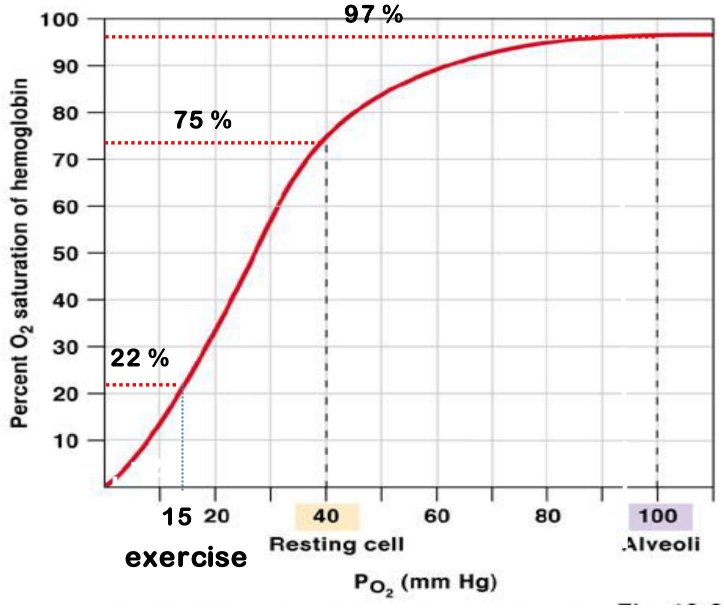
Transport of O_2 during strenuous exercise

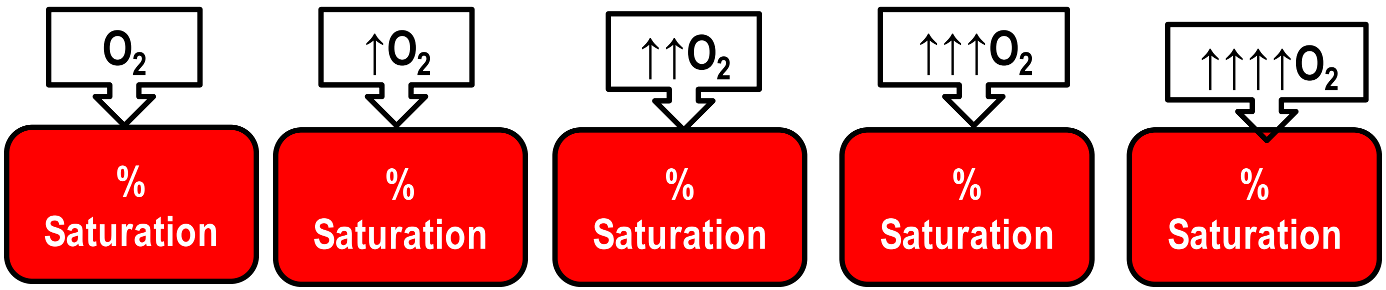
- In heavy exercise interstitial fluid Po_2= 15mm Hg (saturation = 22%)
- 20-folds increase in O_2 transport to tissues
  - 3-folds ↑ O_2 transport by each volume of blood
  - 6-7 folds increase in CO



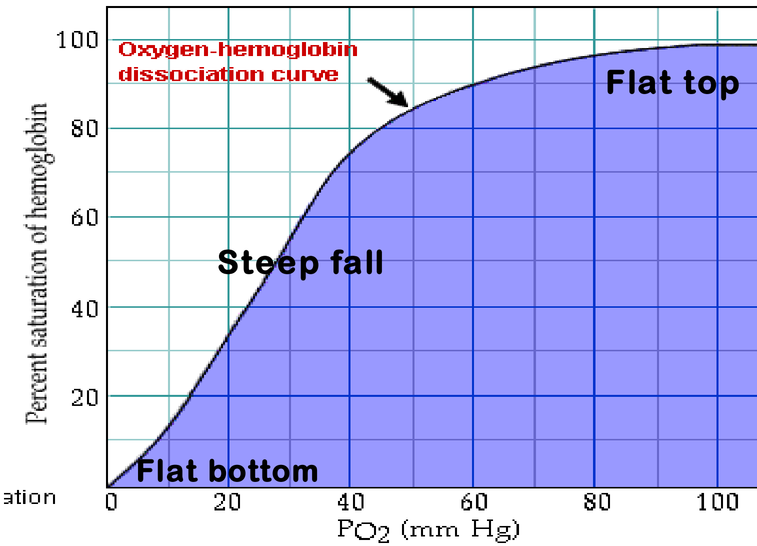
Combined O_2 ml/dL	Arterial blood, Po_2=95mmHg, Hb saturation 97%	Venous blood, Po_2=15mmHg, Hb saturation 22%	Amount of O_2 carried to tissues by each dL of blood (exercise)
Exercise	20.1×0.97=19.5 ml	20.1×0.22= 4.4ml	19.5 – 4.4=15.1ml
Rest	20.1×0.97=19.5 ml	20.1×0.75= 15.1ml	19.5 – 15.1=4.4ml

O_2-Hb dissociation curve

- Definition: curve relating percent O_2 saturation of Hb to the Po_2
- Procedure:
  - 10 tonometers are filled with a known quantity of blood having known Hb%

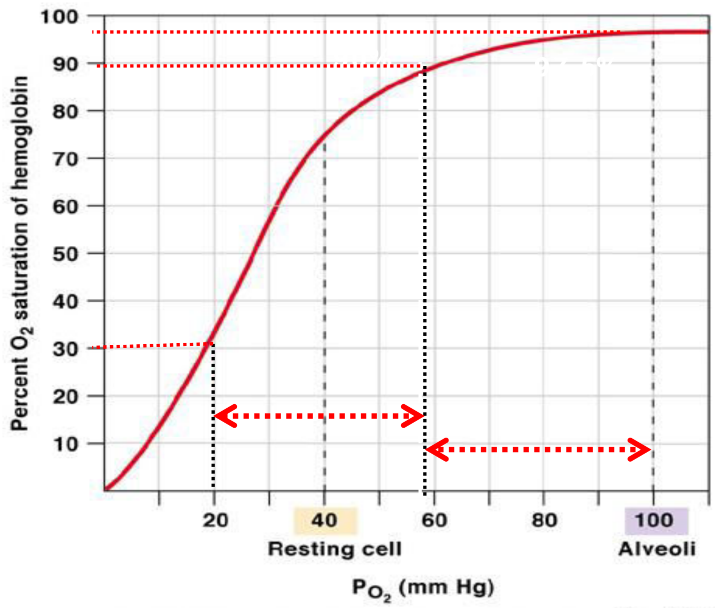


  - The blood in each tonometer is exposed to O_2 at different partial pr.
  - % Saturation of Hb with O_2 is measured.
  - PO_2 and % saturation are plotted→ O_2-Hb dissociation curve



- Shape: S (sigmoid) shaped .
  - High affinity at high O_2 tension (flat) & low affinity at low O_2 tension (steep)

Flat Top (Saturation phase) (PO_2 = 60-100 mmHg)



- ↓ Arterial PO_2 (low PO_2 in inspired air lung disease)→little change in % saturation of Hb
  - PO_2 100mmHg → 97% saturation
  - PO_2 60mmHg → 90% saturation
  - Safety margin for exchange of O_2 in lungs.
- ↑ PO_2 >100 mmHg → no significant increase in % saturation of Hb.

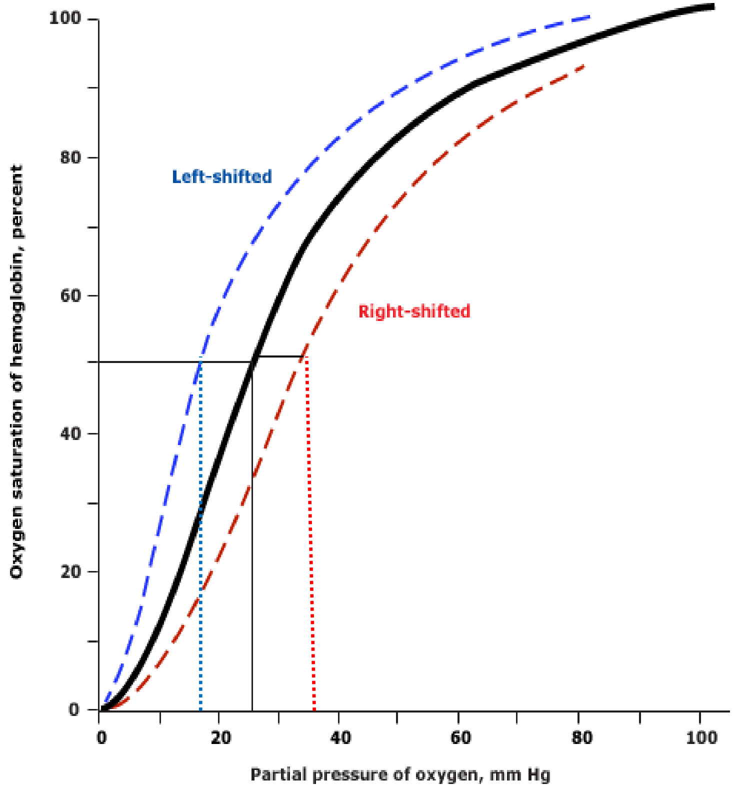
Steep fall (dissociation phase) (Po_2=20-60mm Hg)

- PO_2 = 60 mmHg → 90%
- PO_2 = 20 mmHg → 30%

- Small ↓ in PO_2 → great reduction in % saturation of Hb→ unloading of O_2 to tissues.

Changes in Hb-O_2 dissociation curve

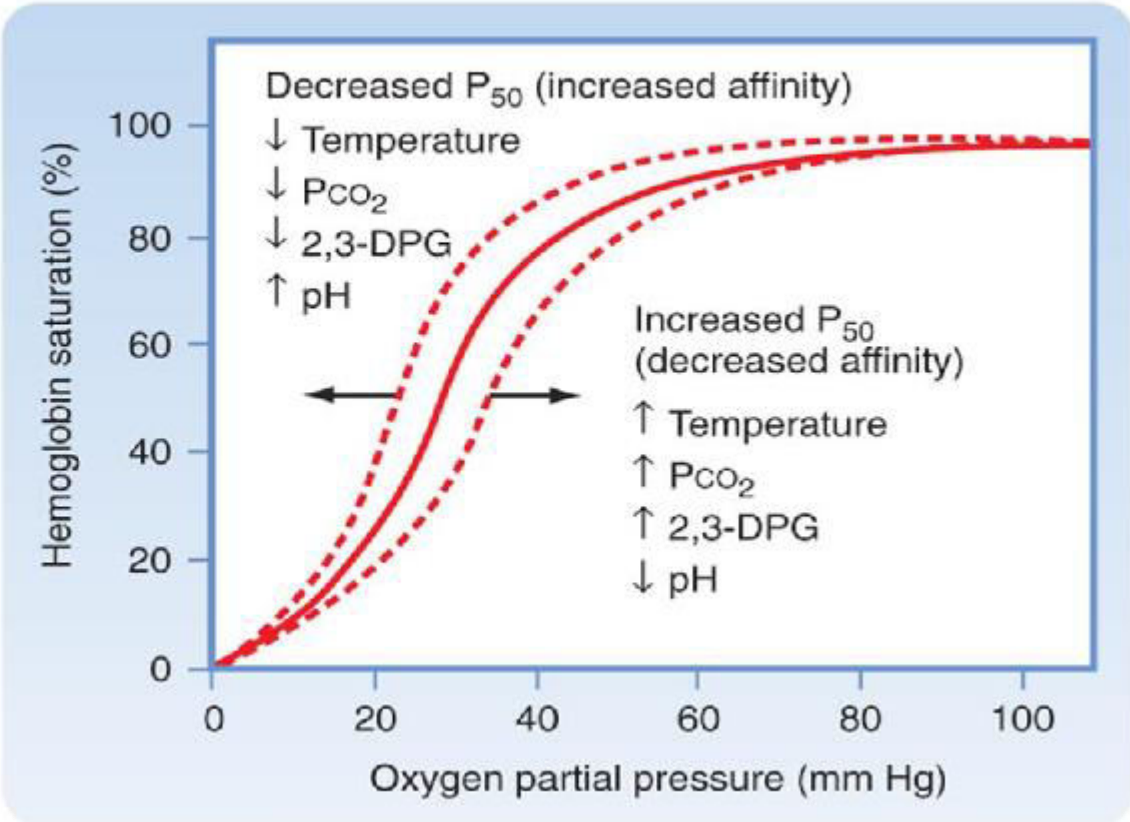
- The position of the O_2-Hb dissociation curve is not fixed & can vary by a few factors → changes in the affinity of Hb for O_2.
- The position of the curve can be defined by the PO_2 at which 50% of Hb is bound to O_2 (P_{50}).
- At normal body temp (37°C) arterial blood with a pH of 7.4, a PCO_2 of 40 mmHg, $P_{50} \approx$ 27 mmHg.
  - ↑P_{50}→↓affinity of Hb for O_2 → the curve is shifted to the right → unloading of O_2 to the tissues
  - ↓P_{50}→↑ affinity of Hb for O_2 → the curve is shifted to the left → unloading of O_2 to the tissues is more difficult



Shift to the right

⇩ Affinity (⇧ P_{50})⇨ unloading of O_2 to the tissues is facilitated.

The Shifting HbO_2 Dissociation Curve



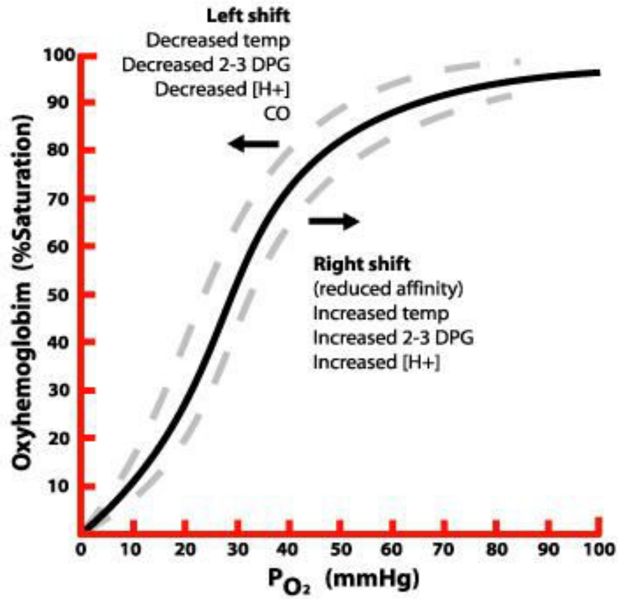
⦿ Causes:

1) ↑ PCO_2
2) ↑ H^+ (↓pH)
3) ↑ Temp
4) ↑ BPG

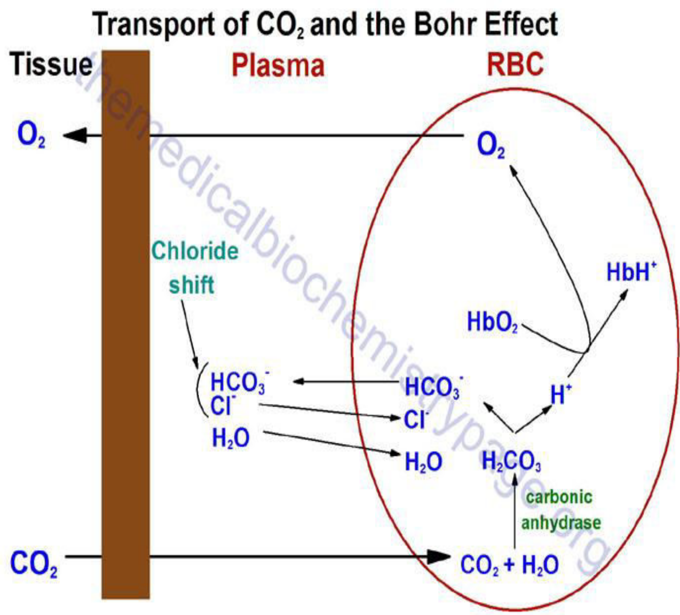
Shift to the right

⇩ Affinity (⇧ P_{50})⇨ unloading of O_2 to the tissues is facilitated.

⦿ ⇧PCO_2 ,⇧H^+ or ⇩ pH

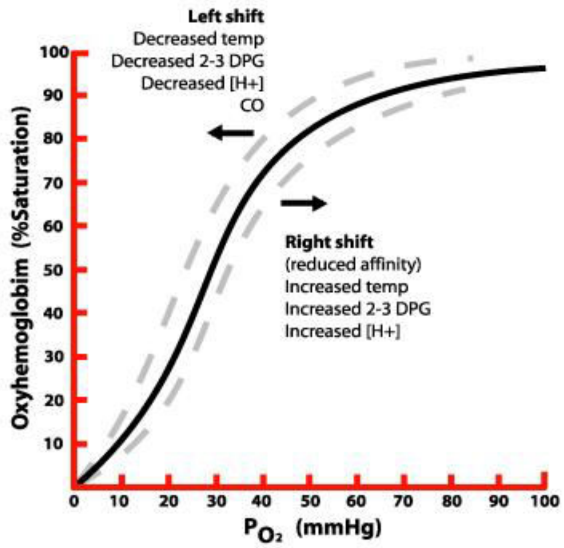


- Exercise: ↑CO_2 production ⇨↑ H^+ ⇨ ↓ pH⇨ shift to the right ⇨ ↑ O_2 delivery to the exercising muscles
- Bohr effect: ↓ in O_2 affinity of Hb when pH of blood falls (deoxy-Hb binds H^+ more actively than does oxy-Hb), deoxy-Hb is weaker acid and a strong buffer)
- Hb unsaturation in tissues:
  - ⇨ ↓ PO_2(98-99%)
  - ⇨ ↑PCO_2 in blood ⟶ ↓pH ⟶the curve shift to the right (1-2%)



⦿ ⇧ Temperature (e.g. exercise):

⦿ ⇧ 2,3-BPG concentration:

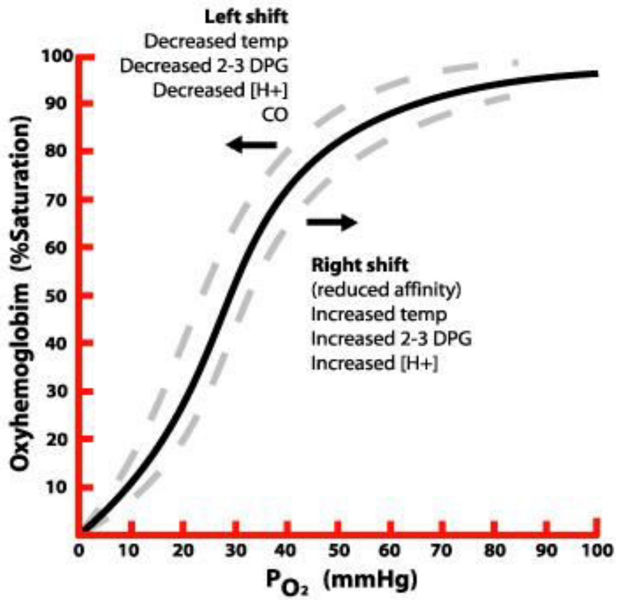


- 2,3-BPG is produced in RBC by glycolysis, is highly charged anion that binds to β chain of deoxy-Hb
- HbO_2 + 2,3-DPG → Hb-2,3-DPG + O_2
- Factors affecting 2,3-DPG
  1) pH of blood
     - ↓ pH → inhibit glycolysis → ↓ 2,3-DPG
     - ↑ pH → ↑ 2,3-DPG: high altitude (low PO_2) → hyperventilation → ↓ CO_2 → ↑ pH → ↑ 2,3-DPG
  2) T_3 &T_4, GH, androgens → ↑ 2,3-DPG
  3) Exercise → ↑ 2,3-DPG (60 minutes), ↑ temp, ↑ CO_2 → ↑ P_{50}
  4) Blood banking → ↓ 2,3-DPG

Shift to the left:

⇧ Affinity of Hb to O_2 → ↓ P_{50} → unloading of O_2 is more difficult.

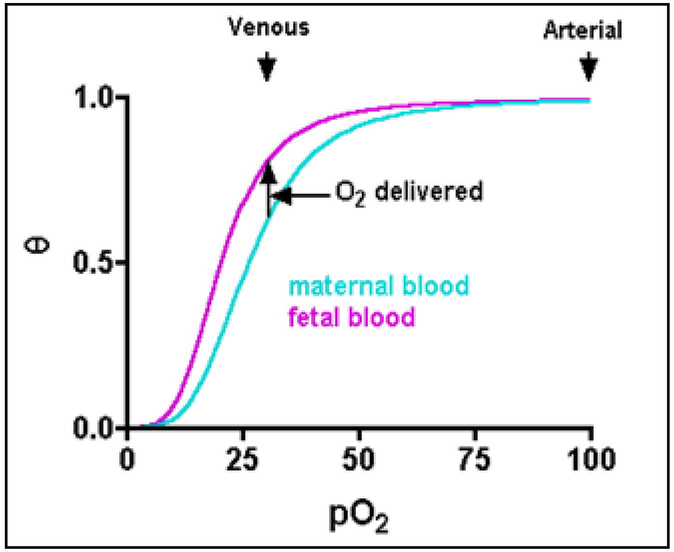
- Causes:
  1. ↓ $[H^+]$ ↓ PCO_2
  2. ↓ Temperature
  3. ↓ 2,3-BPG concentration
  4. Fetal hemoglobin
  5. CO



Fetal Hb (HbF) Adult Hb (HbA)

2α 2γ 2α 2β

← BPG →



- O_2-Hb dissociation curve of fetal Hb is to the left of adult Hb
  - ☛ Facilitates movements of O_2 from maternal to fetal blood

Carbon Monoxide (CO)

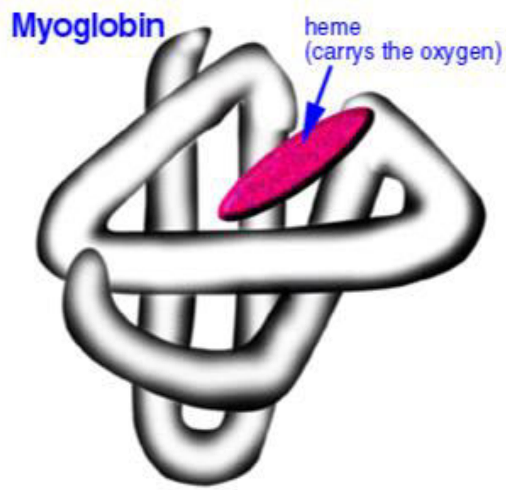
- The affinity of Hb for CO is 230 times that for O_2
  1) CO competitively blocks the combination of O_2 with Hb (Hb-CO)
  2) CO also shifts the O_2-Hb dissociation curve to the left

  1&2 → sever tissue hypoxia

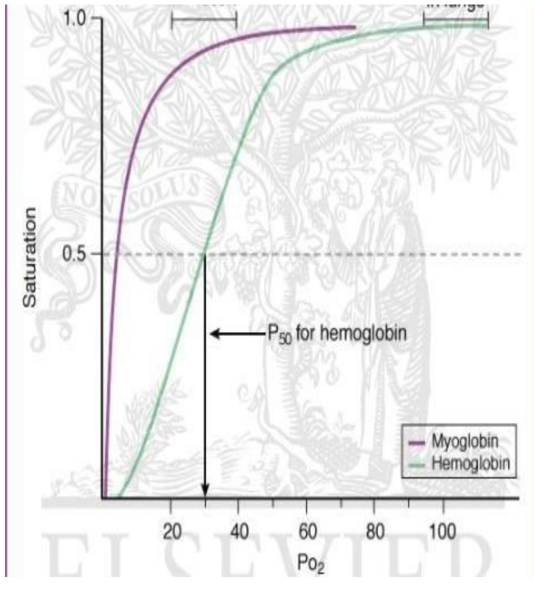
Pco	Hb-CO	$HB-O_2$
0.4mmHg (0.4 ÷ 760 = 0.05%)	50%	50%
0.7mmHg (0.7÷ 760 = 0.09%)	Most of hemoglobin is Hb-Co (lethal)	

- Treatment of CO poisoning:
  - Pure O_2 (high alveolar PO_2 displace CO from Hb)
  - Few % of CO_2 (stimulate respiration → hyperventilation → ↓ alveolar CO →↑CO release from Hb)

Myoglobin



- Iron-containing pigment in skeletal M
- One heme unit → one molecule of O_2
- Myoglobin does not show Bohr effect
- Myoglobin has a lower P_{50} than adult Hb
- The ODC for myoglobin is a rectangular hyperbola
  - The curve is to the left of Hb curve
  - It takes up O_2 from Hb and releases O_2 only at very low PO_2 values
- In exercise (sustained muscle contraction) → compression of blood vessels → ↓PO_2 in the muscle → (muscle utilizes O_2 in myoglobin)
  - Myoglobin acts as temporary store of O_2 in the muscle
  - A man of average size can store 1.5 L of O_2, in his myoglobin at rest



	Hemoglobin	**Myoglobin**
Location	RBC	Muscles (skeletal muscle)
Heme subunits	4	1
Binding with O_2	4 molecules	1 Molecules
Bohr effect	Show	Dose not show
P_{50}	27 mmHg	5 mmHg
ODC	Sigmoid shaped	Rectangular hyperbola

Blood substitutes:

- The solubility of O_2 in plasma is limited. Certain compounds dissolve much more O_2, can be used to totally replace blood for short period (emergency) until blood can be obtained and cross matched.