

neuromuscular disorders. As neuromuscular weakness progresses, the respiratory muscles, including the diaphragm, are placed at a mechanical disadvantage in the supine position due to the upward movement of the abdominal contents. New-onset orthopnea is frequently a sign of reduced respiratory muscle force generation. More commonly, however, extremity weakness or bulbar symptoms develop prior to sleep disturbance in neuromuscular diseases such as amyotrophic lateral sclerosis (ALS) or muscular dystrophy. Patients with respiratory drive disorders do not have symptoms distinguishable from other causes of chronic hypoventilation.

TABLE 296-1 Signs and Symptoms of Hypoventilation

Dyspnea during activities of daily living
Orthopnea in diseases affecting diaphragm function
Poor-quality sleep
Daytime hypersomnolence
Early morning headaches
Anxiety
Impaired cough in neuromuscular diseases

The clinical course of patients with chronic hypoventilation from neuromuscular or chest wall disease follows a characteristic sequence: an asymptomatic stage where daytime PaO_2 and PaCO_2 are normal followed by nocturnal hypoventilation, initially during rapid eye movement (REM) sleep and later in non-REM sleep. Finally, if vital capacity drops further, daytime hypercapnia develops. Symptoms can develop at any point along this time course and often depend on the pace of respiratory muscle functional decline. Regardless of cause, the hallmark of all alveolar hypoventilation syndromes is an increase in alveolar PCO_2 (PAco_2) and therefore in Paco_2 . The resulting respiratory acidosis eventually leads to a compensatory increase in plasma bicarbonate concentration. The increase in Paco_2 results in an obligatory decrease in PAO_2 , often resulting in hypoxemia. If severe, the hypoxemia manifests clinically as cyanosis and can stimulate erythropoiesis and thus induce secondary erythrocytosis. The combination of chronic hypoxemia