Life 25 - Control of respiration – Raven & Johnson Ch 9 & 53 (parts)

Objectives

1: Understand the action of allosteric enzymes in regulating glycolysis and aerobic respiration in cells.

2: Describe how carbon dioxide is transported from tissues to lungs.

3: Understand how the Bohr effect augments oxygen delivery to the tissues.

4: Describe the effects of decreased oxygen and increased carbon dioxide on ventilation of aquatic and terrestrial animals.

5: Explain why aquatic and terrestrial animals use different stimuli to control gas exchange.

Control of cellular respiration

Content of ATP in cells is limited, enough for a few seconds use, must be replenished from ADP by cellular respiration

When ATP is high, key reactions of glycolysis and aerobic respiration are inhibited, slowing ATP production. Feedback inhibition of the pathways

When ATP is low, ADP is high, stimulates carbohydrate catabolism to produce ATP

Glycolysis. The enzyme phosphofructokinase (PFK) catalyses reaction (3),

Fructose 6-phosphate + ATP $\leftrightarrow$ Fructose 1,6-biphosphate + ADP

Reaction lies to the right, not easily reversible, commits substrate to glycolysis

High ADP stimulates PFK, commits more sugar to catabolism. Conversely, high ATP inhibits PFK and slows glycolysis. (Fig. 9.20)

High level of citrate also inhibits PFK. High citrate implies that the Krebs cycle is fully active and does not need further input

Note that Raven & Johnson is confusing here – high citrate inhibits, not low citrate stimulates PFK, low citrate only activates by reducing inhibition

Action of ADP & ATP on PFK is the reverse pattern for normal enzyme kinetics. Usually forward reaction increased by high reactants, reverse reaction increased by high products

Regulatory enzymes have 2 or more active sites – allosteric ("other site") enzymes. One site for catalysis, separate site(s) for modulator(s)

Modulators are molecules (may be unrelated to the reactants or products in the catalysed reaction) that stimulate or inhibit an allosteric enzyme

ATP is a reactant but also an inhibitory modulator of PFK. ADP is a product but also a stimulatory modulator of PFK. Citrate is also an inhibitory modulator of PFK, unrelated to the catalytic reaction

Aerobic respiration. Main regulation of oxidation of pyruvate is at pyruvate decarboxylase, the committing step for carbohydrates to enter the Krebs cycle

Pyruvate decarboxylase is inhibited by a high level of NADH, implying that no more Krebs cycle activity is needed

Krebs cycle also regulated at reaction (1), the combination of oxaloacetate and acetyl-CoA to give citrate. This is catalysed by citrate synthetase, which is inhibited by high ATP. Note arrow has wrong direction in Fig. 9.20

Inhibition stops acetyl-CoA entering the Krebs cycle, and thus ATP production from the electron transport chain. Acetyl-CoA is channelled to fatty acid synthesis for fat storage instead

Control of gas exchange

Physiology of respiration involves an exchange of gases. Oxygen taken up at respiratory surface, circulated to tissues, used, CO_2 produced, transported back to respiratory surface, released (Fig. 53.11)

If the need for oxygen increases due to activity, or its availability in the environment decreases, the ventilation of the gills or lungs must increase

Most aquatic animals use oxygen at the gills as the stimulus to control ventilation; includes annelids, molluscs, crustaceans and fish

E.g. lugworm *Arenicola* (annelid), decrease in O_2 increases ventilation of burrow (OHP Figure)

Increase in CO_2 may have no effect or only slightly increase ventilation in aquatic animals. It may even decrease ventilation due to narcotic effects on nerve cells (e.g. aquatic crab)

But the land crab increases ventilation with increasing CO_2. Also found in insects (opening of spiracles) & land vertebrates. Ventilation is closely linked to oxygen need, but the main stimulus is not lack of oxygen, but build up of CO_2

Can see this by giving animals gases of different composition to breathe. A decrease in oxygen of 8% has only a slight effect, but an increase in CO_2 of 8% increases the ventilation volume several times (OHP Figure)

Why do aquatic and land animals use different stimuli for control? Two major differences between water & air environments:

1: **Variation in levels of gases**. In the open air the levels of oxygen and CO_2 are very stable. Ventilation only needs to be controlled to give extra oxygen for activity, not for environmental changes

CO_2 will be produced in proportion to the oxygen consumed. The level of internal CO_2 is thus an indicator of oxygen demand in a land animal

In water the levels of the gases can change greatly with temperature, decomposition, photosynthesis. Data for gases in water in a rock pool. Normal tension in seawater shown by green line (OHP Figure)

Daytime increase in oxygen and decrease in CO_2 due to photosynthesis. Then tide mixes with seawater. Night time decrease in oxygen and increase in CO_2 due to respiration

In this case CO_2 and oxygen are inversely related, but they need not be. Increase or decrease together for temperature change. So the level of CO_2 cannot be used as an indicator of oxygen availability

2: **Difference in the build up of CO_2** in the tissues. When the gas exchange of an animal is at equilibrium, the CO_2 lost must correspond to the oxygen consumed

The increase in the partial pressure (P) of CO_2 in the medium can be calculated from the decrease in the partial pressure of oxygen in the medium, according to the equation:

$$P_{CO_2}^{e} - P_{CO_2}^{i} = \frac{\alpha\ O_2}{\alpha\ CO_2} \ .\ \frac{\text{moles } CO_2}{\text{moles } O_2} \ .\ (P_{O_2}^{i} - P_{O_2}^{e})$$

The equation relates partial pressures of CO_2 and oxygen in exhaled and inhaled medium, solubility (α) of CO_2 and oxygen, and molar ratio of CO_2 produced to oxygen consumed

Latter is the respiratory quotient RQ. This varies from about 0.7 to 1.0 depending on the diet - for simplicity use a value of 1.0, which would be given by carbohydrates

The equation calculates the increase in P_{CO_2}, but when the inhaled P_{CO_2} is nearly zero, it calculates the partial pressure of CO_2 in the exhaled medium

Look at an animal in water that depletes the oxygen tension from 159 to 100 mmHg. In water the solubility of CO_2 is 30 times the solubility of oxygen. The tension of CO_2 in the exhaled water will be 2 mmHg:

$P_{CO_2} = 1/30 \ .\ 1 \ .\ (159-100) = 2$ mmHg

Now look at a land animal. Oxygen and CO_2 are equally soluble in air, so depleting the oxygen partial pressure by 59 mmHg will give a CO_2 partial pressure of 59 mmHg:

$P_{CO_2} = 1 \ .\ 1 \ .\ (159-100) = 59$ mmHg

Comparing an aquatic and a land animal excreting the same quantity of CO_2 (in moles) …

But the partial pressure in the exhaled medium is much lower for the aquatic animal, because of the different solubility of oxygen and CO_2 in water

Why should the partial pressure of CO_2 in the exhaled medium matter to an animal?

Because for CO_2 to be lost at the gill or lung, its tension in the blood must be slightly greater than the partial pressure in the exhaled medium

So the tension of CO_2 in the blood of an aquatic animal is much lower than in the blood of a land animal. The CO_2 in solution forms carbonic acid, which dissociates into bicarbonate and hydrogen ions and lowers blood pH

Now consider what happens if oxygen consumption is increased, without a change of ventilation. Say that the oxygen tension in the exhaled medium decreases from 100 to 80 mmHg

This corresponds to about a 1/3 increase in oxygen consumption, from a depletion of 59 mmHg to 79mmHg

At equilibrium, the CO_2 tension in the exhaled water will be 2.7 mmHg:
P_{CO_2} = 1/30 . 1 . (159–80) = 2.7 mmHg

The blood CO_2 tension will also rise to the same level. The change in CO_2 tension from 2 to 2.7 mmHg would lower pH by about 0.014 units

In the land animal the CO_2 partial pressure in the exhaled air will be 79 mmHg:
P_{CO_2} = 1 . 1 . (159–80) = 79 mmHg

The blood tension will rise to this level. The change in CO_2 tension from 59 to 79 mmHg would lower pH by about 0.4 units. This would be lethal, as pH is normally kept within a narrow range

Different stimuli are therefore used to control ventilation in water and on land:

In water, CO_2 does not build up appreciably in the tissues, and the effect on pH is fairly small

On the other hand CO_2 in the inhaled water can be very variable, and not linked to oxygen lack. It is best to control ventilation directly using oxygen

On land, blood pH could vary substantially with the level of CO_2, so it is important to control this. Increased ventilation will lower blood carbon dioxide, and will automatically increase oxygen uptake

CO_2 levels in air are very stable and so will not upset the system, and oxygen levels are also stable so no need to monitor at the lungs

Air-breathing fish control ventilation using oxygen, like other fish but unlike other air-breathing animals

This is because CO_2 is mostly lost through the skin or gills and does not build up in the tissues. For regulation, being aquatic is more important than breathing air

Carbon dioxide transport

CO_2 tension in the blood can rise to high levels in land animals, and this could have a substantial effect on pH - a 30% increase in oxygen consumption would potentially lower pH by 0.4 units

pH is normally regulated within much narrower limits than this. It varies by about 0.2 units between different species, less within a single species. Man varies from 7.35 to 7.45.

How is the CO_2 transported without affecting pH? 3 ways (Fig. 53.18):

1: **In solution**, dissolved in the plasma. This has no effect on pH. However, the amount that can be carried is small, only about 8% of the total production

2: **Combined with haemoglobin**. At a different binding site to that of oxygen, with protein not Fe^{2+}, does not compete for active sites. Accounts for about 20% of the total production

3. **As ions**. Most (72%) CO_2 combines with water and is transported as carbonic acid or bicarbonate ions:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \text{ (carbonic acid)} \leftrightarrow H^+ + HCO_3^- \text{ (bicarbonate)}$$

At normal blood pH (7.4) carbonic acid is mostly dissociated to hydrogen and bicarbonate ions - 1 carbonic acid : 20 bicarbonate. H^+ would acidify the blood

But the blood is buffered as the H^+ are removed. The most important buffers are blood proteins, including haemoglobin:

$$Hb^- + H^+ \leftrightarrow HHb$$

So most CO_2 is carried as bicarbonate, and buffers remove the H^+ so pH does not change. Removal of dissolved CO_2 from plasma allows more to diffuse from tissues

Formation of bicarbonate from carbonic acid is instantaneous, but reaction 1 is slow. So the rate is increased by the enzyme carbonic anhydrase. Found in red blood cells, where haemoglobin is available to buffer the H^+

Bicarbonate ions diffuse out of the red blood cell into the plasma, down a concentration gradient. Most CO_2 is transported as bicarbonate in the plasma

A transporter links the loss of bicarbonate to inward movement of chloride ions to maintain electrical neutrality of the red blood cell. Process known as the chloride shift

The reactions of haemoglobin with both CO_2 and H^+ favour dissociation of oxyhaemoglobin to free oxygen. This is a right shift of the dissociation curve, lower oxygen affinity, known as the Bohr effect

So oxygen is released to the tissues where CO_2 is produced. These reactions are reversed in the lung where haemoglobin is oxygenated and CO_2 given off by the blood