglobin
Neutral, cool (lungs),
high O2, low CO2
Hb(O2)4
Oxyhemoglobin
Acid, warm (tissues)
high CO2, low O2

HAEMOGLOBIN IN THE RED CELLS

Haemoglobin…..Contd

- Allosteric protein: has 4 O_2 binding sites
- O_2 binding curve of Hb is sigmoided.
- Shows cooperative effect: i.e. binding of some O_2 molecules males it easy for other O_2 molecules to bind.
- O_2 affinity of Hb is affected by pO_2, pCO_2, H+, 2,3 DPG.



TYPES OF HAEMOGLOBINS

In Adults

Hb	:	~97%	$\alpha_2 \beta_2$
HbF	:	<1%	$\alpha_2 \gamma_2$
Hb A_2	:	2.5 – 3.5%	$\alpha 2 \delta_2$

At Birth

HbF	:	$\beta_2 \gamma_2$
Hb A	:	$\alpha_2 \beta_2$

During Embryonic life

Hb Gower 1

Hb Gower 2

Hb Portland

GLOBIN CHAINS OF Hb

Amino acids in globin chains

α Globin	141 a.a.
β-like globin chains:	146 a.a.

Structure

- Globular
- ~75% and helics
- Have a hydrophobic cavity for binding heme.

HEME GROUP

- Protoporphyrin IX
- It is a tetra pyrolle ring linked together by methylene brides.
- Fe^{++} coordinates with 4 N of the 4 pyrolle rings:
  - Bind with coordinate covalent bond to Histidine F8.
  - Binds to O_2 between Fe^{++} and His E7.
- If Fe is oxidized to ferric (Fe^{++}) the Hb $\rightarrow$ met Hb, which cannot binds O_2.

STRUCTURE OF HEME GROUP