Oxygen and Carbon Dioxide Transport in Blood

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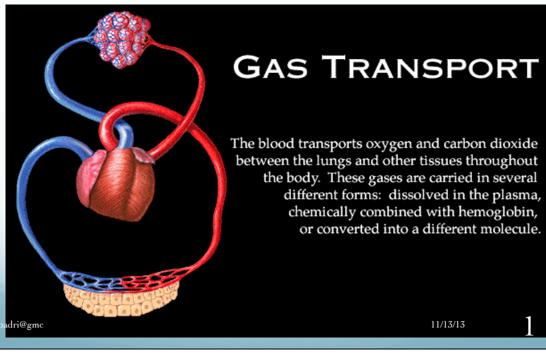
GMC

Introduction



Oxygen Transport

An understanding of oxygen transport is essential to the study of pulmonary physiology and to the clinical interpretation of arterial and venous blood gases.

Basic Mechanism of the Gases Transportation

Two forms of the gases: physical dissolution and chemical combination.

Most of oxygen and carbon dioxide in the blood is transported in chemical combination

Only the gas in physical dissolution express PP and diffuse to a place with low PP.

Dynamic balance between the two forms:

Physical dissolution $\underset{PP\downarrow}{\overset{PP\uparrow}{\rightleftharpoons}}$ Chemical combination

Normal Blood gas values

Arterial blood	Venous Blood
pH=7.35-7.45	pH=7.30-7.40
Pco2=35-45mmHg	42-48 mmHg
Po2=80-100mmHg	35-45 mmHg
HCO3-=22-28mEq/L	24-30 mEq/L

Oxygen Transport

- The transport of oxygen between the lungs and the cells of the body is a function of the blood and the heart.
- Oxygen is carried in the blood in two forms:
  - as dissolved oxygen in the blood plasma
  - chemically bound to the hemoglobin (Hb) that is encased in the erythrocytes, or RBC's

O2 Dissolved in Plasma

- As O2 diffuses from the alveoli into the pulmonary capillary blood, it dissolves in the plasma of the blood.
- At normal body and temperature about 0.003 ml of O2 will dissolve in 100 ml of blood for every 1 mm Hg of Po2
- Vol% represents the amount of O2 in milliliters that is in 100 ml of blood.
- In terms of total oxygen transport, a relatively small percentage of O2 is transported in the form of dissolved O2.

Dissolved Oxygen

- Henry's Law states that the amount of gas that dissolves is proportional to its partial pressure.
- Dissolved Oxygen=0.003 mls x PAo2
  0.003 x 100=0.3mls of dissolved O2

O_2 Bound with Hemoglobin

- Most of the O2 that diffuses into the pulmonary capillary blood rapidly moves into the RBC's and chemically attaches to the hemoglobin.
- Each RBC contains about 280 million Hb molecules, which are highly specialized to transport O2 and CO2.
- The normal hemoglobin value for the adult male is 14 to 16 g% and female is 12 to 15 g%.

Quantity of O2 Bound to Hb

- Each g% of Hb is capable of carrying approximately 1.34 ml of O2 thus:
- O2 bound to Hb = 1.34 ml O2 x g% Hb
- At a normal Pao2 of 100 MM Hg, hemoglobin saturation (Sao2) is about 97%because of normal physiologic shunts:

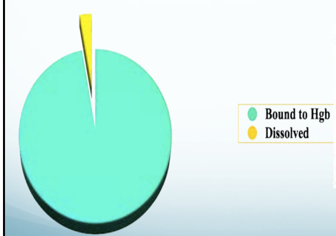
–thebesian veins (Coronary circ.)

-bronchial venous drainage

–V/Q mismatch

Oxygen Transport

Method	Percentage
Dissolved in Plasma	1.5 %
Combined with Hemoglobin	98.5 %



The Hemoglobin Molecule

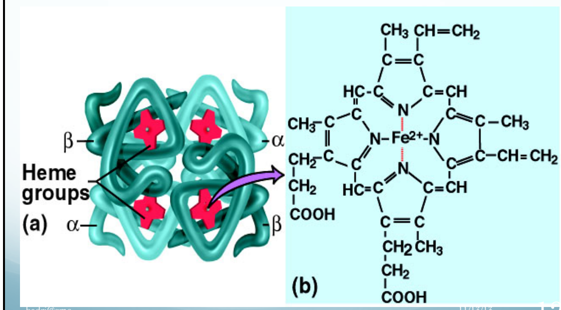
- Normal adult hemoglobin consists of:

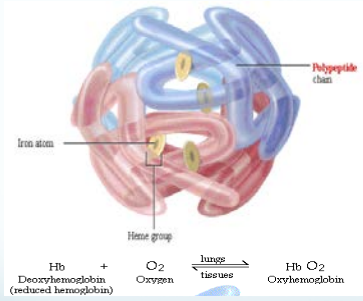
-four hemo groups which are the pigmented, iron-containing non-protein portions

-four amino chains that collectively constitute globin (a protein)

- At the center of each heme group, the iron molecule can combine with one O2 molecule for form oxyhemoglobin: Hb + O2 <> HbO2
- The amount of O2 bound to Hb is directly related to the partial pressure of O2.

Hemoglobin Structure





- Haemoglobin molecules can transport up to four O2's
- Oxygen binding occurs in response to the high PO2 in the lungs
- When 4 O2's are bound to haemoglobin, it is 100% saturated, with fewer O2's it is partially saturated.
- Co-operative binding: haemoglobin's affinity for O2 increases as its saturation increases.

Fetal Vs. Adult Hemoglobin

- The globin, or protein portion of each adult Hb molecule consists of two identical alpha chains and two identical beta chains.
- Normal fetal Hb (Hb F) has two alpha chains and two gamma chains.
- These gamma chains increase hemoglobin's attraction to O2 and facilitates transfer of maternal O2 across the placenta.
- Fetal Hb is gradually replaced with adult Hb (Hb A) over the first year of postnatal life.

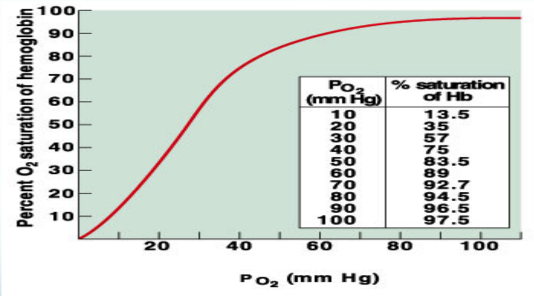
Basic Concepts:

Oxygen Capacity: The maximum quantity of oxygen that will combine chemically with the hemoglobin in a unit volume of blood;
normally it amounts to 1.34 ml of O_2 per gm of Hb or 20 ml of O_2 per 100 ml of blood.
Oxygen Content: how much oxygen is in the blood
Oxygen Saturation: A measure of how much oxygen the blood is carrying as a percentage of the maximum it could carry

Oxygen Dissociation Curve

- The O2 dissociation curve graphically illustrated the percentage of Hb that is chemically bound to O2 at each O2 pressure.
- The curve is S-shaped with a steep slope between 10 and 60 mm Hg and a flat portion between 70 and 100 mm Hg.
- The flat and steep portions of the curve each have a distinct clinical significance.

The oxygen-hemoglobin dissociation curve:



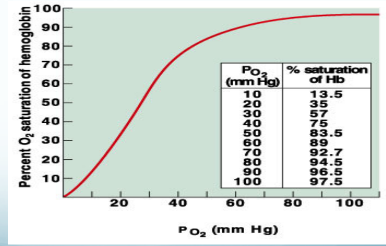
the curve relating percentage saturation of the O_2-carry power of hemoglobin to the PO_2.

The oxygen-hemoglobin dissociation curve

A. Flattened upper portion

B. Steep middle portion

C. Lower portion



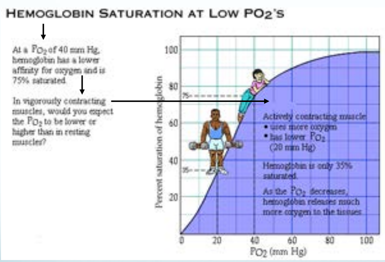
Significance of the Flat Portion

- The flat portion of the curve shows that the P02 can fall from 100 to 60 mmHg and the Hg will still be 90% saturated with 02
- At pressures above 60mm Hg, the standard dissociation curve is relatively flat. This means the oxygen content does not change significantly even with large changes in the partial pressure of oxygen.

Significance of Steep Portion

- PO2 reductions below 60 mm Hg produce a rapid decrease in the amount of O2 bound to hemoglobin.
- Clinically, when the PO2 falls below 60 mm Hg, the quantity of O2 delivered to the tissue cells may be significantly reduced.
- As oxygen partial pressures decrease in this steep area of the curve, the oxygen is unloaded to peripheral tissue readily as the hemoglobin's affinity diminishes.

Haemoglobin Saturation at Low Values



The P50

- A common point of reference on the oxygen dissociation curve is the P50.
- The P50 represents the partial pressure at which the hemoglobin is 50% saturated with oxygen, typically 26.6 mm Hg in adults.
- The P50 is a conventional measure of hemoglobin affinity for oxygen.

Shifts in the P50

- In the presence of disease or other conditions that change the hemoglobin's oxygen affinity and, consequently, shift the curve to the right or left, the P50 changes accordingly.
- An increased P50 indicates a rightward shift of the standard curve, which means that a larger partial pressure is necessary to maintain a 50% oxygen saturation, indicating a decreased affinity.
- Conversely, a lower P50 indicates a leftward shift and a higher affinity.

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Factors that effect the 02 Dissociation

- pH- Change in the blood pH
- Temperature-temp increases the curve moves to the right
- 2,3 Diphosphoglycerate-Increases 2,3 DPG results in decreased affinity
- Carbon monoxide
- 5. Fetal Hemoglobin

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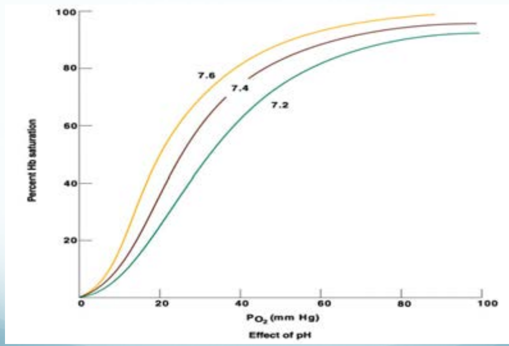
1. pH and PCO_2: Bohr effect



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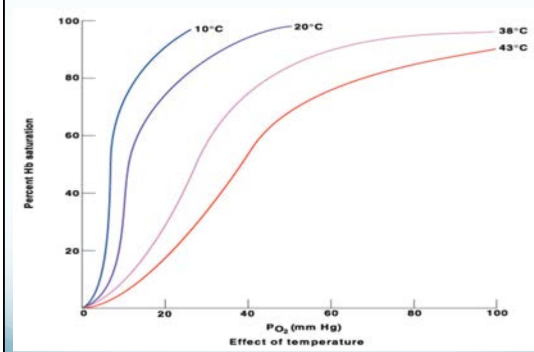
2. Temperature



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3. 2,3-diphosphoglycerate

A byproduct of anaerobic glycolysis.

Present in especially high concentration in red blood cells because of their content of 2,3-DPG mutase.

The affinity of hemoglobin for O_2 diminishes as the concentration of 2,3-DPG increase in the red blood cells.

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Importance:

The normal DPG in the blood …

Hypoxic condition that last longer than a few hours…

Disadvantage:

The excess DPG also makes it more difficult for the hemoglobin to combines with O_2 in the lungs.

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4. Effect of Carbon Monoxide (CO)

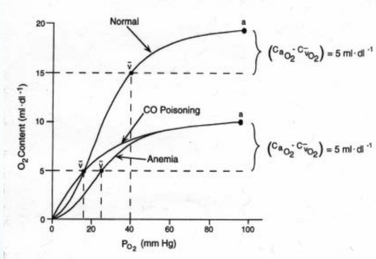
CO combines Hb at the same point as does O_2, and can displace O_2 from hemoglobin.

CO binds with about 250 times as much tenacity as O_2.

Therefore, a P_{CO} only a little greater than 0.4 mmHg can be lethal.

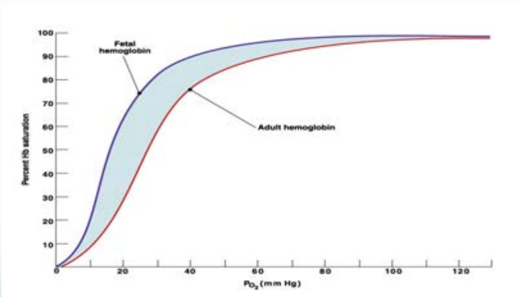
In the presence of CO (low concentration), the affinity of hemoglobin for O_2 is enhanced,

Effect of CO & Anemia on Hb-O_2 affinity



Normal blood with Hb=15 gm/dl, anemia with Hb=7.5 gm/dl, and normal blood with 50% COHb (carboxyhemoglobin).

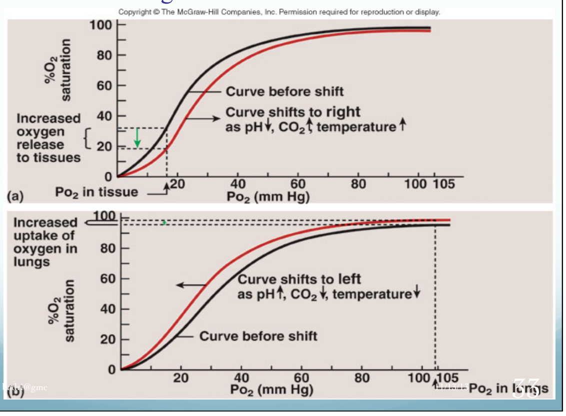
5. Fetal Hemoglobin



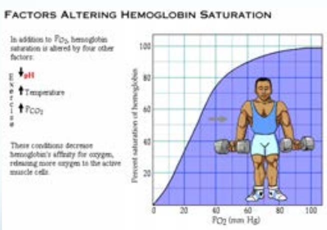
Advantage

Increased O_2 release to the fetal tissues under the hypoxic condition.

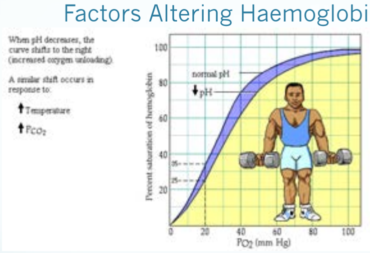
Shifting the Curve



Factors Altering Haemoglobin Saturation



Factors Altering Haemoglobin Saturation



Key Point

- Increased temperature and hydrogen ion (H^+) (pH) concentration in exercising muscle affect the oxygen dissociation curve, allowing more oxygen to be uploaded to supply the active muscles.

Carbon Dioxide Transport

- Carbon dioxide also relies on the blood for transportation. Once carbon dioxide is released from the cells, it is carried in the blood primarily in three ways…
- Dissolved in plasma,
- As bicarbonate ions resulting from the dissociation of carbonic acid,
- Bound to haemoglobin.

Carbon Dioxide Transport

Method	Percentage
• Dissolved in Plasma	7 - 10 %
• Chemically Bound to Hemoglobin in RBC's	20 - 30 %
• As Bicarbonate Ion in Plasma	60 -70 %

Dissolved Carbon Dioxide

- Part of the carbon dioxide released from the tissues is dissolved in plasma. But only a small amount, typically just 7 – 10%, is transported this way.
- This dissolved carbon dioxide comes out of solution where the PCO_2 is low, such as in the lungs.
- There it diffuses out of the capillaries into the alveoli to be exhaled.

Carbaminohemoglobin Formation

- Carbon dioxide molecule reversibly attaches to an amino portion of hemoglobin.

$$CO_2 + Hb \rightleftharpoons HbCO_2$$

Carbonic Acid Formation

- The carbonic anhydrase stimulates water to combine quickly with carbon dioxide.

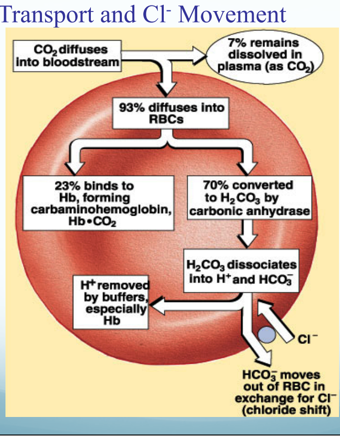
$$CO_2 + H_2 0 \rightleftharpoons H_2 CO_3$$

Bicarbonate Ion Formation

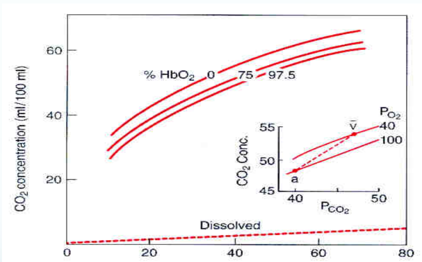
- Carbonic acid breaks down to release a hydrogen ion and bicarbonate.

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

CO_2 Transport and Cl^- Movement



Carbon Dioxide Dissociation Curve



Haldane effect

For any given PCO_2, the blood will hold more CO_2 when the PO_2 has been diminished.

Reflects the tendency for an increase in PO_2 to diminish the affinity of hemoglobin for CO_2.

Mechanism of Haldane effect

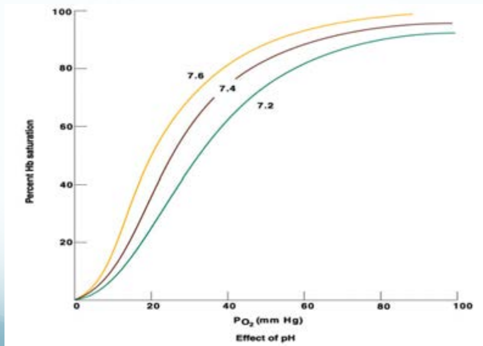
Combination of oxygen with hemoglobin in the lungs cause the hemoglobin to becomes a stronger acid. Therefore:

1)The more highly acidic hemoglobin has less tendency to combine with CO_2 to form CO_2 Hb

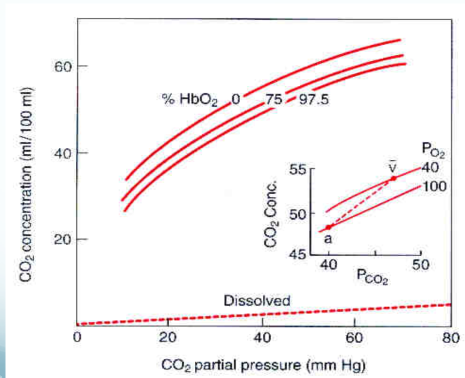
2)The increased acidity of the hemoglobin also causes it to release an excess of hydrogen irons

Interaction Between CO_2 and O_2 Transportation

1. Bohr effect



2. Haldane effect



In Review

1) Oxygen is transported in the blood primarily bound to haemoglobin though a small amount is dissolved in blood plasma.
2) Haemoglobin oxygen saturation decreases.
   1) When PO2 decreases.
   2) When pH decreases.
   3) When temperature increases.

   Each of these conditions can reflect increased local oxygen demand. They increase oxygen uploading in the needy area.

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In Review

3) Haemoglobin is usually about 98% saturated with oxygen. This reflects a much higher oxygen content than our body requires, so the blood's oxygen-carrying capacity seldom limits performance.
4) Carbon dioxide is transported in the blood primarily as bicarbonate ion. This prevents the formation of carbonic acid, which can cause H+ to accumulate, decreasing the pH. Smaller amounts of carbon dioxide are carried either dissolved in the plasma or bound to haemoglobin

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Clinical Significance of Shifts

- Individuals with PaO2's within normal (80-100) limits are rarely affected by shift changes.
- However, when a patients PaO2 falls below 80, a shift to the right or left can have remarkable effects on the hemoglobin's ability to pick up and release oxygen.

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Right Shifts

- Right shift decrease the loading of oxygen onto Hb at the A-C membrane.–– Decreased affinity
- The total oxygen delivery may be much lower than indicated by a particular Pao2 when the patient has some disease process that causes a right shift.
- Right shift curves enhance the unloading of oxygen at the tissue level.

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Left shift

- Left shift curves enhance the loading capability of oxygen enhance the loading capability of oxygen a the A-C membrane.
- The total oxygen delivery may be higher than indicated by a particular Pao2 when the patient has some disease process that cause a left shift.
- Left shift curves decreases the unloading of oxygen at the tissue level.

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"Zoo Psychiatrist"

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Tissue Hypoxia

- Tissue hypoxia means that the amount of oxygen available for cellular metabolism is inadequate.
- There are four main types of hypoxia:
  - hypoxic hypoxia - circulatory hypoxia
  - anemic hypoxia - histotoxic hypoxia
- Hypoxia leads to anaerobic mechanisms that eventually produces lactic acid and cause the blood pH to decrease.

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Hypoxic Hypoxia

- Hypoxic hypoxia or hypoxemic hypoxia refers to the condition in which the PaO_2 and CaO_2 are abnormally low.
- This form of hypoxia is better known as hypoxemia (low oxygen concentration in the blood).
- This form of hypoxia can develop from:
  - pulmonary shunting - low alveolar PO_2
  - diffusion impairment - V/Q mismatch

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Anemic Hypoxia

- Anemic hypoxia is when the oxygen tension in the arterial blood is normal, but the oxygen-carrying capacity of the blood is inadequate.
- This form of hypoxia can develop from:
  - a low amount of Hb in the blood
  - a deficiency in the ability of Hb to carry O_2
- Increased cardiac output is the main compensatory mechanism for anemic hypoxia.

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Circulatory Hypoxia

- In circulatory hypoxia, the arterial blood that reaches the tissue cells may have a normal O_2 tension and content, but the amount of of blood--and therefore the amount of O_2--is not adequate to meet tissue needs.
- The two main causes of circulating hypoxia are:
  - stagnant hypoxia
  - arterial-venous shunting

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Histotoxic Hypoxia

- Histotoxic hypoxia develops in any condition that impairs the ability of tissue cells to utilize oxygen.
- Clinically, the PaO_2 and CaO_2 in the blood are normal, but the tissue cells are extremely hypoxic.
- The PvO_2, CvO_2 and SvO_2 are elevated because oxygen is not utilized.
- One cause of this type of hypoxia is cyanide poisoning.

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Cyanosis

- When hypoxemia is severe, signs of cyanosis may develop.
- Cyanosis is the term used to describe the blue-gray or purplish discoloration seen on the mucous membranes, fingertips, and toes whenever the blood in these areas is hypoxemic.
- The recognition of cyanosis depends on the acuity of the observer, on the lighting conditions, and skin pigmentation.

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Polycythemia

- When pulmonary disorders produce chronic hypoxemia, the hormone erythropoietin responds by stimulating the bone marrow to increase RBC production.
- An increased level of RBC's is called polycythemia.
- The polycythemia that results from hypoxemia is an adaptive mechanism designed to increase the oxygen-carrying capacity of the blood.

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