Systems of the Body 2

Integrated Physiology

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Extraceullar buffers include bicarbonate (key), hemoglobin, phosphate and plasma proteins. Isodhyric principle states that all extracellular buffers work together to resist changes in pH.

The bicarbonate system works on the following reaction:

\[ \text{CO}_2 + \text{H}_2\text{O} = \text{H}_2\text{CO}_3 = \text{H}^+ + \text{HCO}_3^- \]

Carbon dioxide is controlled by the respiratory system and the bicarbonate is controlled by the kidney.

Henry's law states that: Carbonic acid = 0.03 x PCO2. Note the 0.03 is the solubility coefficient. This equation will always be given.

Arterial pH follows all the fours:

\[ \text{pH} = 7.4 = 6.1 + \log \frac{24}{0.03 \times 40} \]

since: 6.1 is the pK of carbonic acid, 24 is the concentration of bicarbonate in the body and 40 is the partial pressure of carbon dioxide.

Thus: pH is dependent on the ratio of bicarbonate and partial pressure of CO₂.

\[ \text{pH} = \frac{[\text{HCO}_3^-]}{[\text{PCO}_2]} \]

pH is inversely proportional to the ratio of bicarbonate and carbon dioxide. When we hyperventilate we reduce the carbon dioxide and so we increase pH leading to alkaloysis. The key here is that the two are in a ratio.

There is a high concentration of bicarbonate in the plasma: 24mmol/L. Carbon dioxide is regulated by the lungs whilst the kidneys will regulate bicarbonate.

The body is a net producer of acid:

- The Krebs cycle produces CO₂
- Metabolism makes H⁺ that consumes bicarbonate. Phosphate and sulphate groups on proteins make phosphoric / sulphuric acid during protein metabolism.
- The majority of the gut below the pylorus secretes bicarbonate into the lumen; this sends H⁺ ions into the blood. Stomach makes HCL which leads to the alkaline tide in the stomach blood; but this effect is smaller than the acidification that occurs in the rest of the gut.

Renal Handling of Bicarbonate

Reabsorption of bicarbonate ions that enter the nephron; but if the plasma concentration exceeds the tubular threshold then this will spill over into the urine (i.e. reach the transport maximum). PCT reabsorbs bicarbonate.
Here, bicarbonate reacts with the H+ to make carbonic acid and then CO₂. This then diffuses into the cell to make bicarbonate.

Regeneration of bicarbonate lost in buffering occurs in the kidney by secreting protons into the nephron that are trapped and excreted by non-bicarbonate buffers and by secreting ammonium.

There is a H⁺ pump. This is buffered with phosphate. Also a H/K exchanger so to secrete H⁺ you reabsorb K⁺ so lots of acid base disturbances will effect K⁺ ions.

CO₂ is regulated by chemoreceptors which act on the respiration rate to return to the normal levels.

A rise in plasma bicarbonate above the tubular threshold will lead to its loss in the urine. A fall in plasma bicarbonate stimulates an increase in net acid excretion by the kidney.

We often need to take an arterial blood gas to monitor acid base disturbances. We put a syringe into the radial artery (with heparin in to stop clots forming in the syringe).

Remember the amount of CO₂ produced is the rate of production / alveolar ventilation (i.e. how fast you’re clearing it). pH depends upon the amount of bicarbonate and carbon dioxide.

The ABG print out will give you:

Name
Sample (venous, capillary or arterial)
pH
PaO₂ (arterial)
PaCO₂
HCO₃⁻
Lactate
Lecture 6: Ageing and Changes in Homeostatic Mechanisms

There are two processes: maturation and deterioration that co-exists. Maturation exceeds deterioration in first 3 decades, and the deterioration will exceed later. Balance changes with life.

As we age we have increased body size, range of function and improved performance (until 18 with growth but through 20’s cognitive ability increases and muscular strength can to). But eventually there is decreased elasticity and flexibility, loss of cells and tissues and decreased range of compliance in the deterioration phase leading to death. Particularly a problem for terminally differentiated tissues; cartilage, heart muscle and neurons. Compliance is the ability to respond to physiological challenges and this falls with age.

Major influences on reducing death are housing, nutrition, public health and vaccination.

Aging is degenerative. There is a linear relationship between death and age. On a Gompertz plot you plot log of death vs age and this gives us the linear relationship. A similar relationship can be plotted for diseases which incidence is age-related. The linear relationship is broken malignant tumours and diabetes which don’t appear to be primary killers in upper age range. Slope steepens for infectious disease as the elderly have more problems coping with infections. Degenerative aging has not been selected out in evolution as it occurs after reproductive age and so does not apply selective pressure.

Free radicals occur naturally and usually involve molecular oxygen. Radicals have an unpaired electron. Most are reduced to water and some will form hydroxyl radicals, H2O2 or superoxide. Radicals damage fatty membranes and with DNA. Malondialdehyde for example can cross link proteins and thus stop protein function. Enzymes such as superoxide dismutase and catalase can control radical levels. Vitamin C (antioxidant) and Vitamin E (becomes incorporated into lipid membrane and can trap free radicals). Smoking generates the greatest amount of voluntary radicals. Thus, free radicals cause aging.

Apoptosis allows for tissue redevelopement. Necrosis is due to accident or injury i.e. external cause.

Genetic causes of ageing. DNA redundancy failure; less than 1% of the DNA is used for function- thus as errors occur the amount of redundant DNA declines which makes errors more likely to be expressed with age. So errors in one sequence; start using the redundant repeat sequences. With time the redundant DNA declines thus the error is now expressed. Failure in chromosome replication due telomeres shorten with time and once they are small enough cells can no longer divide and thus metabolism slows and the cell dies.

Progeria: is a rare, fatal condition associated with accelerated ageing. Children display the characteristics of aging at 1.5-2 years and there is growth failure, hair and skin changes, joint problems and atherosclerosis. Death occurs in the early teens due to heart failure or stroke. Located the LMNA gene: Lamin A protein contributes to nuclear membrane and defective Lamin A leads to nuclear instability.