Department of Anesthesia Techniques
Title of the lecture:- Oxygen transport

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Oxygen transport, Hb types

How is oxygen transported in the blood?

O2 is carried within the circulation from the lungs to the tissues in two forms:

Bound to Hb, accounting for 98% of O2 carried by the blood. Each gram of fully saturated Hb can bind 1.34 mL of O2 (this is called Hüfner's constant).

Dissolved in plasma, accounting for 2% of O2 carried by the blood. The volume of O2 dissolved in blood is proportional to the partial pressure of O2 (this is Henry's law).

Arterial oxygen content = oxygen bound to hemoglobin + oxygen dissolved in plasma
Arterial oxygen content (CaO2) = (hemoglobin)(oxygen saturation) (1.34) + (PaO2) (0.031)

The usual arterial oxygen saturation is close to 100%, and PaO2 is approximately 90 mmHg. Arterial blood normally contains approximately 200 mL of oxygen per liter of blood. If we assume a cardiac output of ~5 L/min then this is an oxygen delivery of ~1 L/min.

The above worked example demonstrates that Hb is a much more efficient means of O2 carriage than O2 dissolved in plasma. However, it would be wrong to think that dissolved O2 is unimportant. The O2 tension of blood is determined from the amount of O2 dissolved in plasma – the PO2 within an RBC is low because all the O2 is bound to Hb. Fick's law of diffusion states that diffusion occurs along a pressure gradient, so O2 diffuses to the tissues from the dissolved portion in the plasma, not from Hb itself. O2 then dissociates from Hb as plasma PO2 falls, replenishing the O2 dissolved in the plasma.

Oxygen consumption Oxygen is carried to the tissues and delivered to cells via the capillaries, where oxygen is taken up (consumed) by cells, so that venous blood contains less oxygen (and more carbon dioxide) than arterial blood. The partial pressure of oxygen in the venous blood (PvO2) is, on average, ~40 mmHg (this corresponds to an oxygen saturation of ~70–75% in the venous blood).

The overall oxygen content of venous blood is ~150 mL of

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oxygen/liter of blood. Overall oxygen consumption is ~250 mL of oxygen per minute; if delivery is ~1 L/min this means we usually extract about 25% of the oxygen delivered. Oxygen consumption (demand) will increase with exercise or fever Sedation, paralysis and hypothermia decrease oxygen consumption.

How do the body's oxygen stores compare with its consumption of oxygen?

Very little O2 is stored in the body, which means that periods of apnoea can rapidly lead to hypoxia. In addition to O2 in the lungs (within the FRC), O2 is stored in the blood (dissolved in plasma and bound to Hb) and in the muscles (bound to myoglobin).

As described above, approximately 20 mL of O2 is carried in each 100 mL of arterial blood, and 15 mL of O2 per 100 mL of venous blood. At sea level, a 70 kg man has approximately
5 L of blood, containing approximately 1000 mL of O2 ;
An adult's resting O2 consumption is approximately 250 mL per minute, which means that apnea can occur for only a few minutes before the onset of significant cellular hypoxia. Hypoxic damage occurs even more quickly when there is reduced O2 -carrying capacity (for example, anemia or carbon monoxide poisoning) or an increased rate of O2 consumption (for example, in children).

What is the oxyhaemoglobin dissociation curve?

The oxyhaemoglobin dissociation curve describes the relationship between SaO2 and blood O2 tension. As discussed above, the cooperative binding of Hb is responsible for the curve's sigmoid shape, which has important clinical consequences:

The upper portion of the curve is flat. At this point, even if PaO2 falls a little, SaO2 hardly changes. However, when PaO2 is already pathologically low (for example, in patients with respiratory disease) and near to the steep part of the curve, a further fall in PaO2 results in a large decrease in SaO2 .

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The steep part of the curve is very important in the peripheral tissues, where PO2 is low: the steep fall in SaO2 means a large quantity of O2 is offloaded for only a small decrease in PO2 .

The position of the oxyhaemoglobin dissociation curve is described by the P50 value – the PO2 at which 50% of Hb is bound to O2 . When the position of the curve moves to the right, the affinity of O2 for Hb is reduced – O2 is more easily offloaded (that is, for a given PO2 , SaO2 is lower). Rightward shift is caused by:

increased PCO2 ;
acidosis;
increased 2,3-diphosphoglycerate (2,3-DPG) concentration.
exercise;
increased temperature;
the presence of HbS in sickle cell disease. (Mnemonic: CADETS – CO2 , acidosis, DPG, exercise, temperature, sickle cell disease.) This rightward shift of the curve is an important physiological mechanism:

The Bohr effect: Metabolically active tissues produce CO2 , heat and H+ ions. When blood arrives at these capillaries, the oxyhaemoglobin dissociation curve is shifted to the right, offloading O2 where it is most needed. This phenomenon is called the 'Bohr effect' or Bohr shift.

Anaerobic metabolism: When cellular PO2 falls below a threshold value, anaerobic metabolism predominates. Energy is produced through the
breakdown of glucose to pyruvate (in a process called glycolysis) which is then converted to lactate. One of the intermediates of the glycolytic pathway is converted to 2,3-DPG in a side pathway. This is thought to be controlled by an O2 -sensitive enzyme in the glycolytic pathway, likely phosphofructokinase. The greater the extent of anaerobic metabolism, the greater the 2,3-DPG concentration. 2,3-DPG binds specifically to the β-chains of deoxyhaemoglobin, stabilizing this configuration , thus reducing the O2 binding affinity of Hb. This mechanism means that additional O2 is offloaded to cells undergoing anaerobic metabolism.

O2 loading in the lungs. When blood reaches the lungs, CO2 is excreted and the pH normalizes. The P50 of the oxyhaemoglobin

dissociation curve then returns to its central position. The binding affinity of O2 therefore increases: dissolved O2 binds to Hb, which in turn lowers the blood O2 tension, facilitating O2 diffusion across the alveolar–capillary barrier. The oxyhaemoglobin dissociation curve is shifted to the left by the following:

the reverse of the above – that is, low PCO2 , alkalosis, reduced 2,3-DPG levels, hypothermia;

carboxyhaemoglobin (COHb);

methaemoglobin (MetHb);

fetal Hb (HbF). Leftward shift of the oxyhaemoglobin dissociation curve results in an increase in O2 binding affinity. This is an important physiological mechanism in fetal life. HbF must be able to extract O2 from maternal oxyhaemoglobin – HbF must therefore have a higher O2 binding affinity than maternal Hb. This is achieved by two mechanisms:

HbF causes a leftward shift in the oxyhaemoglobin dissociation curve, increasing O2 binding affinity.

While 2,3-DPG is present in fetal RBCs, it cannot bind to HbF: 2,3-DPG is only bound by β-globin chains, not the fetal γ-chain. This mechanism further increases the binding affinity of HbF for O2 .

Clinical relevance: blood transfusion Erythrocyte 2,3-DPG concentration rapidly decreases in stored blood, and is effectively zero after 1–2 weeks' storage. Low 2,3-DPG concentration shifts the oxyhaemoglobin dissociation curve to the left, increasing O2 binding. When stored blood is transfused, it takes up to 24 h for erythrocyte 2,3-DPG concentration to return to normal. The increased O2 binding affinity means that transfused blood is not as effective at offloading O2 as native blood. In the anaemic patient facing major surgery, it may be advantageous to transfuse blood 24 h prior to surgery rather than intraoperatively, to gain the full benefit of the transfusion. In contrast, cell-salvaged blood maintains almost all of its 2,3-DPG; O2 binding affinity and O2 offloading are unaffected.

What other forms of haemoglobin are there?

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Types of Hb may be classified as physiological or pathological.

Physiological:

– HbA, which, as discussed above, is the most common form, has two α and two β globin subunits (α2β2).

– HbF is the normal variant during fetal life and is composed of two α and two γ globin subunits (α2γ2). HbF has a higher affinity for O2 than HbA, and may therefore displace O2 across the placenta from maternal blood

HbF is produced up to 3 months of age, when γ globin synthesis switches to the adult β globin; by 6 months of age, all HbF should have been replaced by normal adult variants. However, HbF can persist in conditions where β-globin synthesis is impaired; for example, beta-thalassaemia.

Pathological:

– HbS. Found in people with sickle cell disease, HbS has an abnormal β-globin subunit: a point mutation, where glutamate has been replaced by valine at the 6th position.

– MetHb. Methaemoglobinaemia is where the ferrous iron (Fe2+) within the Hb molecule is oxidized to ferric iron (Fe3+). Fe3+ cannot bind O2 , so MetHb cannot participate in O2 transport.

– COHb. This is formed when Hb binds inhaled carbon monoxide molecules.

– CyanoHb. Cyanohaemoglobin is formed when Hb is exposed to cyanide ions.

Clinical relevance:

anaesthesia for patients with sickle cell disease The principles of management are:

Identifying undiagnosed sickle cell disease. Sickle cell status may not be known by the patient: all patients of at-risk ethnic backgrounds should be tested. Formal screening test is by Hb electrophoresis, but in an emergency the rapid ‘sickledex test’ can be used (but it cannot distinguish sickle cell trait from sickle cell disease).

Preoperative optimization:

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– Identification and optimization of end-organ dysfunction: abnormal physiology; for example, hypoxia, acidosis, hypothermia or hypotension should be addressed.
– Exchange transfusion is sometimes undertaken before major elective surgery, but there is rarely sufficient time before emergency surgery
Intraoperative management:
– Avoidance of known sickling precipitants: hypoxia, acidosis, hypothermia and hypotension.
– Tourniquets are traditionally avoided, but are occasionally used if the benefits outweigh the risk of precipitating sickling.
– Regional anaesthesia has many advantages over general anaesthesia, but neuraxial blockade risks hypotension. Postoperative management:
– Patients should be managed in a highdependency unit, given supplemental O2 and kept warm and well hydrated.
– Analgesia can be challenging, as sickle cell patients are rarely opiate naive.