Pathophysiology of Neuromuscular Respiratory Diseases

Joshua O. Benditt, MD

KEYWORDS

• Neuromuscular disease • Pathophysiology of neuromuscular disease • Respiratory failure
• Pulmonary function assessment • Amyotrophic lateral sclerosis • Muscular dystrophies
• Spinal cord injury

KEY POINTS

- The respiratory pump is designed to bring oxygen into the body to fuel energy generation and remove carbon dioxide as a waste product of cellular metabolism.
- The system is made up of the cortex of the brain that controls voluntary breathing; the brainstem, which is involved with automatic breathing; and the spinal cord and motor neurons that transmit nerve impulses.
- The effects of neuromuscular diseases on the respiratory system range from isolated and mild to protean and severe.
- An understanding of the pathophysiology of specific diseases as well as adopting a general approach to patients with one of these disorders can be helpful and in many cases lead to improvement in quality and quantity of life.

NORMAL PHYSIOLOGY

The respiratory pump is designed to bring oxygen into the body to fuel energy generation and remove carbon dioxide as a waste product of cellular metabolism.[1–3] The system is made up of the cortex of the brain that controls voluntary breathing; the brainstem, which is involved with automatic breathing; the spinal cord and motor neurons that transmit nerve impulses; the respiratory muscles that are the effectors of the system; and a complex system of feedback receptors and nerves that regulate ventilation (**Fig. 1**). The system is remarkably flexible and can precisely maintain CO_2 and acid-base balance. This article discusses each of the components of this complex network.

CENTRAL NERVOUS SYSTEM

Voluntary Breathing Controllers

Voluntary breathing is initiated by signals from the cerebral cortex. Centers located within the parietal cortex send signals that initiate inspiration and expiration.[4] These cortical areas project to the motor neurons in the spinal cord via the corticospinal tracts.

Automatic Breathing Controllers

Automatic breathing is controlled by a complex system that includes respiratory centers in the pons and medulla, nerve tracts in the lower brainstem, pathways in the spinal cord, and the feedback mechanisms that are both chemical and mechanical in nature. There are believed 3 centers that generate the rhythm and drive to breathe: 1 located in the pons and 2 in the medulla. More detailed reviews of this topic are available.[5]

Spinal Cord

The spinal cord and motor nerves conduct nerve impulses from the cortex and brainstem to the anterior horn cells of the motor neurons supplying

Department of Medicine, University of Washington School of Medicine, 1959 NE Pacific Street, Seattle, WA 98119, USA
E-mail address: benditt@uw.edu

Clin Chest Med 39 (2018) 297–308
https://doi.org/10.1016/j.ccm.2018.01.011

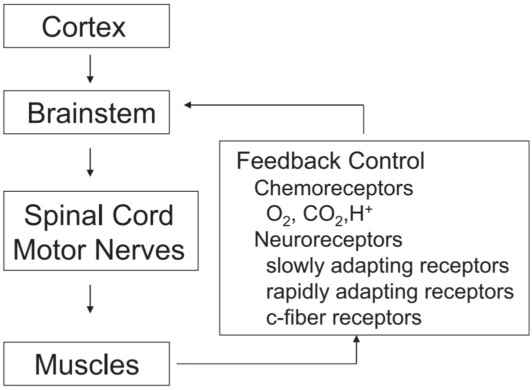

Fig. 1. Schematic of respiratory system, including controllers, effectors, and receptor feedback inputs.

the respiratory muscles. The fibers in both these tracts travel through the spinal cord to synapse with the lower motor neurons.

PERIPHERAL NERVOUS SYSTEM

Lower Motor Neurons

The lower motor neuron has its cell body in the spinal cord (anterior horn cell) but exits the spinal cord to become the spinal nerve roots and the nerves that supply the respiratory muscles. When the nerves arrive at the muscle, they divide into branches known as twigs that, on reaching the muscle fiber, further divide into bulbous projections called boutons that apply themselves to the muscle membrane at a specialized anatomic junction called the motor end plate. These boutons contain acetylcholine, which is the chemical transmitter that serves to excite the muscle to contract. With nerve firing, there is release of acetylcholine at the motor end plate into the cleft between the nerve and the muscle. The acetylcholine binds to receptors on the muscle side of the motor end plate, which results in a suprathreshold excitatory end plate potential and depolarization of the muscle membrane.[6] A muscle action potential then results in contraction of the muscle fiber.

Respiratory Muscles

The respiratory muscles are the mechanical effectors of the breathing system. They are often divided into 3 major groups: (1) the inspiratory muscles, (2) the expiratory muscles, and (3) the accessory muscles of respiration. The muscles that maintain patency of the upper airway during the respiratory cycle are sometimes also considered muscles of respiration because of their close interaction with the other respiratory muscles. Table 1 shows the innervation of the inspiratory muscles.

Table 1
Respiratory muscles and their innervation

Muscle Group	Spinal Cord Level	Nerve (s)
Inspiratory muscles		
Diaphragm	C3–C5	Phrenic
Parasternal intercostals	T1–T7	Intercostal
Lateral external intercostals	T1–T12	Intercostal
Scalenes	C4–C8	
Sternoclydomastoids		
Expiratory muscles		
Lateral internal intercostals	T1–T12	Intercostal
Rectus abdominis	T7–L1	Lumbar
External and internal obliques	T7–L1	Lumbar
Transversus abdominis	T7–L1	Lumbar
Upper airway muscles		
Muscles of mastication		CN V, VII
Laryngeal and pharyngeal		
Abductors		CN IX–XII
Adductors		CN IX–XII

The diaphragm is the major muscle of inspiration and accounts for approximately 70% of the inhaled tidal volume in the normal individual.[7] Contraction of the diaphragm results in a downward piston motion of the muscle as well as outward and upward movement of the ribs through the zone of apposition (Fig. 2).

The intercostal muscles are thin sheets of muscular fibers that run between the ribs in the costal spaces.[8] There are 2 sheets of muscle fibers, the external and internal intercostals. The external intercostals function to expand the rib cage during inspiration. The internal intercostals are deeper and function to decrease rib cage size during expiration. The orientation of the muscle fibers with respect to the ribs results in the increase or decrease in the size of the rib cage, as the muscles contract (Fig. 3).

The abdominal muscles (rectus abdominis, internal oblique, external oblique, and transversus abdominis) serve several functions in respiration that mainly assist expiration but also can function in inspiration. The abdominal muscles also may play a minor role in inspiration if their contraction reduces lung volume below function residual capacity; abdominal muscles can store elastic recoil energy in the chest wall that then assists