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# The Value of Respiratory Muscle Testing in Children With Neuromuscular Disease

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Routine lung function and respiratory muscle testing are recommended in children with neuromuscular disease (NMD), but these tests are based on noninvasive volitional maneuvers, such as the measurement of lung volumes and maximal static pressures, that young children may not always be able to perform. The realization of simple natural maneuvers such as a sniff or a cough, and the measurement of esophageal and gastric pressures during spontaneous breathing can add valuable information about the strength and endurance of the respiratory muscles in young children. Monitoring respiratory muscles in children with NMD may improve understanding of the natural history of NMD and the evaluation of disease severity. It may assist and guide clinical management and it may help the identification and selection of optimal end points, as well as the most informative parameters and patients for clinical trials.

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**ABBREVIATIONS:** CPF = cough peak flow; ΔPgas to ΔPes = ratio of change in gastric pressure to change in esophageal pressure; DMD = Duchenne muscular dystrophy; fR = respiratory frequency; fR/VT = rapid and shallow breathing index; NIV = noninvasive ventilation; NMD = neuromuscular disease; OEP = optoelectronic plethysmography; $P_{0.1}$ = pressure generated in the first 100 milliseconds of inspiration against an occluded airway; Pdi = transdiaphragmatic pressure; Pes = esophageal pressure; Pgas = gastric pressure; Pgas cough = gastric pressure during maximal cough; PImax = maximal static inspiratory pressure; SMA = spinal muscular atrophy; Sniff Pdi = transdiaphragmatic pressure during maximal sniff; Sniff Pes = esophageal pressure during maximal sniff; SNIP = sniff nasal inspiratory pressure; TTdi = diaphragmatic tension time index; TTes = esophageal tension time index; TTmus = noninvasive index of respiratory muscle endurance; VC = vital capacity; VT = tidal volume

Routine lung function and respiratory muscle testing are recommended in children with neuromuscular disease (NMD). Indeed, respiratory muscles are rarely spared in NMD, with respiratory muscle weakness being responsible for most of the morbidity and mortality of these diseases. Routine pulmonary function testing consists of noninvasive volitional tests, such as the measurement of lung volumes and maximal static pressures, that young children may be unable to perform.[1-4] These tests are also "global" respiratory tests that do not allow distinguishing the specific involvement of the different inspiratory muscles (ie, the diaphragm and the accessory

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inspiratory muscles), which may be of importance for clinical management. Indeed, children having a NMD characterized by involvement of the diaphragm should be screened for sleep-disordered breathing.[5-7] Moreover, a precise evaluation of the capacity of the inspiratory and expiratory muscles may be important for the understanding of the natural history of the disease. Finally, identification of the most informative respiratory parameters associated with the most rapid decline in case of a progressive disease may optimize patient selection for therapeutic trials with innovative therapies.[8] For young or noncooperative children, nonvolitional and/or more "invasive" tests may, thus, be required. This review gives an overview of the most recent advances in the field of respiratory muscle testing in children, and the clinical feasibility and usefulness of these tests.

## Respiratory Muscle Testing in Children

The distinction between volitional/nonvolitional and noninvasive/invasive tests is of major importance in children. Tests should be preferentially noninvasive, and for the youngest children, nonvolitional, which restricts considerably the available respiratory muscle tests for this age group.

Respiratory muscle testing should be performed routinely. Ineffective cough or recurrent or severe respiratory infections suggest weakness of the respiratory muscles, but there is no known correlation between clinical symptoms and related objective measures of respiratory muscle weakness.[9] The only situation in which five simple questions (ie, do you feel breathless when you lie down, when you bend forward, when you swim in water or lie in a bath? Have you changed your position in bed? Have you noticed a change in your sleep [waking more, getting up, poor-quality sleep]?) were able to detect sleep-disordered breathing with a high sensitivity and specificity was diaphragmatic paralysis in adults.[10] We will start our review with noninvasive tests, as they are more widely performed than invasive tests (Table 1).

### *Noninvasive Tests*

The monitoring of breathing pattern with the recording of respiratory frequency ($f_R$), tidal volume ($V_T$), and minute ventilation is easy and allows the calculation of the rapid and shallow breathing index ($f_R/V_T$). Although this index is more likely a reflex response to an increase in the respiratory workload than the consequence of respiratory muscle fatigue or weakness per se,[11] it has been shown to be significantly higher in children requiring nocturnal noninvasive ventilation (NIV) as compared with those not requiring NIV.[12]

The analysis of the thoracoabdominal pattern of breathing is another way to quantify the degree of respiratory muscle impairment. This analysis can be performed by respiratory inductive plethysmography. This analysis showed marked abnormalities in thoracoabdominal pattern of breathing in young children with spinal muscular atrophy (SMA) and congenital myopathy.[13]

Optoelectronic plethysmography (OEP) is a way to analyze displacement of the thoracic and abdominal compartments, with the aid of special cameras.[14,15] In children with SMA, OEP has demonstrated abnormal thoracoabdominal kinematics with normalization during NIV.[16,17] Similarly, in patients with Duchenne muscular dystrophy (DMD), the average contribution of the abdominal volume change to $V_T$ in the supine position measured by OEP has been shown to decrease significantly with age and was associated with nocturnal hypoxemia.[18] The OEP was also useful to detect the abnormal chest-wall distortion during cough in patients with NMD.[19]

Ultrasonography is another promising technique for the evaluation of the structure and dynamic function of the diaphragm. However, standardized assessment and imaging protocols have yet to be developed and validated.[20]

Measurement of tidal flow-volume loops by respiratory inductive plethysmography has also shown the adverse effect of bracing in young children with SMA.[21] However, it has to be noted that these deleterious effects were not observed with the Garchois brace, which allows thoracic expansion and, thus, less impairment of respiratory function.[22]

Cooperative children over the age of 5 to 8 years are able to perform reproducible maximal maneuvers. Vital capacity (VC) is the simplest test that has been widely assessed in children with NMD. Technical quality standards have been published that may be difficult to fulfill for young children.[23] Therefore, simpler maneuvers have been used, such as slow VC and maximal inspiratory capacity.[24] Mask spirometry may circumvent the inability to seal lips around a mouthpiece for patients with facial weakness, which is very common in children with NMD.[25] VC in the sitting and supine positions is recommended in case of diaphragm dysfunction, as a $>25\%$ fall while in the supine position is associated with diaphragm weakness.[26] However, a