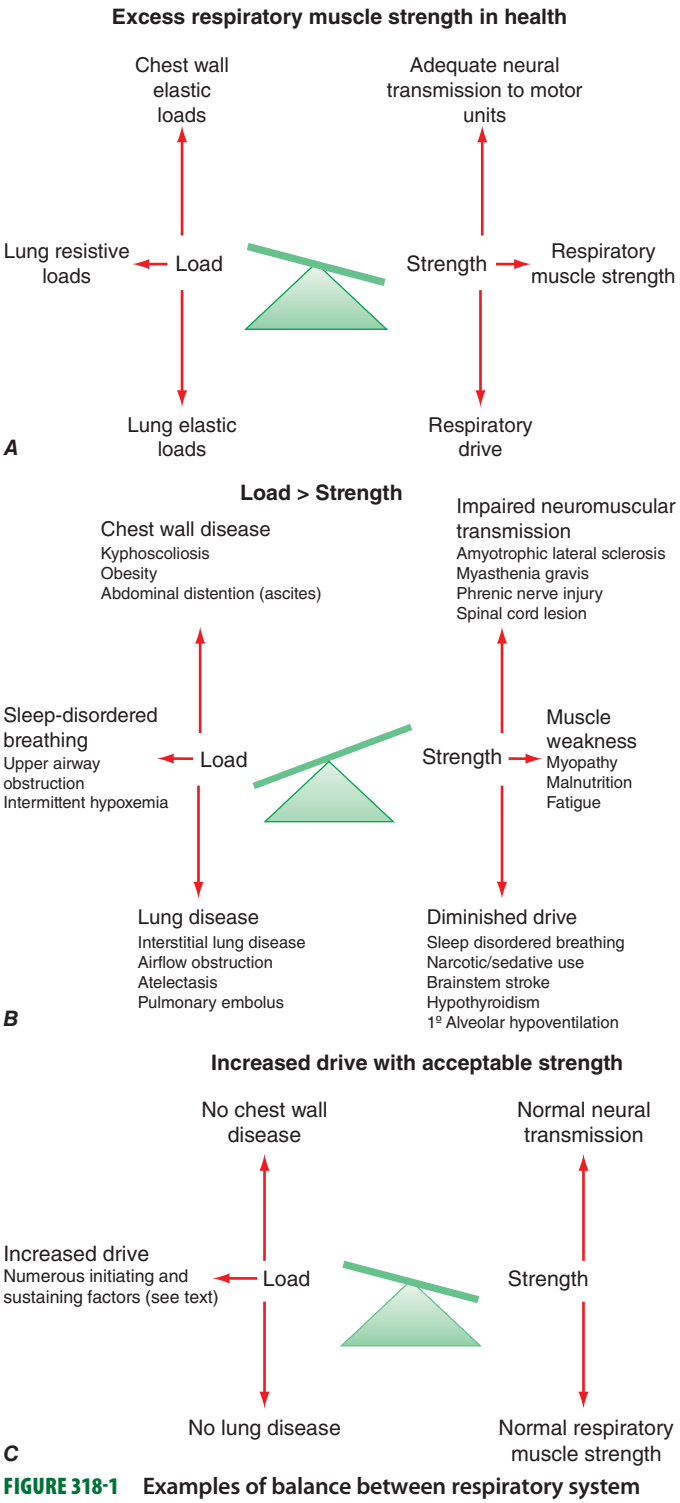

FIGURE 318-1 Examples of balance between respiratory system strength and load. ***A.*** Excess respiratory muscle strength in health. ***B.*** Load greater than strength. ***C.*** Increased drive with acceptable strength.

syndromes are nonspecific (Table 318-1) and vary depending on the severity of hypoventilation, the rate at which hypercapnia develops, the degree of compensation for respiratory acidosis, and the underlying disorder. Patients with parenchymal lung or chest wall disease typically present with shortness of breath and diminished exercise tolerance. Episodes of increased dyspnea and sputum production are hallmarks of obstructive lung diseases such as chronic obstructive pulmonary disease, whereas progressive dyspnea and cough are common in interstitial lung diseases. Excessive daytime somnolence, poor-quality sleep, and snoring are common among patients with sleep-disordered breathing. Sleep disturbance and orthopnea are also described in

TABLE 318-1 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

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.

The clinical course of patients with chronic hypoventilation from neuromuscular or chest wall disease follows a characteristic sequence: an asymptomatic stage where daytime Pa_{O_2} and Pa_{CO_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 P_{CO_2} (PA_{CO_2}) and therefore in Pa_{CO_2}. The resulting respiratory acidosis eventually leads to a compensatory increase in plasma bicarbonate concentration. The increase in PA_{CO_2} results in an obligatory decrease in PA_{O_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 and hypercapnia may also induce pulmonary vasoconstriction, leading eventually to pulmonary hypertension, right ventricular hypertrophy, and right heart failure.

DIAGNOSIS

Elevated plasma bicarbonate in the absence of volume depletion is suggestive of hypoventilation. An arterial blood gas demonstrating elevated Pa_{CO_2} with a normal pH confirms chronic alveolar hypoventilation. The subsequent evaluation to identify an etiology should initially focus on whether the patient has lung disease or chest wall abnormalities. Physical examination, imaging studies (chest x-ray and/or computed tomography [CT] scan), and pulmonary function tests are sufficient to identify most lung/chest wall disorders leading to hypercapnia. If these evaluations are unrevealing, then the clinician should screen for obesity hypoventilation syndrome (OHS), the most frequent sleep disorder leading to chronic hypoventilation, which is typically accompanied by obstructive sleep apnea (OSA). Several screening tools have been developed to identify patients at risk for OSA. The Berlin Questionnaire has been validated in a primary care setting and identifies patients likely to have OSA. The Epworth Sleepiness Scale (ESS) and the STOP-Bang questionnaires have not been validated in outpatient primary care settings but are quick and easy to use. The ESS measures daytime sleepiness, with a score of ≥10 indentifying individuals who warrant additional investigation. The STOP-Bang survey has been used in preoperative clinics to identify patients at risk of having OSA. In this population, it has 93% sensitivity and 90% negative predictive value.

If the ventilatory apparatus (lungs, airways, chest wall) is not responsible for chronic hypercapnia, then the focus should shift to respiratory drive and neuromuscular disorders. There is an attenuated increase in minute ventilation in response to elevated C_{O_2} and/or low O_2 in respiratory drive disorders. These diseases are difficult to diagnose and should be suspected when patients with hypercapnia are