Sleep-Disordered Breathing in Neuromuscular Diseases

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Introduction

The broad categories of NMD that affect children include muscular dystrophies, congenital and metabolic myopathies, neuromuscular junction disorders, peripheral neuropathies, and anterior horn cell disease [1]. However, there are additional acquired pathologies such as acute transverse myelitis, flaccid myelitis syndromes, spinal cord injury, traumatic brain injuries (accidental and non-accidental), hypoxic ischemic encephalopathy and resultant cerebral palsy, etc. that result in altered muscle tone and carry subsequent respiratory implications. Lastly, central nervous defects (such as lissencephaly, myelomeningocele, spinal cord syrinx, etc.) can also result in unfavorable changes in muscle tone and/or respiratory drive. The related presence of sleep-disordered breathing (SDB) results from the combination of altered respiratory drive, upper airway muscle tone, respiratory compliance, and the presence of any associated underlying lung disease.

The incidence of sleep-disordered breathing in any specific neuromuscular disease is variable and depends on the degree of existing muscle weakness. It should be understood that progressive neuromuscular disorders are likely to be associated with sleep-disordered breathing at different time points in the disease progression. Sometimes, though, the underlying pathology may be a static insult (SMA types 1 and 2, congenital brain malformation, cerebral palsy, etc.), but the consequences of such disorders in growing children are progressive, and not infrequently, the onset of sleep-disordered breathing is a function of evolving growth and comorbidities (such as chronic aspiration, recurrent pneumonia, evolving thoracic dystrophy, etc.) and therefore delayed in its onset.

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Neuromuscular disorders have significant impacts on patient well-being. Psychological and psychiatric impacts echo on family relations and within the broader society; social implications abound with many patients and their families experiencing social isolation. High medical costs that relate to other morbidities develop as a result of primary neuromuscular disorders (such as feeding tube dependence, rehabilitative needs, predisposition to malnutrition and bedsores, recurrent infections, etc.). The financial costs are not trivial. In a comprehensive study of the costs associated with amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD), and myotonic dystrophy (DM), it was determined that the total impact on the US economy inclusive of direct medical and nonmedical costs and loss of income was staggering [2] with annual per-patient costs approximated to be $64,000 for ALS, $51,000 for DMD, and $32,000 for DM. On a national scale, the population-wide costs were about $1.023 billion for ALS, $787 million for DMD, and $448 million for DM.

The landscape of pediatric NMD is changing as it relates to emerging novel treatments, and long-term survivorship is increasing. This makes the discussion of sleep-disordered breathing in these patients more relevant than ever.

Pathophysiology and Clinical Presentation

Respiratory complications in NMD occur due to respiratory pump dysfunction. The respiratory pump comprises the respiratory muscles, chest wall, and spine. At rest, the diaphragm is the major inspiratory muscle working as a piston to create an intrathoracic pressure gradient that determines the tidal volume. Other chest wall muscles involved in forceful inspiration include external intercostal muscles, pectoralis muscles, and anterior neck muscles. Exhalation is passive at rest occurring largely due to chest and lung recoil. With exertion or cough, there is additional recruitment of anterior abdominal musculature. The act of active inspiration plays a critical role in maintaining lung recruitment at rest and

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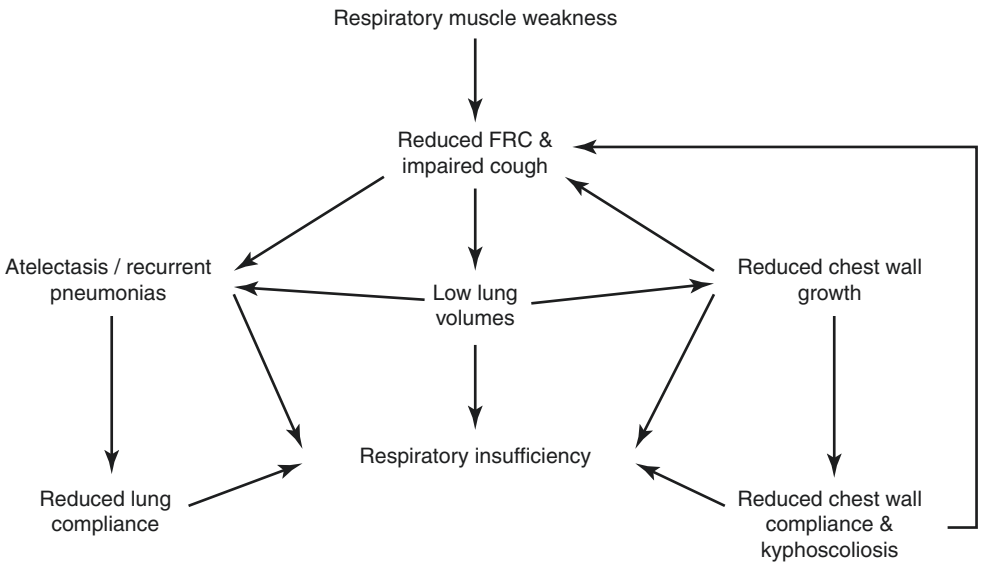

Fig. 42.1 Impacts of respiratory muscle weakness

secretion clearance when followed by a cough. With progressive weakness of respiratory muscles, these functions are impaired.

The impact of respiratory muscle weakness is summarized in Fig. 42.1. With progressive respiratory weakness, the "floor" of maximal expiration (expiratory reserve volume) to residual volume is progressively raised, while the "ceiling" or "height" of maximal inspiration (inspiratory reserve volume) is progressively lowered. Thus, the patient generally experiences narrowing of the range of vital capacity. It is therefore unsurprising that wheelchair-bound patients can lose 60–70% of vital capacity and not appear very symptomatic. Further, when low lung volume states and atelectasis become the norm for these patients, the lung compliance decreases [1], contributing to increased work of breathing and a generally increased catabolic state.

The normal chest wall is integral to normal respiratory function. The weakness of thoracic muscles as seen in SMA type I and other severe myopathies leads to loss of thoracic support. In these younger children, there is increased thoracic compliance in the early stage with obvious respiratory paradox as the negative intrathoracic pressure created by the relatively spared diaphragm is unopposed by the anterior chest wall muscles. The effect is further amplified with respiratory distress and upper airway obstruction (OSA). The persistent abnormal chest wall motion coupled with severe osteopenia of ribs drives subsequent thoracic dystrophy. The chest wall then eventually becomes fixed and poorly compliant with shortening of muscles and stiffening of tissues, resulting in persistent low lung volume states. Most often, there is severe caudal slant of the ribs with loss of anteroposterior depth of the chest (Fig. 42.2). The overall stiffness of the chest wall therefore not only limits vital capacity but also reduces the efficacy of spontaneous cough by reduced deformability. Lastly the spine requires normal muscle strength and tone to maintain its alignment, and the loss of supporting muscle predisposes the child to rotational spine deformities and diaphragm dysfunction. Inadequate vertical spine height translates into lower intrathoracic volumes, limited chest wall growth, and restrictive pulmonary defects (Fig. 42.3) [3].

Scoliosis negatively affects chest wall compliance, compresses or distorts bronchi, contributes to alveolar hypoventilation (Fig. 42.4), diminishes airflow, and decreases the effectiveness of cough [4]. This is generally seen in early childhood onset progressive respiratory weakness. If the onset of respiratory weakness occurs after the chest wall has been fully developed, as in the case in DMD, spinal muscular atrophy type 3, and mid- to late-adolescent spinal cord injury, the degree of thoracic dystrophy that ensues could be milder.

Normally, sleep onset is associated with reduced ventilatory control inputs from higher centers, attenuated sensitivity of central chemoreceptors, medullary and cortical arousal mechanisms, and reduced upper airway muscle tone. The reduction in tidal volume, minute ventilation [5], respiratory rate [6], chemosensitivity [7], and loss of the wakefulness drive [8] results in a 2 to 4 mmHg increase in $PaCO_2$. During rapid eye movement (REM) sleep, skeletal muscle atonia is most pronounced with preserved diaphragm and extraocular muscle function. In supine wake and non-REM (NREM) sleep, the rib cage contributes about 44% of the tidal volume. The atonia of phasic REM sleep reduces this contribution to 19%, decreasing functional residual capacity by 6% to about 15% [9] and rendering tidal volume in phasic REM sleep to be diaphragm-dependent [10, 11]. The load on the respiratory system is compounded by the increase in upper airway resistance during NREM sleep at sleep onset [12] that is fur-

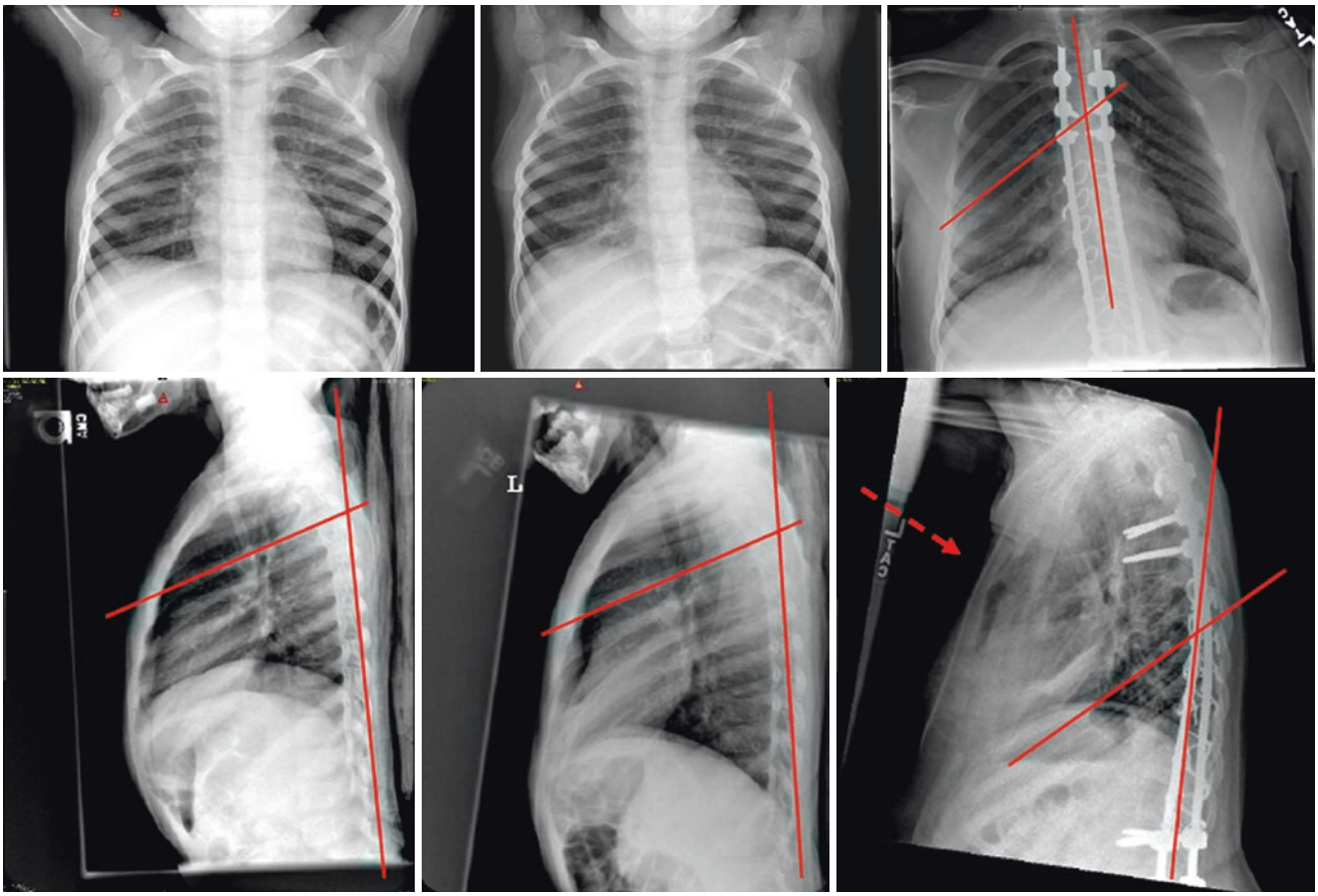

Fig. 42.2 Progressive chest wall changes in a patient with SMA II. Note the early scoliosis at 5 years and loss of antero-posterior diameter of the thorax and progressive sloping of ribs in relation to vertebral axis by 13 years

ther exaggerated during REM sleep with the decreased activity in pharyngeal and laryngeal dilators [13]. These normal phenomena are exaggerated in the presence of muscle weakness with emergence of respiratory instability initially in REM sleep and subsequently including NREM sleep. In severe cases, the instability is notable even while awake. Of course, the nature of the underlying disease will determine the degree of muscle group involvement.

Understanding normal sleep mechanics and chemosensitivity highlights the vulnerability of REM sleep in a patient who either is weak or has altered chest wall mechanics. The diaphragm may initially be able to generate enough negative intrathoracic pressure during REM sleep against a weak or atonic upper airway resulting in its narrowing (hypopnea) or collapse (apnea). Weak intercostal muscles can still contribute to tidal volume in NREM sleep but completely lose this ability in REM sleep. Hence, hypoventilation is initially isolated to REM sleep. With worsening degrees of weakness, there is additional NREM sleep involvement, finally progressing to continuous hypoventilation or respiratory failure [14].

Inherent to this discussion is the definition of hypoventilation. The American Academy of Sleep Medicine (AASM) defines adult nocturnal hypoventilation in two ways: (1) $PaCO_2$ or its surrogate of ≥55 mmHg for ≥10 minutes and (2) a ≥ 10 mmHg increase in $PaCO_2$ or its surrogate compared to wake to a value >50 mmHg for ≥10 minutes [15]. Using the first and second definitions, the prevalence of hypoventilation with daytime eucapnia in neuromuscular disease is 4% and 9%, respectively [16]. The AASM pediatric definition of hypoventilation is >25% of the total sleep time with $PaCO_2$ or its surrogate >50 mmHg. This definition captures 24% of children with neuromuscular disease [17]. Early in the process, symptoms of SDB are poorly perceived with roughly 64% having daytime somnolence, headache, snoring, or sleep disturbance. Notably, these symptoms do not predict the presence of SDB [18]. In a larger population of boys with DMD, only 17% of patients with abnormal PSG findings were noted to have related symptoms [19]. The insidious onset is partially due to impaired mobility and the inability to tax the respiratory system [20]. Subtle symptoms may include unrefreshing sleep, and multiple nighttime

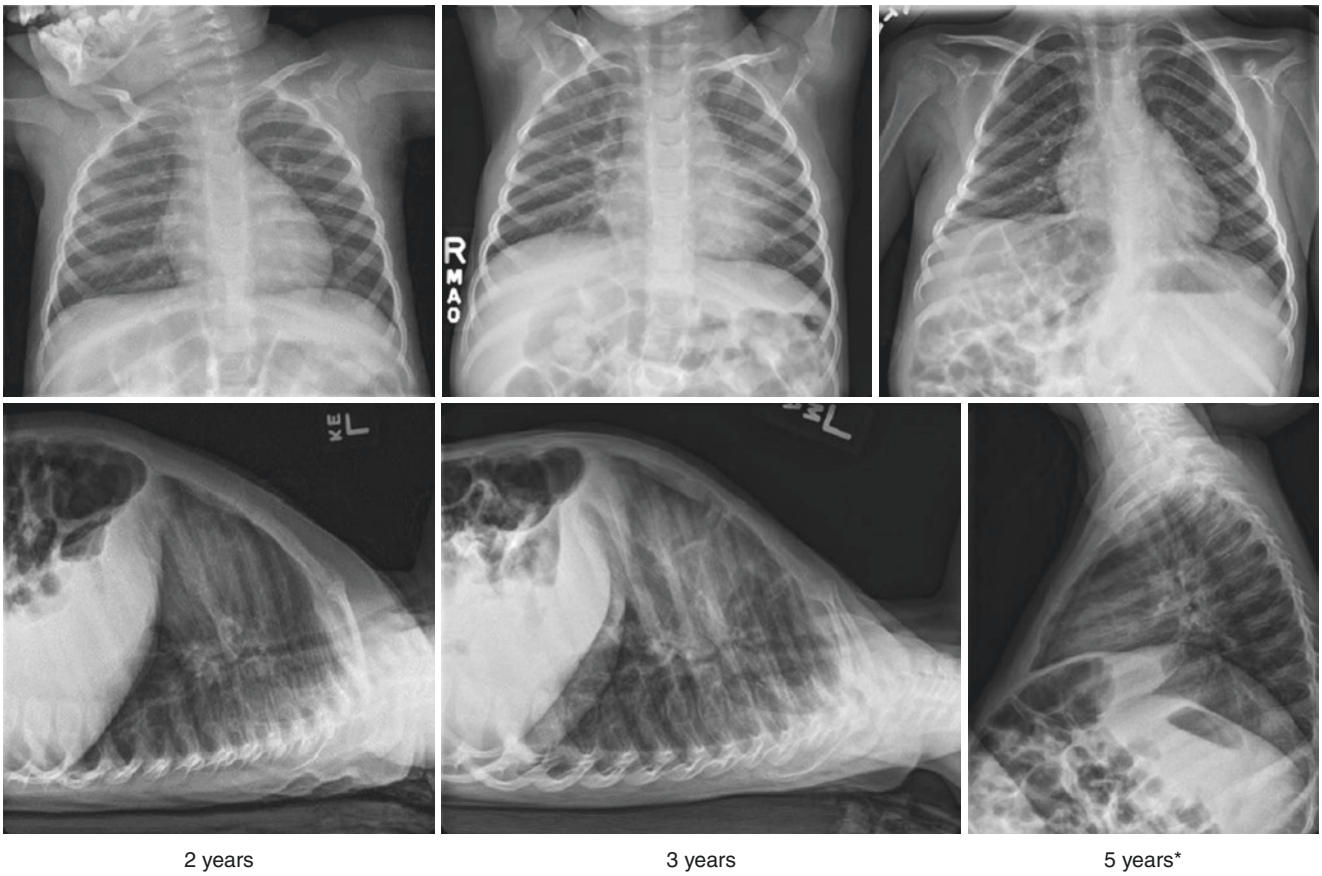

Fig. 42.3 Inadequate thoracic height despite growth, contributing to low lung volumes in a girl with SMA II

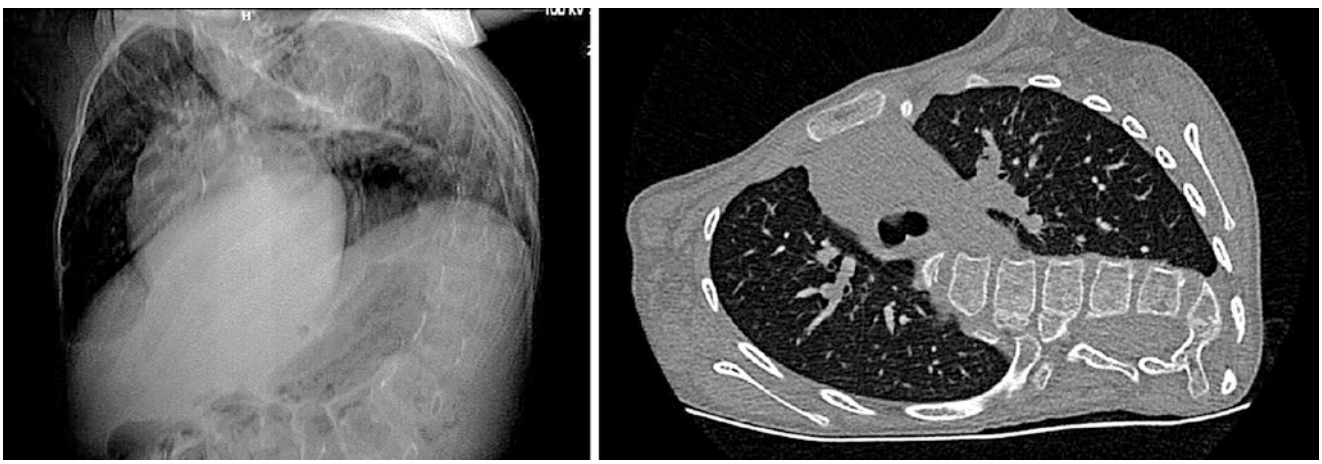

Fig. 42.4 Severe scoliosis in a young boy with congenital muscular dystrophy shown with X-ray (left) and chest CT scan (right). Note the severe rotational thoracic defect, levels of the diaphragm (left), and the multiple vertebral bodies running horizontally within a single frame (right). Asymmetric crowding of ribs is also noted

arousals due to sleep fragmentation. Parallel PSG findings include increased NREM1 [21, 22] and decreased REM sleep [23]. Such findings should raise suspicion for sleep-disordered breathing in patients with neuromuscular disorders.

In 2007, the portable monitoring task force of the AASM recommended that portable monitoring may be used as an alternative to in-laboratory PSGs for the diagnosis of OSA in adults with high pretest probability of moderate to severe OSA [24]. Thus far, studies on portable monitoring have been performed on otherwise healthy children. Children with NMD are at high risk for hypoventilation, and the lack of reliable capnometry monitoring may be a significant limiting factor to allowing for safe and reliable home studies.

In a study to assess the role of overnight pulse oximetry and daytime blood gases in accurately detecting nocturnal hypoventilation in children with long-term noninvasive respiratory support, it was observed that 42% of these subjects experienced nocturnal hypercapnia without nocturnal hypoxemia [25]. In fact, daytime capillary arterialized carbon dioxide levels were normal in 85% of these patients.

Therefore, capnometry monitoring is important in children in whom there is concern regarding nocturnal hypoventilation, regardless of the primary underlying issue (neuromuscular disease, underlying lung disease, or obesity hypoventilation). Most HSAT testing devices do not include any capnometry monitoring. This is a critical aspect of testing as nocturnal hypoventilation in NMD may occur in isolation, and not associated with classic clinical symptoms of sleep-disordered breathing, nocturnal desaturation, or daytime hypercapnia.

Finally, the American Academy of Sleep Medicine (AASM) recommends that HSAT for diagnostic evaluation of suspected OSA should be performed only in conjunction with a comprehensive sleep evaluation, preferably by a sleep medicine specialist, and may be used as an alternative to PSG in patients with a high pretest probability of moderate to severe OSA. As such, patients at risk for central apneas, hypopneas, or hypoventilation should not be tested with such devices. The accuracy of HSAT in these patients is unknown.

Sleep Studies in NMD: Findings

Sleep-disordered breathing in patients with neuromuscular disorders has been well established. However, the type of SDB, timing of onset, and treatment options can vary depending on the underlying disorder. A baseline understanding of the effect of neuromuscular disease on sleep is imperative to suspicion, timely evaluation, diagnosis, and treatment. The findings on polysomnography in a patient with a neuromuscular disorder can be subtle until respiratory insufficiency is more overt. In keeping with the history of non-restorative sleep and frequent nocturnal awakenings, the sleep architecture on PSG will likely reveal increased Stage 1 NREM sleep [21, 22] and decreased REM sleep [23]. Sleep-disordered breathing often manifests as obstructive sleep apnea that is REM sleep predominant. Oximetry on the hypnogram may have a sawtooth pattern versus the prolonged desaturations of hypoventilation [26]. As weakness progresses, the difficulty in polysomnogram analysis lies in differentiating obstructive from non-obstructive respiratory events. Snoring may be absent due to reduced ability to generate a high enough inspiratory flow to produce upper airway vibration. Additionally, thoracoabdominal asynchrony (paradoxical respirations) may be present at baseline, further limiting the ability to detect obstructive events. Respiratory events called "pseudocentral" events or diaphragmatic events are characterized by attenuated intercostal EMG and signals from chest/abdominal belts by the lack of respiratory muscle effort (Fig. 42.5). These events are not from the lack of respiratory drive but instead result from the combination of REM sleep atonia and chest wall muscle and diaphragm weakness [22]. These tracings are similar in appearance to central hypopneas, however, with differing etiologies. Esophageal manometry can facilitate differentiating between such events.

One of the difficulties of neuromuscular sleep medicine is detecting the onset of hypoventilation. Monitoring of ventilation via end-tidal or transcutaneous capnography in addition to respiratory rate is paramount. At the onset, hypoventilation is compensated by an increased sleep fragmentation preventing prolonged desaturations [26], slightly increased end-tidal CO_2 with mild tachypnea and clinical symptoms of unrefreshing sleep due to fragmentation, and morning headaches. Such findings on polysomnography often do not meet the current definition of hypoventilation, further highlighting the importance of recognizing compensatory mechanisms in play during sleep. Lastly, adaptive suppression of REM sleep occurs, thereby reducing the effects of REM-related sleep-disordered breathing in neuromuscular diseases [27].

Spinal Muscular Atrophy

The muscle weakness due to spinal muscular atrophy (SMA) can be a continuum spanning from fetal onset respiratory failure at birth to late-onset SDB in adulthood. In general,

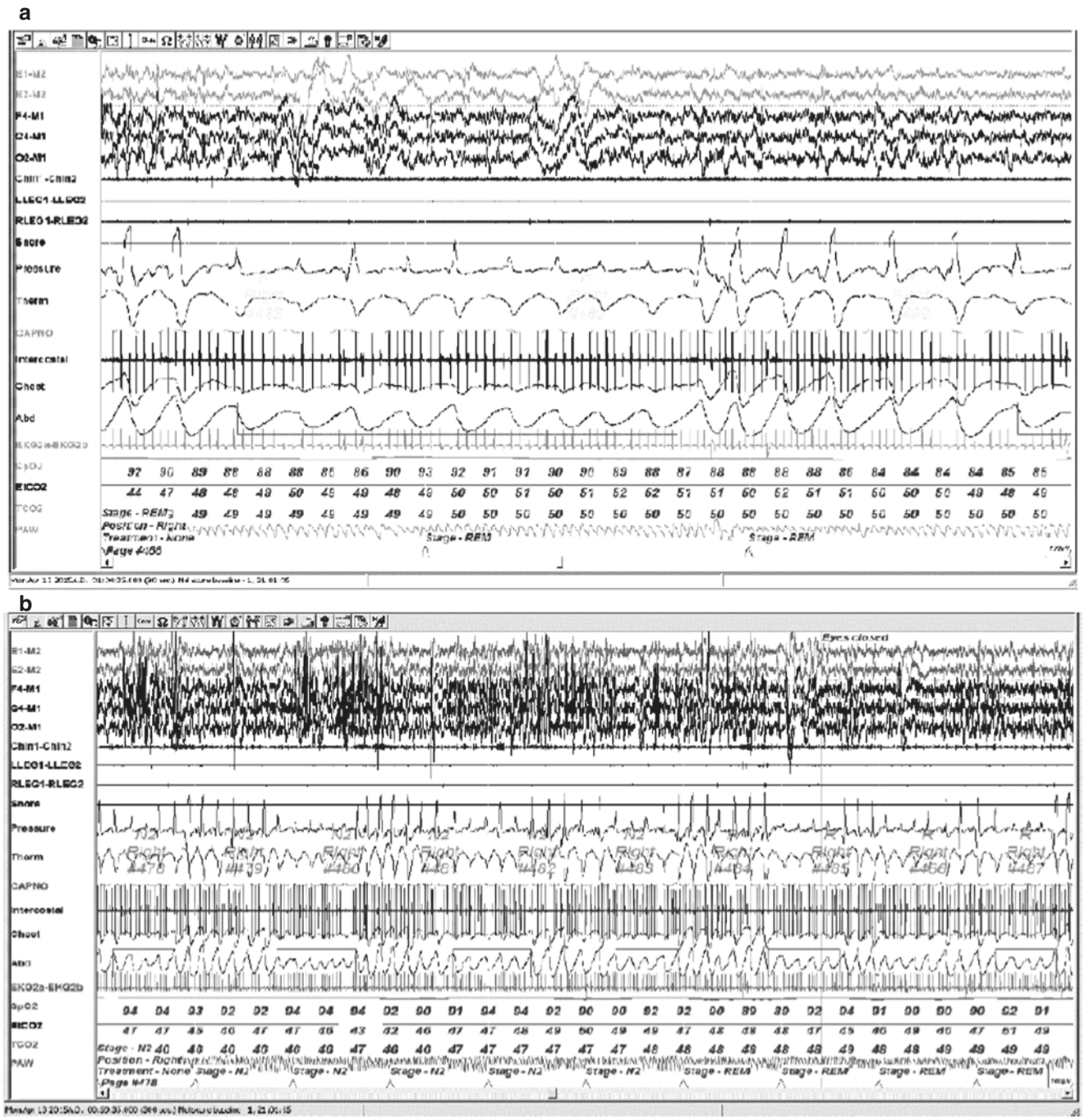

Fig. 42.5 (**a**) REM sleep portion (90 seconds) of a sleep study of a 15-year-old boy with Duchenne muscular dystrophy. Note the non-obstructive respiratory paradox with periodic reduction in intercostal activity during the event. The patient exhibits hypoventilation and hypoxemia at baseline, made worse by this event. (**b**) REM sleep portion (5 minute) of a sleep study of the same 15-year-old boy with Duchenne muscular dystrophy. Note the waxing and waning character of the events

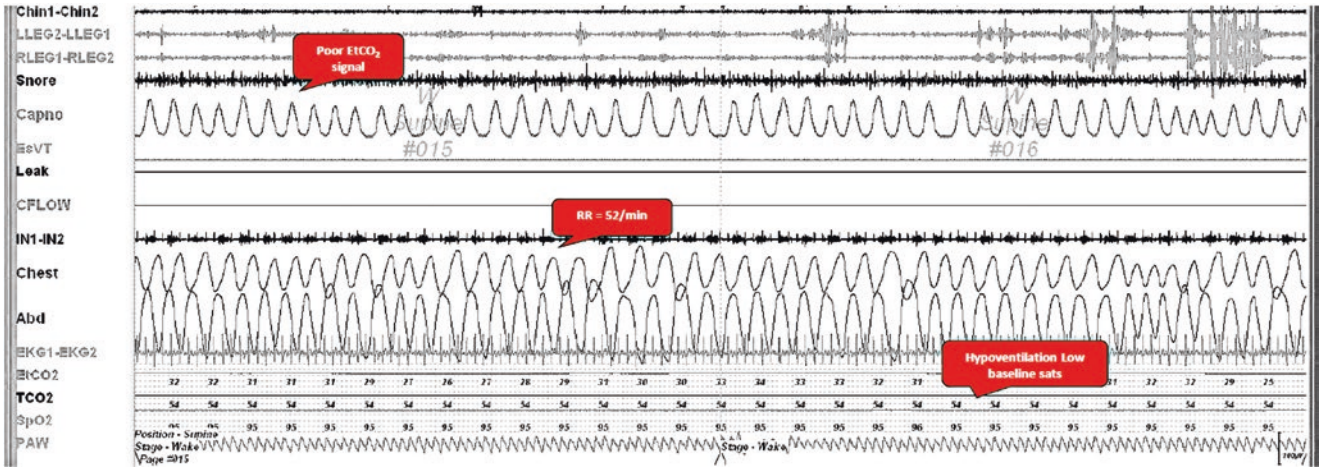

Fig. 42.6 Awake portion (1 minute) of a sleep study of a 5-year-old boy with SMA type I. Note the respiratory paradox, tachypnea, and consequent absence of plateau of end-tidal capnometry waveform (Capno channel) that produces lower related readings ($EtCO_2$) when compared to the transcutaneous CO_2 (TCO_2) channel. Low baseline saturations are also observed

the diaphragm is relatively spared, and remaining muscles are variably affected. Recommendations for children with SMA I, who are unable to sit on their own, are to have a very low threshold to obtain a polysomnogram [28]. The onset of SDB in SMA I is often manifested with upper airway instability, and in very severe cases, patients exhibit airway obstruction even while awake. While awake, patients with SMA I will often manifest tachypnea and respiratory paradox and with greater degrees of weakness also experience hypoventilation and hypoxemia (Fig. 42.6).

Duchenne Muscular Dystrophy

Sleep-disordered breathing in patients with Duchenne muscular dystrophy (DMD) has an anticipated progression. In young boys with DMD and treated with glucocorticoids, there appears to be initial presentation of SDB in the form of REM sleep-related OSA. Continuous nocturnal hypoventilation and ultimately respiratory failure are typically events of the second to third decade. The onset of SDB in steroid-treated patients with DMD has been reported as young as 12 years of age with corresponding FVC% predicted of over 70% [19]. The etiology is multifactorial as chronic glucocorticoid therapy generates obesity in addition to the relentless disease progression. The study affirmed that reduced FVC was associated with a greater risk of hypoventilation, showing that the odds of hypoventilation increased by 20% for every 10% reduction in FVC (OR, 0.80; 95%CI, 0.74–0.87; $P = 0.001$). Interestingly, 16.4% of DMD subjects experienced hypoventilation at a very young age (11.6 ± 3.3 years), and although not significant, this group tended to have lower FVC and respiratory muscle strength profiles compared to their normal or SDB peers. The identification of this small unique group of younger subjects with alveolar hypoventilation and without significant apnea raises the importance of capnometry measurement during PSG acquisition. In steroid-naïve patients with DMD, the decline in lung function occurs about 3 years earlier, and the onset of hypoventilation should be expected at a younger age [29]. DMD patients have normal respiratory drive and respond to hypercarbia and hypoxia by increasing their respiratory rate (Fig. 42.7) compared to age-matched controls who increased their tidal volumes [30, 31]. Using optoelectronic plethysmography, Lo Mauro et al. showed that DMD patients cope with the progressive impairment of the diaphragm by increasing the recruitment of the inspiratory ribcage muscles in order to maintain minute ventilation and do so by increasing their respiratory rate rather than tidal volume [32]. These findings provide evidence that diaphragm weakness in boys with DMD occurs early in the disease. Progression of weakness in DMD is variable, and diurnal hypoventilation occurs as inspiratory muscle weakness progresses [33, 34].

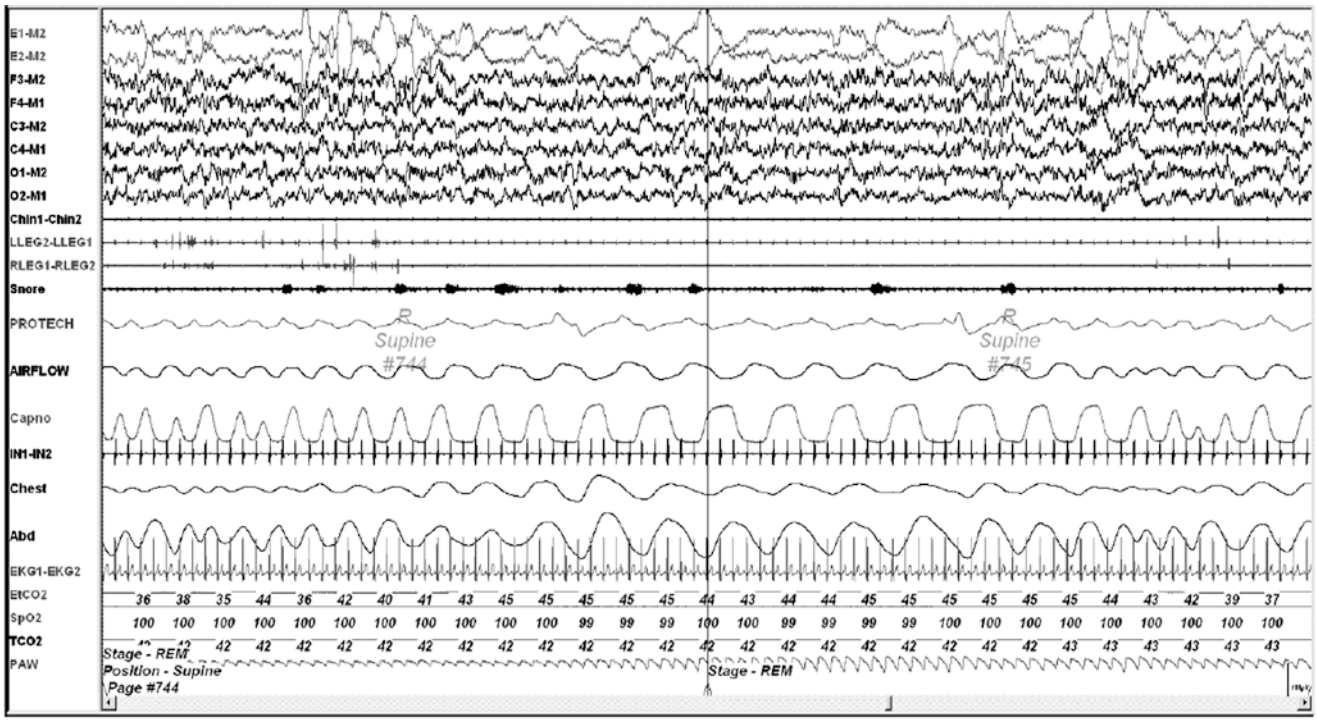

Fig. 42.7 REM sleep portion (1 minute) of a sleep study of a 15-year-old boy with Duchenne muscular dystrophy. Note the range of end-tidal CO_2 ($EtCO_2$) despite a respiratory rate of about 30/min. The $EtCO_2$ channel bears intermittent low values due to the absence of plateau of the related waveform. The respiratory rate is non-physiologic for this age and indicative of compensatory mechanisms at play. Phasic REM sleep exhibits greatest degree of respiratory variability

Congenital Muscular Dystrophy

Congenital muscular dystrophy (CMD) is a rare, inherited neuromuscular disease that comprises heterogeneous subgroups. CMD manifests clinically by early-onset progressive muscle weakness that presents from birth to up to 2 years of age [35]. Certain subtypes are known for early-onset weakness with the inability to sit unassisted, and others present in adulthood. Interestingly, patients with Col6-, LAMA2-, LMNA-, and SEPN1-related CMD are known to have significant diaphragm weakness and may experience hypoventilation even while they are still ambulatory [36]. Diaphragm involvement can be detected with sitting and supine spirometry, noting a fall in FVC% by greater than 20% [37]. In general, it is recommended that there be a low threshold to study these patients by polysomnography.

Spinal Cord Injury

Patients with spinal cord injuries (SCI) are also prone to SDB. Here, characterization of SDB is dependent on the level of the lesion, with higher cervical spine injuries more likely to involve the diaphragm. Patients with SCI may have SDB with or without hypoventilation. The disruption in neural control, abnormal respiratory mechanics with paralysis of intercostal muscles, resultant low lung volumes, and use of CNS suppressants in cervical SCI patients results in roughly 90% of patients with SCI experiencing SDB during the acute phase. The predilection toward central sleep apnea is due to a narrow window between eucapnic and hypocapnic apneic thresholds, sometimes resulting in a periodic breathing pattern [38]. In the setting of cervical (C5–C7) spinal cord injury, about 63% of subjects manifested central apneas, and 88% had periodic breathing. In the case of thoracic spinal cord injury (T1–T6), the incidences of central sleep apnea and periodic breathing were much lower (13% and 38%, respectively). Patients with thoracic SCIs are prone to risk factors suffered by the general population, namely, obesity and subsequent tendency to manifest OSA. The incidence of SDB in the long term is between 22% and 68%, with additional observations of natural loss of function over time and blunted CO_2 sensitivity and respiratory drive [39].

Other Diseases

Metabolic disorders can also present with significant, occult sleep-disordered breathing. SDB including OSA and hypoventilation is common in infants with infantile alpha-

glucosidase deficiency (Pompe disease) [40]. Infants and children with severe neurologic injury or developmental mishaps are very prone to developing chronic respiratory failure from either difficulty maintaining a patent airway free of secretions, abnormal respiratory drive, obstructive sleep apnea, or a combination of a variety of these factors. As they grow, their metabolic needs increase, and pulmonary morbidities from aspiration, infection, and bronchiectasis add to the pulmonary management challenges. These patients merit frequent assessments and warrant polysomnography evaluations repeatedly to optimize their ventilation and growth.

Management Approaches

The detection of respiratory insufficiency seems fairly straightforward if the presentation occurs during an acute crisis such as high spinal cord injury, infantile SMA with acute respiratory infection, etc. However, detection of occult respiratory insufficiency from respiratory weakness presents a greater challenge in wheelchair-bound patients who may present for an ambulatory visit. This rings especially true for young boys with DMD and glucocorticoid therapy. These patients can be quietly tachypneic and are yet able to hold conversations comfortably. Gentle rocking back and forth is subconsciously aimed at increasing inspiratory and expiratory capabilities. In patients with congenital muscular dystrophy, hypoventilation while still ambulatory has also been described. Physical examination of all of these patients often reveals tachypnea, reduced chest excursions with respiratory effort (or sometimes obvious respiratory paradox), and reduced breath sounds due to shallow respirations. Percussion of the lung fields in the mid-clavicular line can reveal hepatic dullness in a higher than usual position (second–fourth intercostal space) providing evidence of low lung volumes at rest (reduced functional residual capacity (FRC)).

Once a deficiency in ventilation or airway clearance is identified, it is critical that it be addressed expediently and effectively. There are, however, a variety of different approaches to doing so that are based on both the age and needs of the patient. Regardless, the goals are re-establishment of appropriate FRC, optimization of tidal volumes, and normalization of gas exchange. These goals are rewarded with maintenance of lung recruitment and prevention of progressive atelectasis.

Nocturnal Ventilation

The goals of initiation of NIV are to normalize ventilation, reduce the work of breathing and provide respiratory muscle rest, improve sleep architecture by reducing sleep fragmentation, and treat SDB. Initiation of NIV has been shown to enhance the quality of life and functional status of patients with NMDs, to prolong survival, and in some patients to attenuate the loss of FVC [41]. The optimal time to initiate NIV in NMD is not clearly defined and universally agreed upon, but consideration should be given to the fact that children may need a little more time to adjust to NIV. The delay in initiation of such support until the first lower respiratory illness-related admission is fraught with unnecessary increased morbidity and perhaps mortality risk.

Patients may be treated with pressure- or volume-cycled modes of ventilation. In pressure-cycled ventilation, a higher designated driving inspiratory pressure is delivered above the end-expiratory pressure until the ventilator cycles into passive exhalation to the designated end-expiratory pressure. In volume-cycled ventilation, flow is delivered until a specific tidal volume is reached; the inspiration then cycles off, and airway pressure returns to the end-expiratory pressure. Regardless of the patient's ability to trigger the ventilator and the chosen mode of ventilation, a backup rate (with a physiologic inspiratory time) must always be included to maintain minute ventilation and provide respiratory muscle rest (Fig. 42.8). Improvement in tidal volumes and minute ventilation may produce reflex central apneas, and the use of a backup rate prevents related respiratory arousals and sleep fragmentation.

The end-expiratory pressure increases resting lung volume to an appropriate FRC, improves ventilation by preventing airway collapse and atelectasis, and treats obstructive apnea by pneumatically stenting the upper airways at the end of exhalation. The inspiratory pressure optimizes minute ventilation and treats obstructive hypopneas and hypoventilation. Technically, the pressure difference between the peak inspiratory pressure and the end-expiratory pressure forms the degree of pressure support the patient receives for spontaneously triggered breaths. Therefore, it stands to reason that the spontaneous and the ventilator breaths need to be as similar as possible to harmonize respiratory rhythm. If the patient is unable to maintain acceptable spontaneous inspiratory time due to severity of weakness, the pressure support volumes will appear much lower. Adding a pressure control feature instead then allows the ventilator to guarantee the set inspiratory time for the triggered breath as well and, hence, an appropriate tidal volume. The level of positive pressure required to normalize gas exchange can be closely approximated at the bedside, but polysomnography would allow for finer adjustments with extended monitoring of carbon dioxide and oxygen levels and sleep architecture.

Isolated continuous positive airway pressure (CPAP) should *never* be used in an attempt to support ventilation in

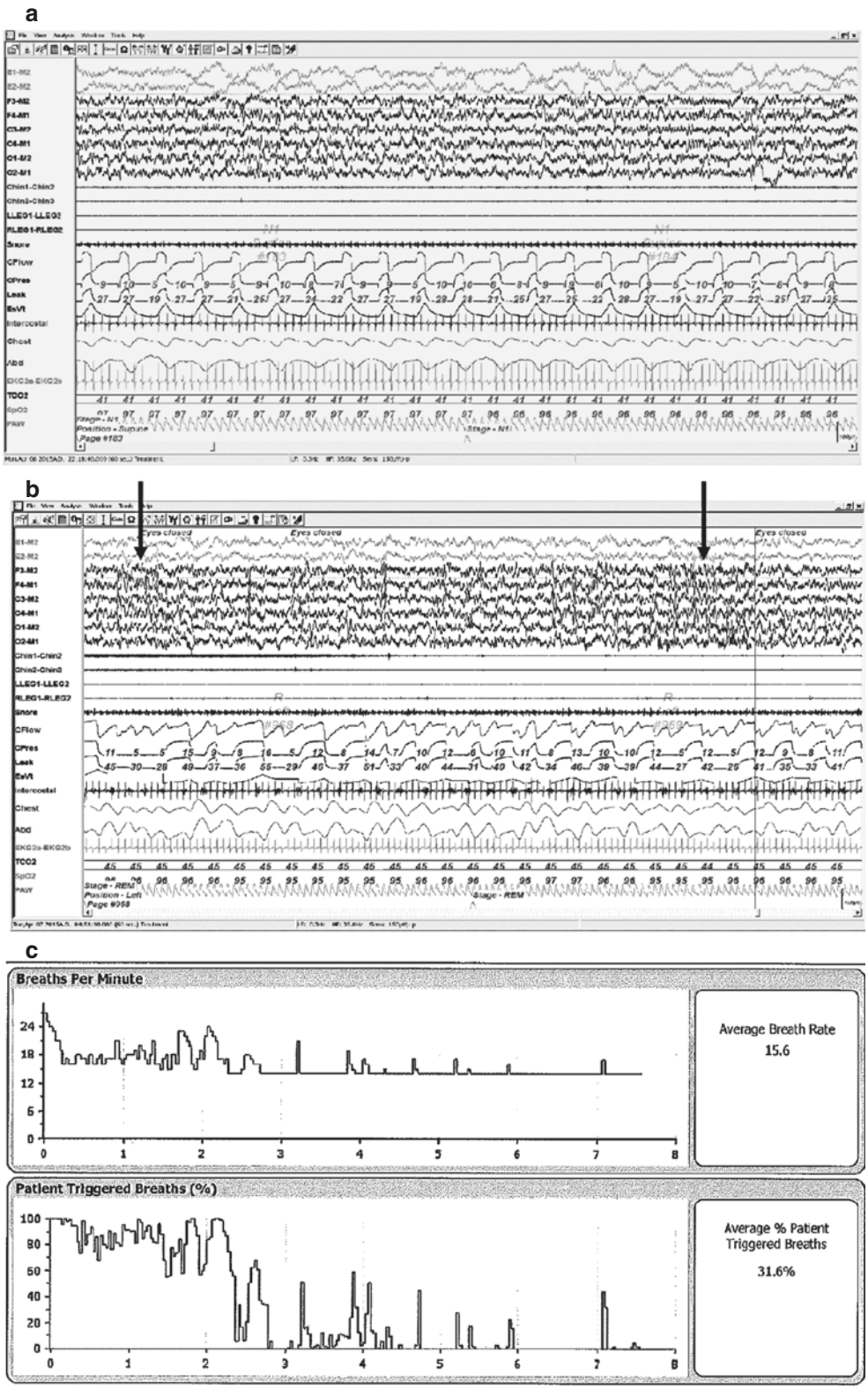

Fig. 42.8 (**a**) This is a 1-minute screen of a sleep study of a 15-year-old girl with SMA II. She appears fully supported with her current pressures and a full respiratory rate of 20/min with little additional spontaneous effort. The respiratory rate of the patient is entirely driven by the ventilator. (**b**) 1-minute screen of a sleep study of the same 15-year-old girl with SMA II, later in the study after withdrawing the backup rate. She appears to be in REM sleep, tachypneic (respiratory rate of 38/min) with acceptable capnometry, with arousals (arrows). Saturations are lower as well. (**c**) This is an overview of 8 hours of a ventilator download of a 20-year-old man with SMA II. Note the complete dependence on the ventilator rate following sleep onset. Occasional awakenings overnight are reflected with the increase in frequency of patient-triggered breaths

patients with NMD since it does not augment the tidal volume, nor does it allow for setting a rate to provide respiratory muscle rest. The only exception to this is a situation where obstructive sleep apnea exists in the presence of preserved respiratory muscle strength.

Titration of pressures or volumes in the sleep lab should be performed incrementally with careful documenting of the impacts on heart rate, respiratory rate and pattern, character of apneas, saturations and capnometry, tidal volume, leak, and sleep architecture. Higher pressures can lead to increased leak that could precipitate increased obstructive events, arousals, and ineffective ventilation. The management of these patients requires the careful follow-up with repeated assessments of ventilator downloads and periodic re-titration in the sleep lab to assure adequate ventilator support in the face of disease progression.

Diurnal Ventilation

Patients with progressive NMD often begin to spontaneously extend the use of nocturnal NIV into the day. This extension typically occurs many years after initiation of nocturnal NIV and is typically guided by the patient. Patients become increasingly symptomatic despite the use of assisted ventilation during sleep. In severe pediatric forms of NMD, such as congenital myopathies or SMA type I, patients may require 24-hour ventilator support from birth.

Past guideline from the American Thoracic Society (ATS) recommended starting diurnal ventilator support after the onset of daytime hypercapnia [42]. Subsequent studies have reported that 95% of patients with DMD complained about daytime dyspnea with the onset of hypercapnia [43, 44]. Clinical observations suggest that patients maintain normal PCO_2 by altering their position and breathing pattern to maintain ventilation as described earlier. Institution of diurnal ventilation has been met with resolution of dyspnea and symptoms and reducing the risk of respiratory fatigue and failure [45, 46]. For practical reasons, the type of respiratory support and existing wheelchair design need to be mutually compatible for successful use by the patient.

Interfaces for Ventilation

The options of interfaces for delivering daytime ventilator support include nasal and face masks (as a direct extension of nocturnal ventilation), mouthpiece (for sip or "sip and puff" ventilation), and tracheostomy.

Mask Interface

Suitable respiratory support for neuromuscular patients also warrants applying appropriate interfaces. There are a variety of different nasal masks and cannula interfaces, which are the most preferred. A nasal interface allows for continued speech, as patients learn to use the nasally provided ventilator breaths to speak during exhalation. A nasal mask may also protect against aerophagia, abdomen distension, and aspiration of vomitus. These issues are critical consideration for patients who lack the ability to spontaneously remove a full-face mask in the event of emesis. For patients with persistent oral air leak despite the use of a chinstrap, oronasal or full-face masks are considerations with the right precautions (venting gastric tubes, timing of feeds, etc.). Nasal masks can be used by patients too young and/or unable to tolerate upright position (e.g., SMA I infants and children) or mouthpiece ventilation. Some users of mouthpiece ventilation may prefer the nasal mask when travelling as it would be less prone to dislodgment and also allow for napping. Due attention must be paid to maintenance of related skin health. A mask interface can certainly be used for continuous ventilation [45].

Mouthpiece

Mouthpiece ventilation (MPV) is an on-demand system that is attached to the patient's wheelchair for daytime use. This system suits the wheelchair-bound patient best if there is a preserved ability to form a seal around the mouthpiece. The interface consists of a plastic or silicone tube that is held between the lips and teeth. Usually, a sipping action or tapping the tube with the tongue is sufficient to trigger the ventilator. MPV has gained popularity and is now being offered as the first mode of ventilation for daytime support. MPV is an effective interface that is inexpensive, easy to use, and safe. The preferred mode of ventilation in MPV is assist control with a larger desired tidal volume (about 2.5–3 times the inspiratory capacity).

Tracheostomy

Tracheostomy is the interface of choice in cases when the use of NIV (despite the wide variety of interfaces) provides less than ideal ventilator support and the need for such support is deemed to be continuous. This is especially true for infants and children under the age of 5 years or when bulbar symptoms are dominant and handling of oral secretions is

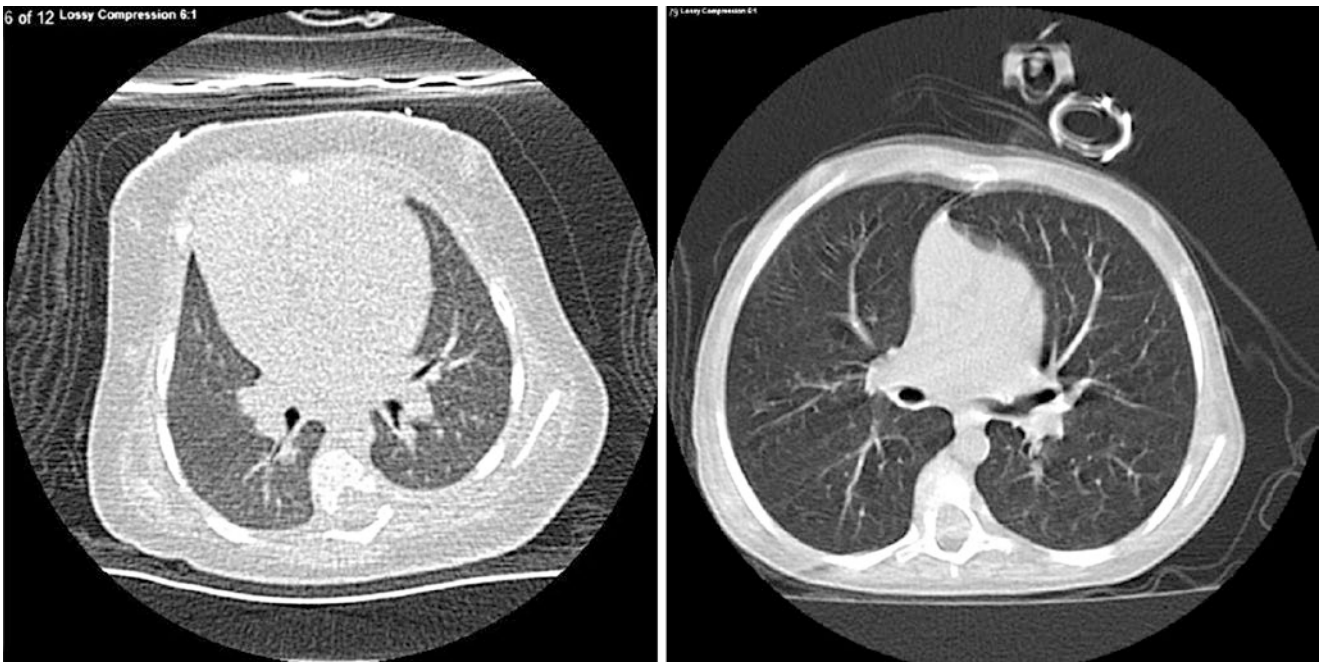

Fig. 42.9 These are CT scans of the same child at 8 months (left) and at 3 years (right). The patient has a congenital myopathy and received a tracheostomy shortly after birth. She presented with chronic respiratory failure at 6 months. Mechanical ventilation was instituted with clinical improvement. A CT scan at 3 years showed resolution of previously noted thoracic dystrophy

severely impaired. In the smaller growing child, it protects against the typical mid-face deformity that occurs from long-term NIV initiated at an early age, and allows for maintenance of normal thoracic architecture (Fig. 42.9). However, ventilation by tracheostomy requires focused care and maintenance, and is not without controversy, especially in NMD that are incurable or progressive.

Conclusions

The spectrum of neuromuscular respiratory disease in children is broad, and it is important that patients' diagnoses not be the only consideration when determining evaluation and management strategies. Rather, it should be their physiology state (or disruption) that needs to determine what the management course should look like. There are some diagnoses that are progressive and some that are static. However, in a growing child, the consequences are almost often progressive. This means that the testing and management strategies need to be adjusted based on their medical and social needs. There is constant discovery of novel treatment agents, and longevity of patients with SMA and DMD is increasing. It is therefore important that clinicians be aware of related guidelines and consensus statements that make recommendations to provide the best outcomes for these patient populations.

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