CONTROL OF VENTILATION

SENSORS / FEEDBACK

Central Chemoceptors The most important receptors involved in the minute-by-minute control of ventilation are those situated near the ventral surface of the medulla in the vicinity of the exit of the 9th and 10th nerves. The central chemoreceptors are surrounded by brain extracellular fluid and respond to changes in its H+ concentration. An increase in H+ concentration stimulates ventilation, whereas a decrease inhibits it. CO2 is able to cross the blood brain barrier but is normally impermiable to H+ and HCO3. CO2 therefore crosses the barrier and hydrates to carbonic acid, which ionises to give a pH inversely proportional to the log of CO2. A hydrogen sensor is thus made to respond to changes in CO2. The response in ventilation is (respiratory depth and rate) is linear over the range that is usually studied. There is a compensatory shift in CSF bicarbonate concentrations when the patient has prolonged CO2 retention which happens over hours.

Peripheral Chemoceptors are located in the carotid bodies at the bifurcation of the common carotid arteries, and in the aortic bodies above and below the aortic arch. The carotid bodies are the most important in humans. The peripheral chemoreceptors respond to decreases in arterial PO2 and pH, and increases in arterial PCO2. The carotid bodies have a very high blood flow for their size, and therefore in spite of their high metabolic rate, the arterial-venous O2 difference is small. The peripheral chemoreceptors are responsible for all the increase of ventilation that occurs in humans in response to arterial hypoxemia. The response of the peripheral chemoreceptors to arterial PCO2 is less important than that of the central chemoreceptors. However, their response is more rapid, and they may be useful in matching ventilation to abrupt changes in PCO2. In humans, the carotid but not the aortic bodies respond to a fall in arterial pH. This occurs regardless of whether the cause is respiratory or metabolic. Interaction of the various stimuli occurs. Thus, increases in chemoreceptor activity in response to decreases in arterial PO2 are potentiated by increases in PCO2 and, in the carotid bodies, by decreases in pH.

Airway Reflexes Nose: irritants may cause sneezing, or apnoea. Pharynx: mechanceptors that respond to pressure play a major role in activation of the pharyngeal dilator muscles. Larynx: Three main groups, mechanoceptors respond to changes in transmural pressure and act on the pharyngeal dilators, cold receptors are found on the vocal cords and their activation generally depresses ventilation and irritant receptors cause cough, laryngeal closure and bronchoconstriction. Cough Reflex may be elicited by chemical or mechanical stimuli arising from the larynx, trachea, carina or main bronchi. It may be voluntary and has three phases, inspiratory, compressive (expiration against a closed glottis) and explusive.

Lung Reflexes Pulmonary stretch receptors are believed to lie within the airway smooth muscle. main reflex effect of stimulating these receptors is a slowing of respiratory frequency due to an increase in expiratory time. This is known as the Hering-Breuer inflation reflex. The opposite response is also seen; that is, deflation of the lungs tends to initiate inspiratory activity (deflation reflex). The reflexes are largely inactive in adult humans unless the tidal volume exceeds 1 liter, as in exercise.

Baroreceptors An increase in arterial blood pressure can cause reflex hypoventilation or apnea through stimulation of the aortic and carotid sinus baroreceptors. Conversely, a decrease in blood pressure may result in hyperventilation.

Proprioceptors Impulses from moving limbs are believed to be part of the stimulus to ventilation during exercise, especially in the early stages.

Pain and Temperature Stimulation of many afferent nerves can bring about changes in ventilation. Pain often causes a period of apnea followed by hyperventilation. Heating of the skin may result in hyperventilation.

CENTRAL CONTROLLER

Suprapontine Cortex - Breathing can be voluntarily interrupted and the pattern of respiratory movements altered within the limits determined mainly be changes in arterial blood gas tensions. The neurones involved in this cortical overide of respiration may completely bypass the respiratory centres and act driectly on LMNs. In addition to volitional changes in the pattern of breathing suprapontine changes are important in reflexes such as sneezing, mastication, swallowing and coughing as well as coordination during speech. The Limbic and hypothalamus may also affect breathing for example in emotional states such as fear and rage.

Pons Pontine neurones fire in synchonry with different phases of respiration and are referred to as the pontine respiratory group PRG. They influence the medullary respiratory neurones via a multisynaptic pathway contributing to fine control of the respiratory rhythm.

Medulla The medulla is accepted as the area of the brain where the respiratory pattern is generated and where the various demands on respiratory activity are coordinated. Respiratory neurones in the medulla are mainly concentrated in two anatomical areas, the ventral and dorsal respiratory groups (VRG and DRG) which have numerous interconections. The DRG is primarily concerned with the timing of respiration and the inspiratory phase. The VRG comprises a column of respiratory neurones. In influences both inspiratory and expiratory phases and most inportantly has the pre Botzinger complex which is believed to be the location of the central pattern generator. Unlike the heart there is no single pacemaker, but rather a group pacemaker hypothesis. concentrated in the CPG. Groups of neurones influence the three main phases of respiratory cycle. The inspiratory phase, the pharyngeal dilators first contract then there is a ramp increase in inspiratory neurone firing leading to inspiratory muscle activation. The second phase (expiratory phase I) is a passive let down of inspiratory muscles. The final phase (expiratory phase II) involves active expiration if required, the inspiratory neurones are now silent.

Upper Motor Neurones The intergration of respiratory control which took place in the CPG continues to take place at the junction of the UMN with the anterior horn cells supplying the LMN. There are three groups of UMN from separate anatomical locations integrated here. The involuntary rhythmic control of inspiration and expiration group from the CPG, the voluntary control of breathing group (speech etc) and in the involuntary non rhythmic control of breathing group (cough, sneezing, swallowing).

OVERRIDE

EFFECTORS

Muscles of Respiration These include the pharyngeal and laryngeal muscles, in particular the pharyngeal dilator muscles, including gleniglossus and tensor palati. The diaphram is the most important effector of respiratory activity. The internal and external intercostals and accessory muscles such as sternomastoids are also important but to a lesser extent. The abdominal muscles are important in forced expiration.

Carbon Dioxide The most important control of ventilation under normal conditions is the PCO2 of the arterial blood. In the course of the day with periods of rest and exercise the arterial Pco2 is probably held within a 3mmHg range. Following a rise in Pco2 the respiratory depth and rate increases until a steady state of hyperventilation is achieved after a few minutes, this can be maintained in healthy subjects for up to 8 hours. The response is linear over the range usually studied. Most of the response comes from the central chemoceptors but the peripheral chemoceptors also contribute and their response is faster. The response is enhanced if the PO2 is lowered.

Oxygen Because the PO2 can normally be reduced so far without evoking a ventilatory response, the role of this hypoxic stimulus in the day-to-day control of ventilation is small. Only peripheral chemoceptors are involved. However, on ascent to high altitude, and in long term hypoxemia secondary to chronic lung disease, hypoxia drive can become important.

pH A reduction in arterial blood pH stimulates ventilation. In practice it is often difficult to separate the ventilatory response to decreased pH and increased CO2. In normal conditions peripheral chemoceptors are the only sensors, however in disease states it is possible that the BBB may leak resulting in central chemoceptor action.

Exercise Increased ventilation in exercise remains largely unknown. Possible explanations have included, oscillation of arterial Pco2 and Po2, propriocetors in muscles and joints, impulse from the motor cortex and increases in body temperature.