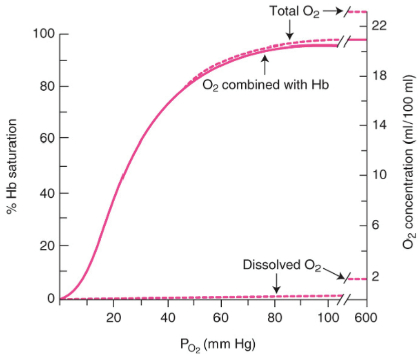
GAS TRANSPORT IN THE BLOOD

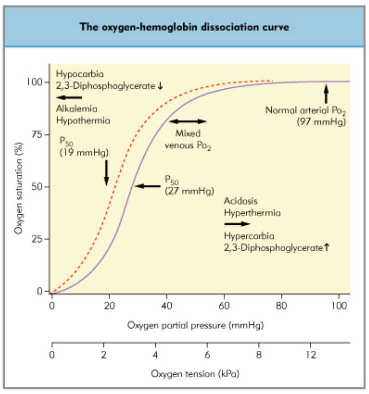


Carriage of oxygen in the blood Oxygen is carried in the blood in two forms: dissolved and combined with hemoglobin. Dissolved O2 obeys Henry's law, that is, the amount dissolved is proportional to the partial pressure. For each mm Hg of PO2 there is 0.003 ml O2 per 100 ml of blood. Thus, normal arterial blood with a PO2 of 100 mm Hg contains 0.3 ml O2 per 100 ml.

Haemoglobin is a tetramer of heme with four globin chains (two alpha and two beta). Each molecule is capable of binding four molecules of O2 to heme. From this observation, and from the molecular weight of Hb (63 500 Da) it is possible to calculate that at 100% Hb saturation (all sites occupied) 1.39ml of O2 will combine with 1g of Hb. The measured value of 1.34 is slightly less due to some of the Hb occuring in the ferric form (metHb) and carboxyHb and sulphHb which is unable to bind O2.

It is possible therefore to calulate the bound O2 by the formula

O2 bound = [Hb] x SaO2 x 1.34	the normal value is 140 x 0.975 x 1.34 = 183 ml per litre (often quoted as 18-20 ml per 100ml)
O2 Delivery = Cardiac Output (O2 bound + O2 dissolved)	the normal value is 5(183 + 3) = 930ml (often quoted as 1000ml per minute)



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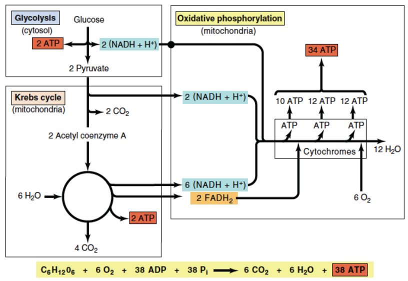
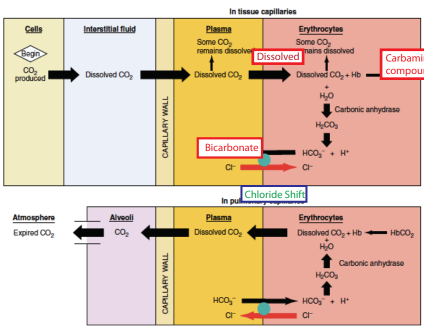
O2 Dissociation Curve Whilst the amount of O2 dissolved has a linear relationship with the PO2 (Henry's Law) the amount of O2 bound to Hb does not. Haemoglobin exists in two conformational states the 'T' or Tense state which has a low affinity for O2 and the 'R' or relaxed stated which has a high affinity for O2 binding. The electrostatic binding of a single O2 to a deoxyhaemoglobin leads to a conformational change to the R state. Additional O2 groups may be then added until full saturation, the dissociation constant of the last step $Hb(O2)_3 \rightarrow Hb(O2)_4$ is much higher than the others which compensates for the reduced binding sites and the slowing caused by the law of mass action. As a result of the complex kinetics of the chemical reaction between oxygen and haemoglobin, the relationship between Po2 and percentage saturation is non linear, and the precise form of the non linearity (a sigmoid curve) is of fundamental biological importance.

When assessing the influence of various factors on the O2-Hb dissociation curve the P50 (pressure at 50% saturation) is often used as a reference point. An increased P50 results from a right shift and decrease in O2 affinity, a decreased P50 indicates a left shift and increased O2 affinity. When O2 is unloaded the beta chains pull apart. This allows the glycolytic metabolite 2,3 diphosphoglycerate (DPG) to slide between and bind, resulting in lower affinity of haemoglobin. The importance of this step has been overstated in the past although it remains important for transfused blood with minimal DPG. Several other factors lead to a propensity towards the T conformation and a lower affinity. The Bohr effect has important effects within physiological ranges and results from the transfer of CO2 and subsequent change in pH. This occurs along capillaries and although the actual change in CO2 and pH is small, it has been suggested that up to 25% of the uploading of O2 to Hb in the pulmonary capillaries and offloading in the systemic circulation is due to the Bohr effect. Temperature has a large effect on the dissociation curve with an increase causing a right shift and offloading of O2 (which occurs in warm exercising muscles) and a left shift in cold tissues.

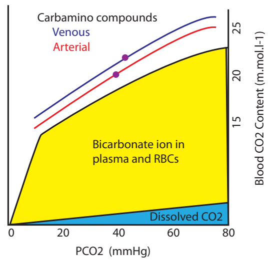


Carbon dioxide is the end product of metabolism. Glucose is converted to CO2, H2O and energy according to the formula $C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O$ + energy. The actual process is a three stage conversion of glucose via glycolysis into lactate/pyuvate, conversion via the Krebs cycle and finally oxidative phosphorylation pathway within the mitochondria creating a total of 38 units of ATP. Carbon dioxide is therefore at its highest concentration at the mitchondria and follows a reverse path to oxygen down partial pressure gradients to the lungs (noting however that despite the lesser change in partial pressures, the increased solubility makes the exchange similar to O2 250ml to 200ml per minute respectively).

Carbon dioxide carriage in blood occurs in three main forms; dissolved, in the bicarbonate ion and bound to Hb as carbamino compounds. 1. Dissolved CO2, like O2, obeys Henry's law, but CO2 is about 20 times more soluble than O2, its solubility being 0.067 ml per dL per mmHg. As a result, dissolved CO2 plays a significant role in its carriage in that about 5-10% of the gas that is evolved into the lung from the blood is in the dissolved form. The dissolved CO2 reacts with water to form carbonic acid. This is usually a very slow reaction and does not occur to any significant effect in the plasma. In the red blood cells however the presence of carbonic anhydrase catalyses the reaction leading to rapid production of carbonic acid. This then dissociates rapidly to the bicarbonate ion and hydrogen ions. The Bicarbonate ion then leaves the red blood cell, however the ionic H+ remains. To balance the charge of the RBC a phenomenon known as chloride shift occurs with Cl moving into the RBC. Bicarbonate is the most important step accounting for approximately 70-90% of CO2 carriage. In addition to reacting with H2O, CO2 also reacts with the exposed amine groups of Hb to form carbaminocompounds. This occurs in a greater exent in RBCs but does also occur in the plasma. Carbamino compounds contribute approximately 20-30% to CO2 carriage.



The Hb characteristics discussed above relating to electrostatic bonds and conformational changes of Hb also have an influence on CO2 carriage. This is known as the Haldane effect and results in improved CO2 carriage in the deoxygenated conformations rather than the oxygenated forms of Hb. This enables better uploading of CO2 from the tissue and offloading at the lungs.



Carbon dioxide dissociation curve Several important features are noted from the CO2 dissociation curve. Firstly, within physiological ranges the curve is mostly linear. Secondly, whilst bicarbonate and dissolved CO2 increase in a linear fashion according to PCO2 levels carbamino compounds vary mainly in respect to the oxygenation of the blood as evidenced by the seperate lines according to arterial and venous blood. This is the component of the Haldane effect discussed above (the other relates to the improved buffering of deoxygenated haemoglobin).

Oxygen and Carbon Dioxide stores The quantity of carbon dioxide and bicarbonate ion in the body is very large - about 120 litres, which is almost 100 times greater than the volume of oxygen. Therefore, when ventilation is altered out of accord with metabolic activity, carbon dioxide levels change only slowly and new equilibrium levels are attained after about 20-30 minutes. In contrast corresponding changes in oxygen are very rapid. In spite of great biological importance, oxygen is a very difficult gas to store in a biological system. Hb is the most efficient chemical carrier, but total blood volume usually carries only 1000ml of O2. The concentration of O2 in blood far exceeds the concentration of any other body fluid. Even so, the quantity of O2 in the blood is barely sufficient to last three minutes metabolism at the resting state. Other stores include the lungs which have approximately 500ml (breathing 100% O2 increases this to 3000ml - hence pre-oxygenation in anaesthesia), dissolved in tissues around 50ml and in myoglobin 200ml. In comparison to the 120 litres of CO2, the stores of O2 equate to only 1.75 litres.

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