Ventilatory Control and the Thoracic Pump

BY WILLIAM W. ECKHARDT, BS, CRT, RPSGT — ASSOCIATE EDITOR

Ventilatory control during wake and sleep, and in patients with obstructive sleep apnea (OSA), has been the subject of much research. Our knowledge in this fascinating aspect of sleep medicine is increasing but much is still largely based in theory. This article will provide the reader a basis of ventilatory control and ventilatory control during sleep.

We have three states being wake: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Each has differences in respiratory control. The respiratory control system is regulated by two anatomically distinct parts that may work in conjunction with each other. These are often referred to as the metabolic and the behavioral (voluntary) respiratory control systems. Blood gas homeostasis (stability in normal states within the internal environment of our bodies) is the function of the metabolic control whereas voluntary control from the cortex provides us the ability to speak and sing or hold our breath.

Maintaining homeostasis is accomplished via a negative feedback control system. The metabolic control of breathing must respond to the changing environment (e.g., changes in ambient pressure, physiologic and metabolic changes associated with exercise and diseases like chronic obstructive pulmonary disease and obstructive sleep apnea). This control of breathing system utilizes external respiration for mediating the gas exchange between the blood (gases) and alveolar gases at the alveolarcapillary membrane and blood gas values at the chemoreceptors involved in the ventilatory process.

Our bodies strive for carbon dioxide homeostasis or a balance between our metabolic rate (rate at which CO₂ enters the venous blood) and alveolar ventilation (how much CO₂ is eliminated in the lung). The Metabolic Control is a function of physiological control systems in which the controllers (central and peripheral chemoreceptor neurons in the brain stem) send neural signals to the effectors. The inspiratory and expiratory motor neurons modify their activity and affect the chest wall and upper airway muscles called the thoracic pump and lungs or “plant.” This initiates the process of inspiration and results in increased ventilation for a given PO₂ but it is the combined stimulus that will exceed

The PaCO₂ is a means of assessing the adequacy of ventilation and probably the most important stimulus to the control system maintaining levels of CO₂ or H⁺ concentration on a breath-by-breath basis. During wake in a normal individual the PaCO₂ is held to within 3 mm Hg. PO₂ increases about 2 mm Hg in NREM sleep and another 1-2 mm Hg in REM sleep. PO₂ increases normally stimulate both the peripheral and central chemoreceptors. Even a slight increase is a stimulus; it may be the concomitant increase in hydrogen-ion concentration in the extracellular fluid governed by the CSF and arterial blood that really cause the stimulus but changes in carbon dioxide lead to changes in hydrogen ion concentration [H⁺] and it is difficult to ascertain which is the stimulus and it maybe both. The PaCO₂ increases, CO₂ diffuses into the CSF from the cerebral blood vessels releasing H+ ions stimulating the chemoreceptors.

Ventilation stimuli due to decreases in PO₂ are mediated by the peripheral chemoreceptors and require a substantial decrease. Peripheral chemoreceptors are located in the carotid and aortic bodies; they directly monitor changes in the arterial blood. The carotid bodies seem to be more important in man than the aortic bodies. The carotid bodies respond to changes in the PaO₂, pH and in the PaCO₂. Their response is quite rapid even within a single ventilatory cycle. They are believed to cause the increased ventilation in response to arterial hypoxemia (decreased PaO₂). Their response to arterial PO₂ seems less important than the central chemoreceptors but more rapid and may influence ventilation due to abrupt changes in PaCO₂. They produce a reflex inhibition of ventilation in response to an increase in PaO₂ or a decrease in PaCO₂ or decrease hydrogen-ion concentration. Hypoxemia has been shown to stimulate ventilation by its action on the peripheral chemoreceptors. The PaO₂ must be reduced to about 60-50 mm Hg before an increase in ventilation is seen.

Hypercapnia and hypoxia are causes of arousal from sleep either individually or as a combined stimulus. An increase in PaCO₂ will increase ventilation for a given PO₂ but it is the combined stimulus that will exceed
the sum of the independent stimuli causing a greater increase in ventilation. The carotid and aortic bodies also react to increases in hydrogen-ion concentration other than caused by increases in PCO₂, but result in a lowering of PCO₂ in order to restore a more normal hydrogen-ion concentration.

Mechanoreceptor reflexes of the lungs also come in to play and serve as protective mechanisms that respond to over inflation of the lungs, irritation, and injury. The Hering-Breuer reflex prevents over expansion of the lungs seen during exercise. Pulmonary stretch receptors are thought to be in the smooth muscle of the airway. They too come into play during exercise and may be important to infants. Bronchoconstriction is a reaction by irritant receptors that are stimulated by substances foreign to the lung e.g. cigarette smoke, dust and cold air. Irritant receptors are between the epithelial cells in the airway. The nose also contains irritant receptors, which may cause sneezing. Coughing and sneezing serve as a protective mechanism. There are joint and muscle receptors that during exercise stimulate ventilation from the movement of our limbs.

Arterial baroreceptors react to increases in arterial blood pressure by causing a reflex hypoventilation or apnea. These baroreceptors are located at the aortic and carotid sinuses. A decrease in arterial BP would cause a reciprocal response of hyperventilation.

The airway must remain patent in order for ventilation to take place. This is dependent on the pharynx (nasopharynx, oropharynx, hypopharynx) remaining patent despite the fact it is compliant (compliance — a measure of the ease with which a structure or substance may be deformed, especially a measure of the ease with which a hollow organ may be distended) and forces act to cause collapse. Compliance depends on and changes with muscle activity. The compliant extrathoracic airway has a tendency to collapse during inspiration and increases in diameter during expiration. Other airway structures being of a cartilaginous nature i.e. nasal passage, larynx and trachea do not have this characteristic. Control of the upper airway muscle activity is of paramount importance in the patency of the airway.

Pharyngeal dilator muscle activity of the genioglossus [a muscle that serves to advance and retract and also to depress the tongue] and tensor palatine [tenses and flattens the soft palate — soft palate is fleshy and moveable, it is made of muscle which regulates the opening between the oropharynx and the nasopharynx] changes from wake to sleep, between young and old and those with OSA to normals, and yes, between women and men. The genioglossus has a greater EMG activity during sleep, between young and old and those with OSA to normals, and yes, between the oropharynx and the nasopharynx) changes from wake to sleep. EMG and appears to be independent of the respiratory drive.

Control in wake is mediated by automatic impulses that come from the brain stem area e.g. the pons, medulla and the less well defined respiratory centers. There are three main groups of neurons, the medullary respiratory center in the reticular formation this being composed of the dorsal group (inspiration), ventral group (expiration). The apneustic center is in the lower pons and is questionable whether comes into play in normal human ventilation. The pneumotaxic center in the upper pons seems to tweak the system but is not necessary for ventilation. It regulates inspiratory volumes preventing over inflation.

Normally the transition from wake to sleep is a time of increased upper airway resistance and decreased minute ventilation. The upper airway dilator muscle activity also decreases at sleep onset but increases again being similar to the activity of wakefulness during stable [non-cp] NREM sleep. Irregularity of respiration during wake tends to be from behavioral control of the ventilatory pattern.

Sleep appears when the wakefulness system decreases and sleep-promoting neurons or groups of neurons become active. Tonic efferent input to the skeletal muscles in non-REM and REM sleep decreases leaving the airway more compliant and more susceptible to increased resistance and obstruction. Synchronized neuronal networks characterize NREM sleep whereas REM sleep is a desynchronized or paradoxical sleep. SWS is associated with the secretion of large amounts of growth hormone. REM sleep seems to have an influence on nervous system functions. Sleep brings about changes in lung volume, suspension of thermoregulation (REM sleep), decreased central respiratory drive, increased airway collapsibility and loss of tonic muscles (atonia in REM). Sleep (NREM) brings about a more regular pattern of ventilation than wake in normal individuals although with a decrease in tidal volume. REM sleep is characterized by a more chaotic ventilatory pattern with a further decrease in tidal volume.

Mechanoreceptors response to stimuli is generally decreased during sleep and our normal wake response to obstruction is reduced or gone during sleep. The hypoxygenia and hypercapnia associated with obstruction cause an increase in drive to the upper airway and thoracic pump but seldom does this lead to the opening of the airway until arousal ensues. Of course then the pathology causing the obstruction reoccurs and the cycle repeats (can anyone say microsleep).

Sleep brings about a loss of the “wakefulness drive” changing respiratory control, which can lead to instability. Muscle activity of the upper airway decreases and therefore upper airway resistance increases. This is thought to contribute to the increase in periodic breathing seen during sleep onset and light sleep. Arousal and hyperpnea cause changes in the respiratory control system creating higher controller gains [changes in afferent signals to the brain] and instability to the system. Upper airway resistance is similar between NREM and REM sleep.

The thoracic pump’s contribution to ventilation changes when supine, the abdominal distention being the major contributor and the chest wall the lesser contributor to the tidal volume. However, with sleep onset the muscle activity is increased in the intercostals as compared to wake and decreased in the abdomen. This is important as we go from NREM to REM sleep. The intercostals or muscles of the chest wall become ineffective due to a greater degree of muscle atonia of the chest wall muscles without much effect on the diaphragm. When you see your thoracic belts go bad during REM this is a likely cause. Do not run in and fix them. Also, the chest wall can move inward during inspiration acting paradoxi—

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PCO₂ has a much different effect during sleep vs. wake. Hypercarbia has its effect of stimulating ventilation but unlike during wake hypocapnia has a more contributory role in reduced ventilatory drive during sleep. This becomes very important during the change from wake to sleep, as hyperventilation is often associated with this time of transition. The ventilatory response to hyperventilation may be sleep onset apneas and may affect OSA microsleeps and respiratory events.

The ventilatory response to the PO₂ or the hypoxic stimulus during NREM sleep is decreased in men when compared to wake. This is much less so in women. Both sexes have a similar decline in hypoxic response in REM compared to NREM. The genioglossal response to hypoxia is also decreased and lower in REM vs. NREM vs. wake.

NREM sees a rise in PCO₂ of about 2-4 mm Hg from wakefulness. This occurs because of a decrease in ventilation at the alveolar level and even with a decrease in metabolic rate translates to an increase in PCO₂. Breathing in NREM sleep is generally a more regular pattern compared to either wake or REM sleep. The increase in PCO₂ does not seem to increase genioglossal activity as it would in wake.

REM sleep contributes another 1-2 mmHg rise in PCO₂ due to a decrease in alveolar ventilation with a concomitant decrease in tidal volume/minute volume from NREM sleep. REM sleep also produces a disordered breathing pattern which is independent of the peripheral metabolic changes e.g. pH of the blood, PCO₂ and PaO₂. REM sleep is controlled by neural responses in the brain stems pneumotaxic centers located in the upper pons. Metabolic control during REM sleep is still debated but it would seem to have a role with other influences also coming into play.

The control system is very stable in wake with compensation to perturbations within the system usually occurring within a few breaths. This changes when sleep commences allowing perturbations to influence the controller regulating the plant with greater changes over longer periods and at times producing an oscillatory behavior. Perturbations caused by OSA and by the technologist treating the patient with PAP further confound the system. Understanding the control system can give the technologist further incites into changes and outcomes while treating the OSA patient.

About the Author

Will Eckhardt is the Director of Education at Sleep HealthCenters in Boston, MA. He also teaches part time at Northern Essex Community College in the polysomnography program. He has been a member of the APT since 1992 and is an Associate Editor of A2Zzz Magazine, and the 2004 recipient of the APT Dr. Allen D. V. Bliss Literary Award.