Effect of 2,3-BPG

- It is an important regulator of O_2-binding
- It is the most abundant organic phosphate in the RBC

$$[2,3\text{-BPG}] = 4\text{-}5\ mM = [Hb]$$

- It is synthesized from an intermediate of the Glycolytic Pathway
- High affinity for O_2 in its absence

P_{50} is 7 to 10 mm Hg

- BPG stabilize the T state
- BPG binds the β subunits in (1:1) in a pocket lined with positively charged amino acids
- BPG conc. is increased in response to chronic hypoxia. e.g
  - chronic obstructive Pulmonary disease [COPD] like emphysema
  - High altitude
  - Chronic anemia. e.g. PK deficiency

- Stored blood in Blood Bank.

storage → ↓ 2,3-BPG → O_2-trap

- transfused blood restore BPG in 6–24 hrs.
- supplement of Adenine and changes of H^+, Phosphate and hexoses restores ATP and improves [BPG] → ↑ storage time from 21 d to 42 days

CO_2 Transport

Hb is impt in the transport of CO_2 from tissues where it is generated to the Lung where it is excreted:

A. Dissolved CO_2 - accounts for ~ 10%

B. Carbamin Hb:- accounts for 15-20% of CO_2 transported

$$R-NH_2 + CO_2 \rightarrow R-\overset{H}{\underset{|}{N}}-\overset{O}{\overset{||}{C}}-O^- + H^+$$

Deoxy Hb is more reactive

C. Bicarbonate is the major form transported

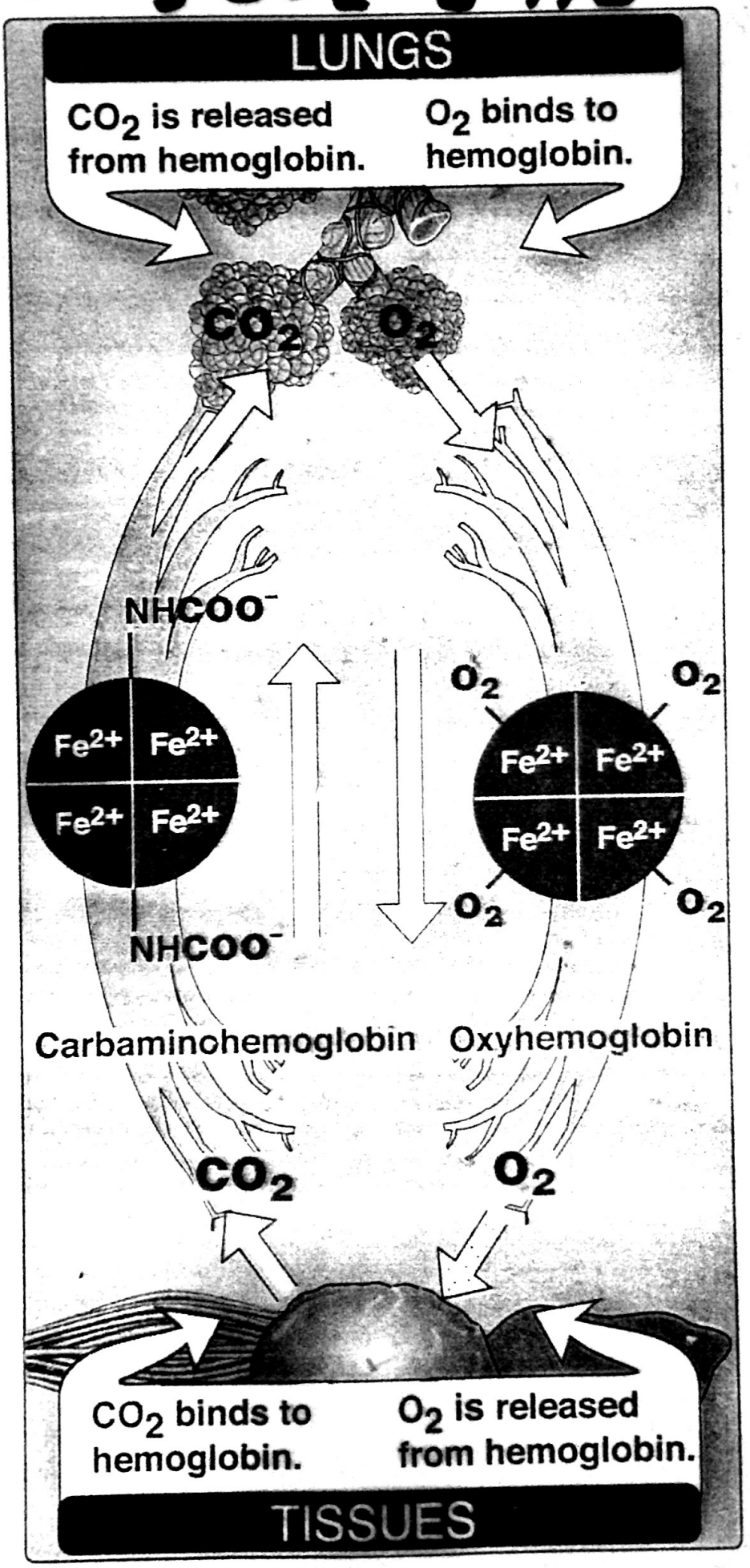
$$CO_2 + H_2O \overset{C.A.}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

1- Isohydric shift
2- Chloride shift

- Distribution of the H^+ generated during normal CO_2 transport:-

Buffering: Hb buffer 50%
other buffers 10%
Isohydric Mechanism 40%

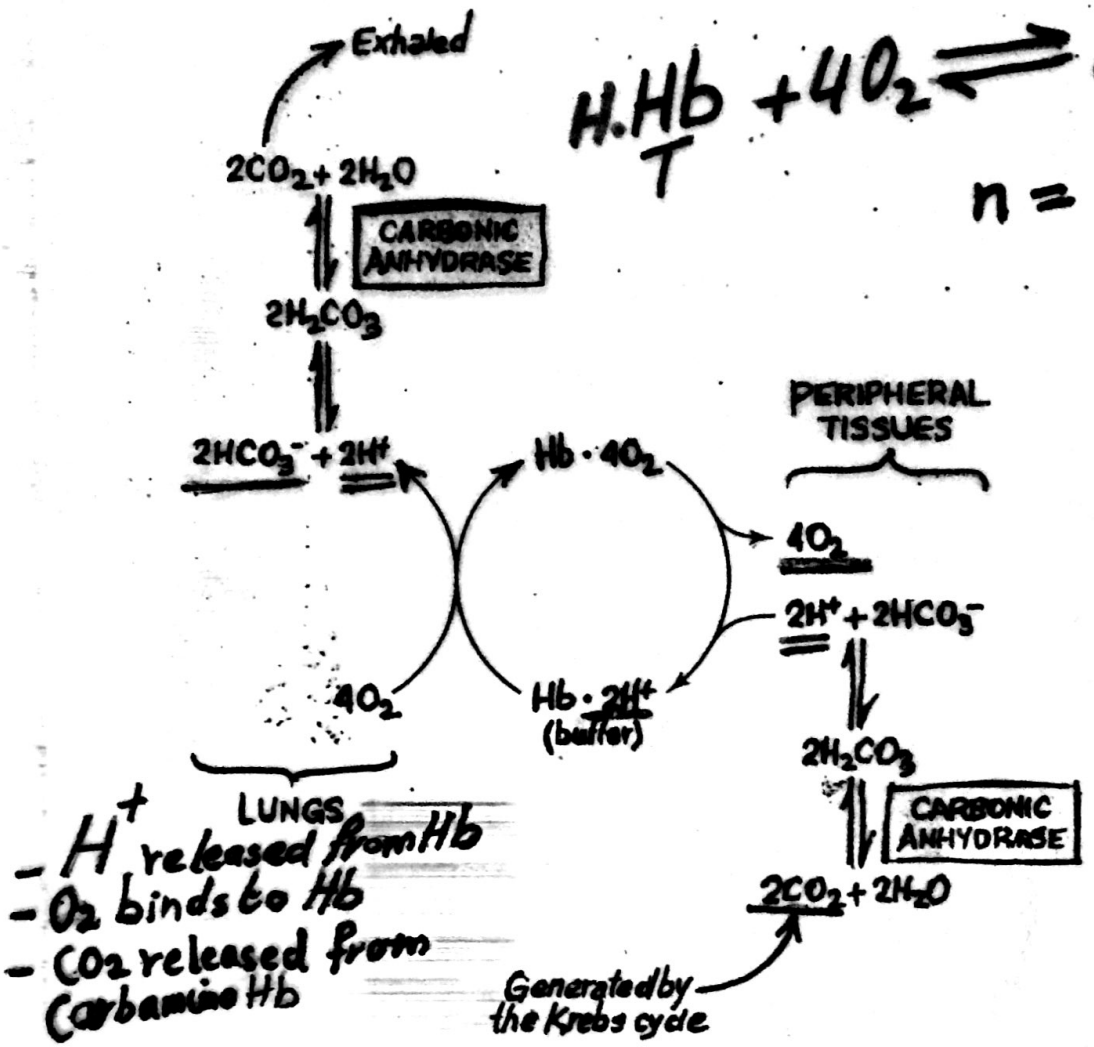
Transport of CO_2 by Hb



BOHR EFFECT :-

$$H.Hb_{T} + 4O_2 \rightleftharpoons Hb(O_2)_4 + nH^+_{R}$$

$n = 1.2$ to 2.7



- H^+ released from Hb
- O_2 binds to Hb
- CO_2 released from Carbamino Hb

Figure 6–9. The Bohr effect. Carbon dioxide generated in peripheral tissues combines with water to form carbonic acid, which dissociates into protons and bicarbonate ions. Deoxyhemoglobin acts as a buffer by binding protons and delivering them to the lungs. In the lungs, the uptake of oxygen by hemoglobin releases protons that combine with bicarbonate ion, forming carbonic acid, which when dehydrated by carbonic anhydrase becomes carbon dioxide, which then is exhaled.

Mechanism of the Bohr Effect :-

pKa of N-terminal α-amino groups and some his residues e.g β146 his is INCREASED upon deoxygenated

pK 7.3 → 7.7 (oxy → deox)

- Protonated
- charged
- formation of ionic bonds in T state

Mechanism of Bohr Effect

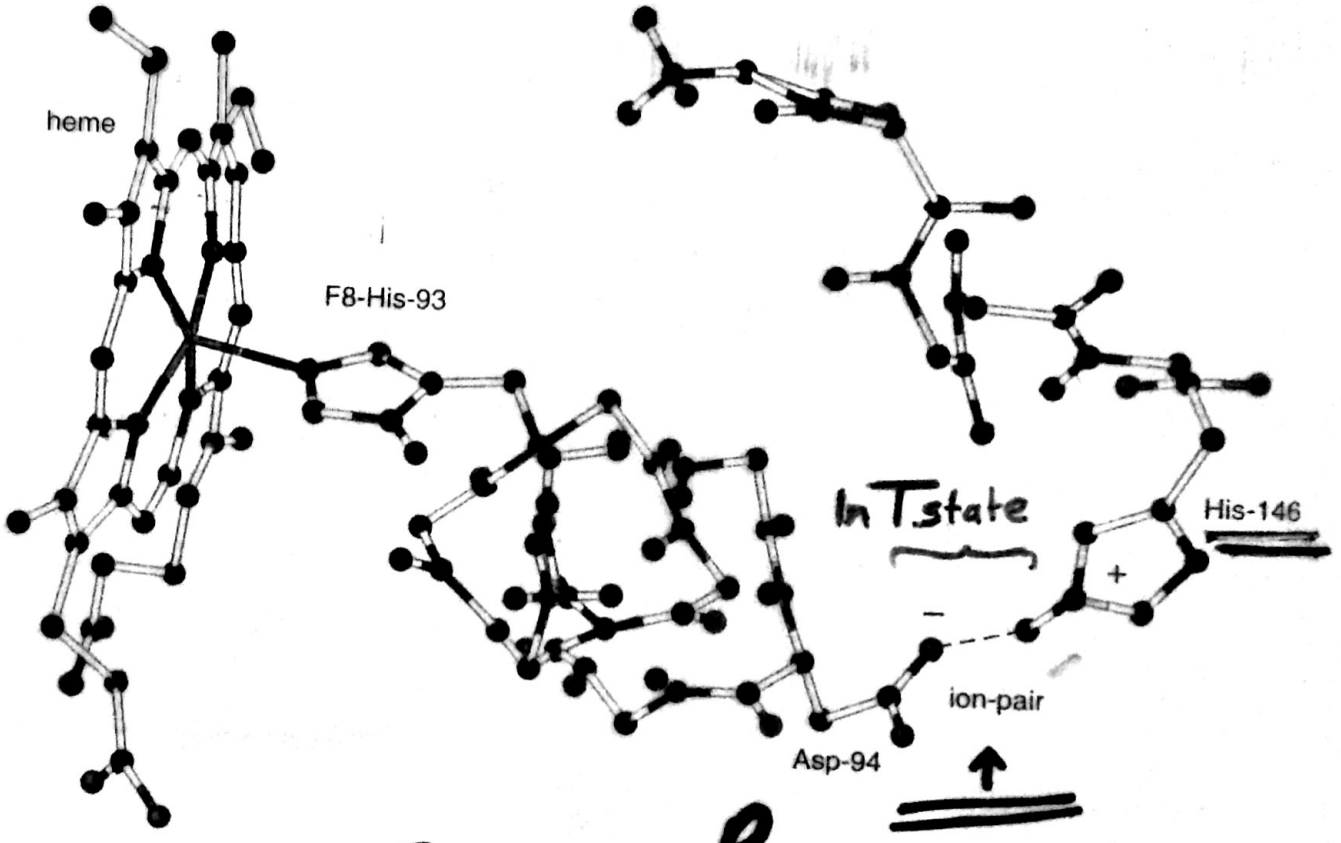


FIGURE 9.29

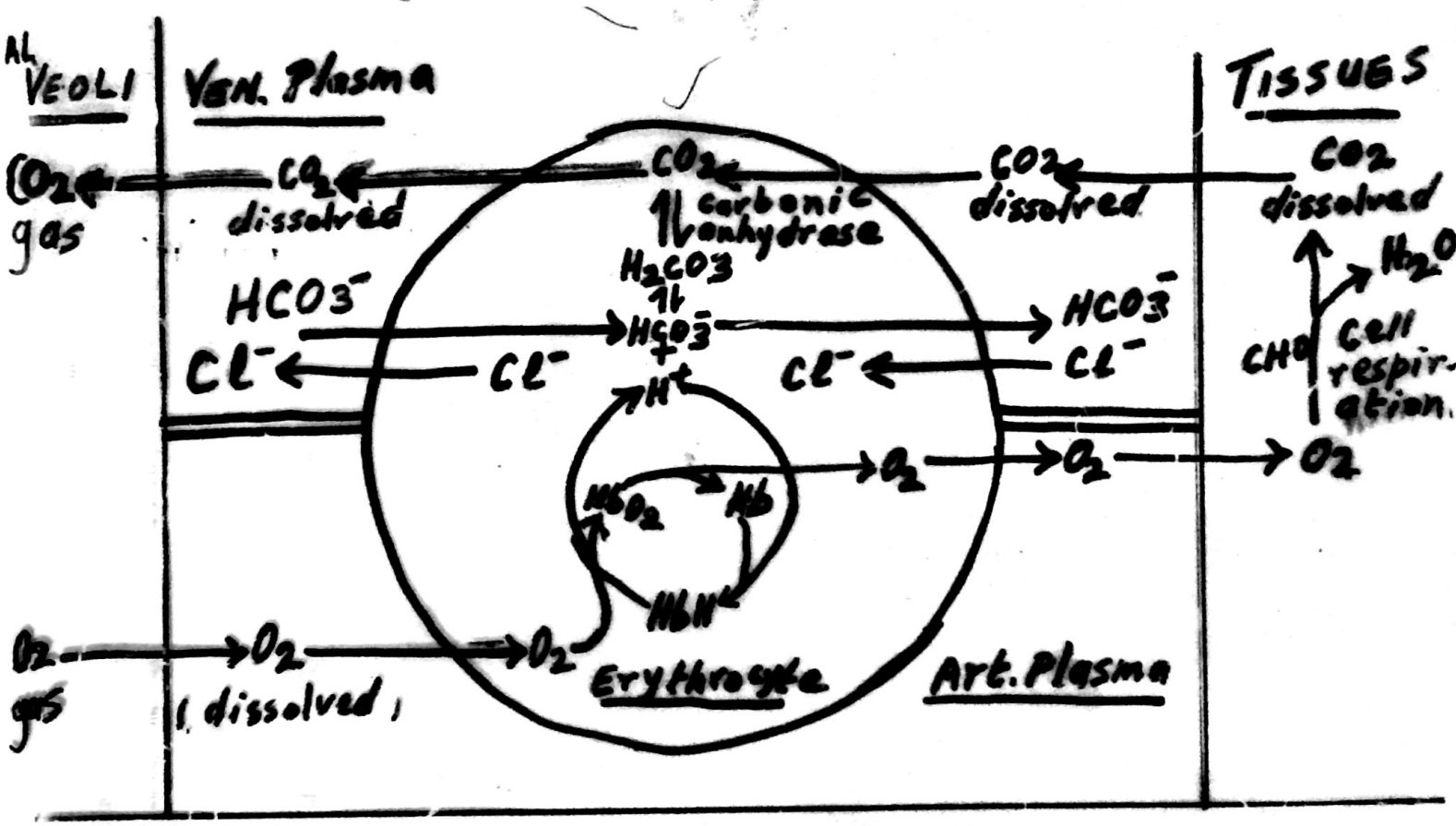
Ion-pair between the βHis-146 imidazolium and the βAsp-94 carboxylate side-chain groups in the deoxy(T)-conformation of hemoglobin.

T
β His-146
pKa 7.7

R
β-His-146
pKa = 7.3

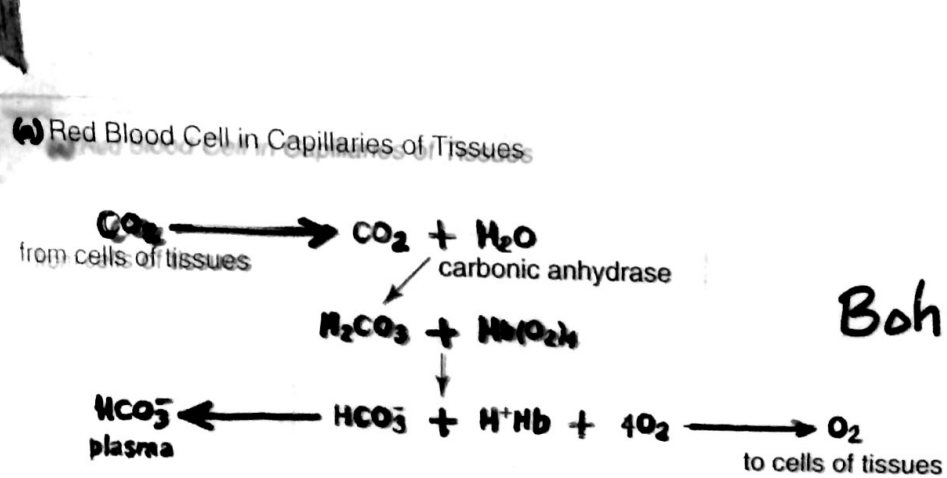
50% of proton release come from β-his 146

BOHR Effect
Haldane Effect



Isohydric shift

Chloride shift



Bohr effect

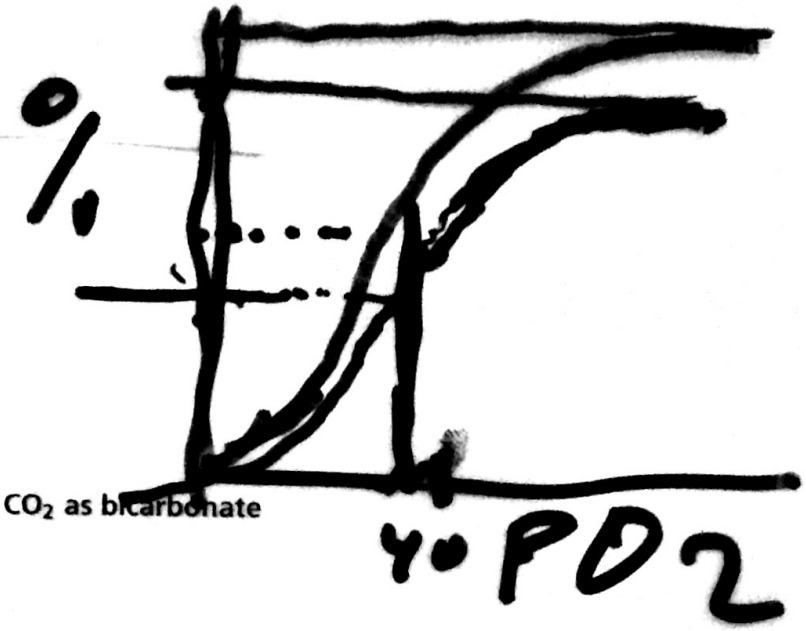
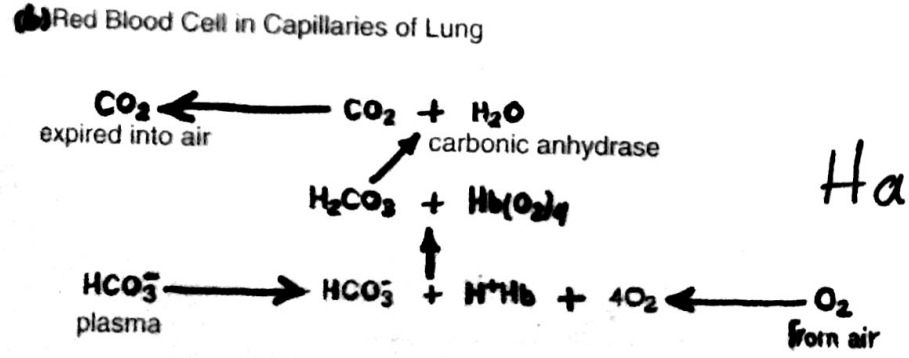


FIGURE 9.31
The isohydric transport of CO_2 as bicarbonate



Haldane effect

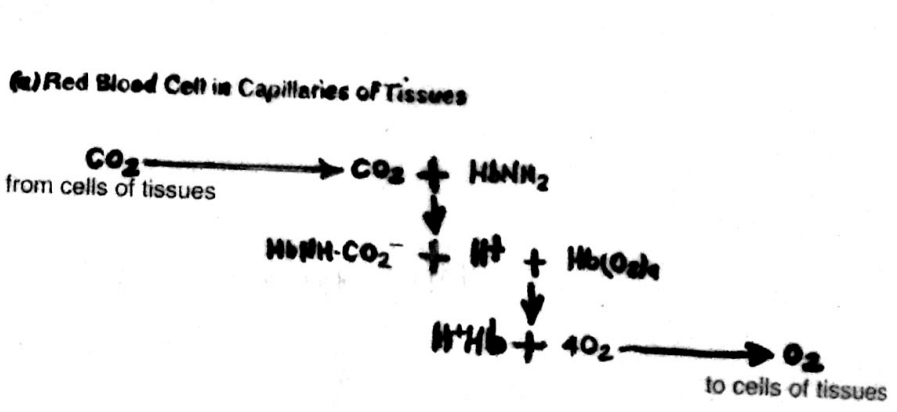


FIGURE 9.32
Transport of CO_2 as carbamino-hemoglobin.