

## Weaning and extubation readiness in pediatric patients\*

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**Objective:** A systematic review of weaning and extubation for pediatric patients on mechanical ventilation.

**Data Selection:** Pediatric and adult literature, English language.

**Study Selection:** Invited review.

**Data Sources:** Literature review using National Library of Medicine PubMed from January 1972 until April 2008, earlier cross-referenced article citations, the Cochrane Database of Systematic Reviews, and the Internet.

**Conclusions:** Despite the importance of minimizing time on mechanical ventilation, only limited guidance on weaning and extubation is available from the pediatric literature. A significant proportion of patients being evaluated for weaning are actually ready for extubation, suggesting that weaning is often not con-

sidered early enough in the course of ventilation. Indications for extubation are even less clear, although a trial of spontaneous breathing would seem a prerequisite. Several indices have been developed in an attempt to predict weaning and extubation success but the available literature would suggest they offer no improvement over clinical judgment. Extubation failure rates range from 2% to 20% and bear little relationship to the duration of mechanical ventilation. Upper airway obstruction is the single most common cause of extubation failure. A reliable method of assessing readiness for weaning and predicting extubation success is not evident from the pediatric literature. (*Pediatr Crit Care Med* 2009; 10:1–11)

**KEY WORDS:** weaning; extubation; mechanical ventilation; respiratory support; spontaneous breathing

**R**espiratory disorders are the main cause of respiratory failure in children. Unfortunately, respiratory failure fits no well-defined clinical description; it may have an abrupt onset or may occur

insidiously with gradual and progressive deterioration of pulmonary function. Insufficient alveolar ventilation from any cause results in hypoxemia and hypercapnia that may contribute to further depression of ventilation, culminating in frank respiratory failure. The major intervention to prevent morbidity and death is mechanical ventilation (MV). The average pediatric intensive care unit (PICU) has about 30% (range 20%–64%) of its patients mechanically ventilated for a mean of 5–6 days (1, 2).

Although mechanical ventilation is often life saving, it can be associated with complications such as ventilator-induced lung injury and nosocomial pneumonia. Endotracheal tubes (ETT) are uncomfortable for patients and increase the need for sedatives. An ETT in the upper airway can be associated with airway injury, particularly in mobile young patients. Furthermore, positive pressure ventilation may contribute to cardiovascular instability from heart–lung interactions. Therefore, it is important that MV be discontinued as soon as the patient is capable of sustaining spontaneous breathing. However, the experience in adults suggests that premature extubation may also be prob-

lematic and result in emergent reintubation with attendant complications, including the potential of catastrophic morbidity (3). A high mortality rate has been documented in both pediatric (4) and adult (5, 6) patients who have required reintubation after extubation failure. Extubation failure is independently associated with a five-fold increased risk of death in pediatric patients (7). Consequently, although expeditious weaning and extubation are the goal, premature extubation can be lethal.

Over 50% of ventilated PICU patients will have been extubated by 48 hrs after admission, but the rest often require prolonged ventilatory support. Failed planned extubations in the latter group average 8.0% (unpublished observations from Kurachek et al [7]) but range up to 20% in some studies. Conversely, 50% of unplanned extubations end in success (8), implying that some patients could be extubated earlier. Both premature and delayed extubation increases morbidity and mortality as well as costs. Initiation of weaning and timing of extubation have been largely neglected in the pediatric literature. This review examines available data in children and

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Table 1. Definitions—summary of terms

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Weaning is the transition from ventilatory support to completely spontaneous breathing, during which time the patient assumes the responsibility for effective gas exchange while positive pressure support is withdrawn. Note that spontaneous breathing is a prerequisite for weaning to begin and decreasing ventilator support is not the sole criterion of successful weaning

Extubation is the removal of the endotracheal tube. Criteria for extubation include spontaneous ventilation, hemodynamic stability, intact airway reflexes, and manageable airway secretions. Success is defined as 48 hrs of spontaneous breathing without positive pressure support. Early extubation failure is defined as that which occurs within 6 hrs of extubation; intermediate extubation failure is that which occurs from 6 to 24 hrs of extubation; and late extubation failure is defined as that which occurs from 24 to 48 hrs of extubation

Spontaneous breathing test is a subjective determination of whether the underlying disease process necessitating mechanical ventilation has improved sufficiently to allow the patient adequate gas exchange with spontaneous breathing

Extubation readiness test is a formal trial of spontaneous breathing to evaluate readiness for discontinuation of the endotracheal tube and/or ventilatory support. This may be performed with variable pressure support assist but we propose spontaneous breathing be evaluated for 2 hrs on continuous positive airway pressure  $\leq 5$  cm H<sub>2</sub>O or T-piece (zero end-expiratory pressure). Criteria of failure, both subjective and objective, are proposed in Table 3

Ventilator free days is an outcome measure consisting of the number of days in a given time period (conventionally 28 days) the patient does not require ventilator support. Successful discontinuation of ventilator support requires a minimum of 48 hrs without positive pressure ventilation. Patients who die are considered to have zero ventilator free days

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adults and makes recommendations for weaning and optimal timing of extubation in children receiving ventilation for respiratory failure.

### Concepts of Weaning, Spontaneous Breathing and Extubation Readiness Trials

*Overview of Factors Impacting Weaning.* There is no standard method of weaning. Indeed, there is disagreement about when the onset of weaning actually occurs and no validated, objective criteria as to when a patient can be extubated. For definitions of common terms regarding weaning and extubation readiness see Table 1.

The course of MV begins with intubation and the onset of ventilatory support (Fig. 1). As the disease progresses, MV is fine tuned to provide effective gas exchange. When the acute phase of the disease subsides, noted by a decrease in the mean airway pressure required, weaning begins. The end of weaning can be defined as the time at which the patient's spontaneous breathing alone can provide effective gas exchange, although how this point can best be determined is unclear. At the end of weaning is extubation, or the act of removal of the ETT.

The length of weaning depends on a number of factors, among them fluid status. When total body water increases, lung compliance decreases due to increased lung water, chest wall, and diaphragm edema. In adults with acute respiratory distress syndrome (ARDS) it is clear that the injured lungs should be managed dry (9, 10). Patients managed with a conservative fluid regime had fewer MV days and a quicker return of

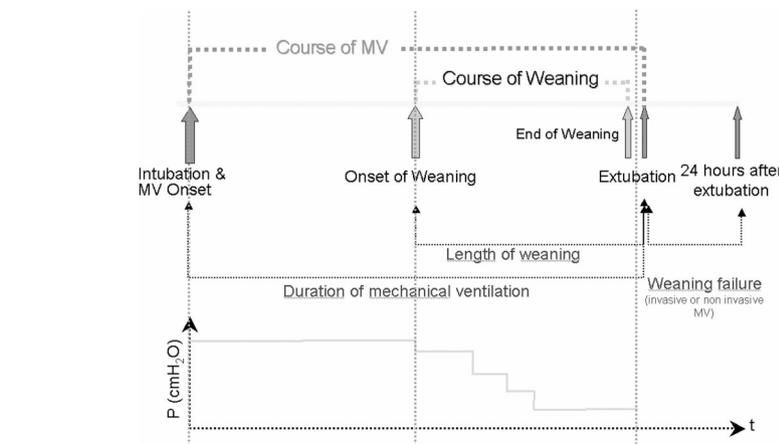


Figure 1. A schematic of the time and pressure courses of mechanical ventilation (MV), along with the defined phases, in a pediatric intensive care unit patient.

normal lung function than those receiving a more liberal regime (9). The importance of fluid balance in children is not as clear. A retrospective study of cumulative fluid balance showed no effect on weaning or extubation success (11). However, two retrospective studies of children with multiple organ failure showed survival may be associated with less fluid overload (in the setting of continuous renal replacement therapy) (12, 13). Similarly, a review by Swaniker et al (14) of 128 children placed on extracorporeal life support for respiratory failure showed increased survival with fluid removal and return to dry body weight.

Positive end-expiratory pressure (PEEP) is another factor that may impact the length of weaning. Early institution of PEEP generally improves oxygenation in ARDS but neither decreases the incidence of ARDS (15) nor changes the weaning times or outcomes if a low-

tidal volume lung protective strategy is used (16).

Sedation further complicates weaning and extubation (17–19). Oversedation may depress central respiratory drive whereas under sedation can leave a child restless. Thrashing movements can result in airway trauma from the ETT. Two groups have shown an association between sedation level and extubation readiness (18, 19), but this has not been validated prospectively in infants and children. Sedation assessment tools are being developed for this purpose (17, 20).

Pulmonary hypertension is another important factor in determining readiness for weaning because of its effect on the patient's oxygenation (21, 22). Supplemental oxygen and ventilatory support are the mainstays of treatment for pulmonary hypertension and there is reluctance to withdraw these too quickly in

the absence of direct measures of pulmonary arterial pressure or resistance.

Differences in diaphragmatic function may relate to longer weaning times in infants and young children. Accessory respiratory muscles are not as developed as in older children (23). As diaphragmatic dysfunction develops with prolonged MV the duration of weaning can increase.

Steroids may play a role in weaning and extubation by reducing tracheal inflammation associated with tracheal injuries from the ETT, as they do in another cause of subglottic edema in children, croup (24). One randomized, controlled trial in children (25) showed steroids prevented upper airway obstruction (UAO) whereas the only other such study (26) did not. Studies in adults have shown the same dichotomy. It is noteworthy that the successful randomized controlled trials in both adults and children have started steroids 6–24 hrs before extubation whereas the unsuccessful ones have started the drug under 6 hrs before extubation.

Finally, other factors are probably important to the weaning process, but there is a dearth of research in these areas, and they are not further discussed. These include disease reversibility (rapid—respiratory syncytial virus bronchiolitis vs. slow—respiratory syncytial virus pneumonia/ARDS [27]), cardiac function, postoperative, neurologic, and nutritional status.

## Predictive Indices for Weaning

Several indices have been developed to predict success in weaning and extubation. Although these indices have been variably used in research, they have not found common use in clinical care—likely because of their complexity and lack of proven benefit over clinical judgment.

**Rapid Shallow Breathing Index (RSBI =  $f/V_T$ ).** The RSBI was devised by Yang and Tobin (28) and found to be a good discriminator of weaning success and failure. This test has become widely used in practice and research with varying success. Recently, the issue has been revisited in a meta-analysis of 41 RSBI studies (29). An editorial that accompanied the meta-analysis (28) suggests that during weaning, the  $f/V_T$  index can be thought of as a screening test with high sensitivity and low specificity, and therefore should be used early in the course of MV to identify patients who can breathe

on their own. Specificity is obtained by applying a confirmatory test such as esophageal pressure trend measurements (30) which are easy to apply in a PICU setting (31).

**Compliance, Resistance, Oxygenation, Pressure Index (CROP Index) (Dynamic Compliance  $\times$  Maximal Negative Inspiratory Pressure  $\times$  ( $PaO_2/PAO_2$ )/Respiratory Rate).** Thiagarajan et al (32) found that spontaneous respiratory rate  $\leq 45$ /min, spontaneous tidal volume  $\geq 5.5$  mL/kg, RSBI  $\leq 8$  breaths/min/mL/kg body weight, and Compliance, Resistance, Oxygenation, Pressure Index (CROP Index)  $\geq 0.15$  mL/kg body weight/breaths/min were good predictors of successful extubation. Baumeister et al (18) used a modified RSBI and CROP indices to predict successful extubation. Their threshold values (RSBI  $\leq 11$ , CROP index  $\geq 0.1$  mL/kg body weight/breaths/min) differed from Thiagarajan's. As with adults, conflicting studies by others (18, 33, 34) found that those indices did not reliably predict extubation outcome in children. Manczur et al (34) studied 47 patients under continuous positive airway pressure (CPAP). Seven failed extubation (14.9%) with low-tidal volume ( $< 6$  mL/kg) and minute ventilation ( $< 180$  mL/kg) associated with failure. RSBI did not predict outcome.

**Volumetric Capnography.** Hubble et al (35) used volumetric capnography to predict successful extubation in 45 children. A volumetric capnogram plots  $CO_2$  concentration in airway gas against expired volume. The slope of an expired, single-breath  $CO_2$  waveform can be used to calculate the physiologic dead space ( $V_D/V_T$ ). They found that  $V_D/V_T \leq 0.50$  reliably predicted extubation success with 75% sensitivity and 92% specificity, whereas a  $V_D/V_T > 0.65$  identified patients at risk for failure. Volumetric capnography requires an arterial or a capillary blood gas.

## Techniques of Weaning

The most common approach to weaning infants and children is gradual reduction of ventilatory support. Weaning with intermittent mandatory ventilation (IMV) or synchronized IMV (SIMV) occurs by reducing the ventilatory rate. With pressure-support (PS) ventilation, the inspiratory pressure is initially set to provide the required support and then reduced gradually. PS is often combined with IMV/SIMV during weaning. Volume support and volume-assured pressure

support are special forms of PS available in certain ventilators that guarantee a minimal tidal volume per assisted breath. Weaning with volume support is semiautomatic, where the PS level required to maintain a certain tidal volume is reduced automatically as respiratory mechanics improve. Extubation occurs from a low level of ventilatory support or after an extubation readiness test (ERT) (see later in this review). Unlike in adults, it seems it is common practice to extubate infants and children from a low level of ventilatory support (4).

A second school of thought recommends moderate amounts of ventilatory support to rest the patient's respiratory muscles and performing a daily ERT. MV is discontinued if the ERT is passed (36, 37). This approach has been more commonly used to wean adult patients than children.

In a small number of patients, weaning is attempted with alternating periods of complete ventilatory support and graded spontaneous breathing with assistance. This "sprinting" is performed on the theory that the respiratory muscles can be slowly trained to sustain complete spontaneous breathing. There is currently little evidence that such an approach is an effective way of training muscles. There are also no data comparing such an approach with more traditional approaches of weaning (38). A recent multicenter randomized control trial comparing three modes of weaning found that there were no significant differences between having no protocol, weaning by PS, or volume support (19).

Adult trials have often used standardized weaning protocols (39, 40) to minimize the time on a ventilator and provide uniform decisions about weaning (see a recent review by Fessler and Brower [41]). Studies in children have begun to follow suit (2, 42–44), and the utility of ventilator protocols in this age group has been reviewed (45). These weaning trials embraced a daily ERT, and all have used ventilator free days (see Table 1 for definition) as their primary outcome. The concept of ventilator free days (46) is implicitly based on having a low failed extubation rate from any cause other than the original cause of respiratory failure. This standard is likely to be adopted in pediatric trials (2) but may be inappropriate since there is not only a higher rate of failed extubations in this group, but up to 40% may involve UAO (7). Thus, for pediatric research, it may be important to

define the end of successful weaning in a way short of extubation. Whether the extubation is successful or not may be of secondary importance. This approach was taken by Schultz et al (47) in their pediatric weaning study and was allowed in the ARDSnet low-tidal volume trial (37) in adults, both of which studies allowed achievement of minimum support settings short of extubation. Ideally, the timing of extubation should coincide with the determination that the patient is ready to sustain adequate gas exchange by spontaneous breathing alone. It is clear from the published studies that there is no such pediatric standard.

### Adult Studies of Weaning and Extubation

In 2001, a task force facilitated by the American College of Chest Physicians, the American Association for Respiratory Care and the American College of Critical Care Medicine published evidence-based guidelines for weaning and discontinuing ventilatory support (48). They classified adult studies on weaning from mechanical ventilation into the following: 1) trials of discontinuation assessment strategies or ERTs; 2) controlled trials of stepwise reduction in mechanical support; and 3) controlled trials of alternative discontinuation strategies.

In a study by Esteban et al (3), 2-hr trials of unassisted breathing using PS of 7 cm H<sub>2</sub>O were compared with T-piece alone. More patients in the PS group tolerated the trial and were extubated at the end of the trial than the T-piece group (86% vs. 78%; relative risk of failure, 0.64; 95% confidence interval, 0.43–0.94). There was no difference in the rate of reintubation. A second similar study by Esteban et al (48), also showed no difference in reintubation rates between groups. However, the shorter T-piece trial benefited patients by reducing ICU and hospital duration (2 days and 5 days shorter, respectively).

Five randomized controlled trials compared alternative methods of reducing ventilatory support in patients in whom clinicians thought extubation was still several days away (36, 50–53). The most informative results come from the two largest studies by Esteban (50) and Brochard (36). Both showed that when patients were first evaluated for extubation using a T-piece, about 76% could be extubated without weaning. The remaining patients were randomized to be

weaned using 2-hr spontaneous breathing trials (SBT) with several different modalities: multiple daily T-piece/CPAP breathing; PS mode; and SIMV. The trial by Esteban et al (50) also included a fourth arm, once daily T-piece tests. There was no difference in the duration of ventilation between T-piece and PS, the trends going in opposite directions in the two studies: Esteban et al (50) favored weaning with T-piece whereas Brochard et al (36) favored PS. Both studies showed shorter duration of ventilation with T-piece compared with SIMV. In the comparison of PS with SIMV, both studies found trends in favor of PS, although the effect in the study by Brochard (36) was much larger. Jounieaux et al (51) randomized 19 patients to SIMV + PS vs. SIMV alone. The duration of the weaning process was approximately 1 day shorter in the group that received PS.

Two adult studies examined the use of noninvasive positive pressure ventilation to facilitate stepwise reductions in ventilatory support for patients hospitalized with chronic obstructive pulmonary disease exacerbations who failed a 2-hr T-piece trial (52, 53). The control strategies in both studies included PS with or without CPAP. In the larger study, Nava et al (52) found that noninvasive positive pressure ventilation reduced the duration of MV and ICU. The study by Girault (53) did

not show differences in ICU or hospital stay, but noninvasive positive pressure ventilation did allow earlier extubation and decreased duration of ventilatory support.

Several adult studies have shown that protocol-based weaning, whether conducted by physicians or nonphysicians, results in earlier and faster weaning with no increase in complications. On average, protocol-based weaning results in a reduction of 1–2 days in weaning time (54–57).

### Pediatric Studies of Weaning and Extubation

Pediatric studies relating to weaning and extubation fall into two broad categories—those that describe practice (usually within a single PICU) (7, 22, 58, 59), and those that seek to identify predictors of successful extubation, usually retrospectively (4, 18, 32–35, 60–62). Less commonly, prospective studies (19) have been done where patients are randomized and extubated after reaching a predetermined physiologic goal. A number of studies give data about failed extubations and the major ones are listed in Table 2.

Although protocol-based weaning results in faster, earlier weaning with better outcomes in adults, the data are less solid for children. No advantage over clinical weaning was shown in one prospective

Table 2. Days of mechanical ventilation and rates of failed extubation

Author	Tests Done Preextubation or Postextubation Decision <sup>a</sup>	N	Variables	FE (%)	LMV (days)
Khan et al (60)	Retrospective	208	RSBI, V <sub>T</sub> /kg	16	5.1
Baumeister et al (18)	Retrospective	47	RSBI <11	19	?
Thiagarajan et al (32)	Retrospective	227	RSBI <8	11	4.9
Farias et al (64)	Prospective	84	SBT: T-piece	16	6.0
Manczur et al (34)	Retrospective	47	OI, V <sub>T</sub> /kg, MV	14	?
Hubble et al (35)	Retrospective	45	V <sub>D</sub> /V <sub>T</sub> <0.5	4	5.9
Venkataraman et al (33)	Retrospective	312	RSBI, V <sub>T</sub> /kg	16	5.1
Edmunds et al (59)	Retrospective	632	Clinical	4.9	6.5
Farias et al (61)	Prospective	418	SBT: T-piece	14	6.5
Randolph et al (19)	Prospective	313	SBT; PS/positive end-expiratory pressure	16	7.0
Harrison et al (22)	Prospective	202	SBT; PS/positive end-expiratory pressure	10	?
Kurachek et al (7)	Prospective	2794	Clinical	6.2	4.8
Baisch et al (58)	Retrospective	3193	Clinical—5 yrs	4.1	5.9
Fontela et al (62)	Retrospective	124	Clinical	10.5	5.8
Chavez et al (65)	Retrospective	70	SBT: T-piece	7.8	3.3

RSBI, rapid shallow breathing index; SBT, spontaneous breathing trials; LMV, length of mechanical ventilation; FE, failed extubation; OI, oxygenation index.

<sup>a</sup>Retrospective and prospective refer here as to whether the physiologic measurements were taken after or before a decision had been made clinically to extubate the patients, respectively.

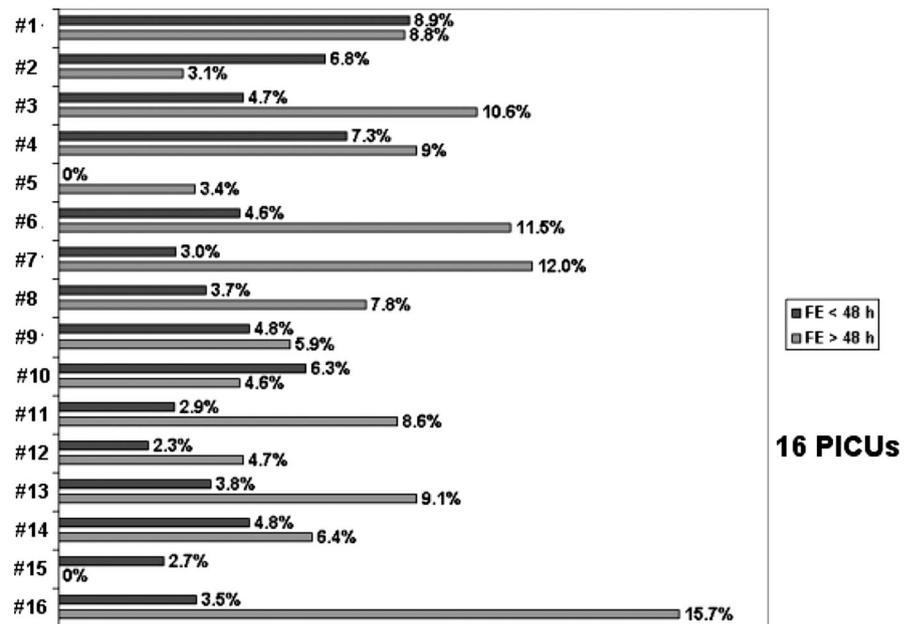
study (19), but shorter weaning (by 12 hrs) against historical controls was shown in another (63). A study by Shultze et al showed shorter weaning times on a protocol which was respiratory therapist initiated (10 vs. 0.8 hrs), but surprisingly had no overall difference in hours of MV (47).

A comprehensive and prospective study on intubation and extubation practices from 16 US PICUs gave valuable insight into the variability of length of MV and failed extubations (7). Defining extubation failure as reintubation within 24 hrs, they reported a failure rate of 6.2% (range 1.5%–8.8%) in 1459 patients intubated for at least 48 hrs and ventilated for a mean of 4.8 days (range 3–7 days). Risk factors for extubation failure included age <24 months, dysgenetic or syndromic condition, chronic respiratory disorder, chronic neurologic condition, and the need to replace the ETT at admission for any reason. UAO accounted for 37% of failed extubations. Previously unpublished data from this study showed that contrary to common perception there was no relationship between the duration of MV and rates of failed extubation, even when excluding patients ventilated for <48 hrs (Figs. 2 and 3). In this study, patients who failed extubation and required reintubation went on to have longer average durations of ventilation.

Among single-center studies, Edmunds et al (59) reported a 7.9% failed extubation rate in 280 patients intubated for at least 48 hrs. They used clinical criteria to determine the appropriate time to extubate and found that a higher incidence of extubation failure was associated with longer durations of ventilation. UAO accounted for almost 25% of failures. In 2005, Fontela et al (62) studied 124 infants and children intubated for at least 12 hrs. They excluded patients who failed extubation due to UAO. Extubation failure, defined as reintubation within 48 hrs, was associated with younger age, mean oxygenation index (OI) >5, longer duration of MV (>15 days), increased sedation (>10 days), and use of inotropes. Baisch et al (58) reported a 4.1% extubation failure rate within 48 hrs in 3193 infants and children. Extubation failures were younger (median age of 6.5 months vs. 21.3 months), had longer durations of intubation, PICU, and hospital stay but no difference in mortality.

Many studies have described extubation practices in pediatrics, most of them conducted in a single PICU (7, 18, 19, 22, 32, 33, 35, 58–61, 64, 65). Only two were

Mean (Range): FE < 48 h = 4.2% (0 - 8.9%)  
FE > 48 h = 8.0% (0 - 15.7%)



**All planned extubations decided upon clinically; no sedation or inotrope scores**

Figure 2. The failure rate of planned extubations of patients within the first 48 hrs of arrival in the pediatric intensive care unit (PICU) is, on average, half that of the rate for patients ventilated for longer than 48 hrs. This presents previously unpublished data from the 2003 report of Kurachek et al (7) of extubation practices in 16 PICUs across the United States. FE, failed extubation.

multicentered, one reporting clinical practice over 16 PICUs (7) and the other using an ERT as part of a weaning protocol in 10 PICUs (19). Most studies reporting clinical practice outcomes suggest that a failed extubation rate <10% is the norm as supported by the Kurachek study (7). Trials using an ERT all report a higher rate of failed extubation—around 14%–20% in the Randolph study (19). The disparity may be, in part, caused by the inclusion of patients extubated in less than 24–48 hrs. When the failed extubation data from the 16 PICUs is reanalyzed excluding those patients, the failed extubation rate increases from a mean of 4.2%–8%.

**Spontaneous Breathing Trials and Extubation Readiness Tests**

In 2001, Farias et al (4) compared SBT using PS of 10 cm H<sub>2</sub>O vs. a T-piece. The use of PS was, in their reasoning, to overcome the resistance of the ETT. The 257 subjects had to tolerate the 2-hr long trial (either on PS or T-piece) to be considered for extubation. The primary physician could terminate the SBT for objective (e.g., increased respiratory rate or SpO<sub>2</sub> <90%) or subjective signs (e.g., dia-

phoresis or increased respiratory work) of poor tolerance. There were no differences in the rate of extubation failure within 48 hrs (15.1% vs. 12.8%) or SBT failure (20.8% vs. 22.7%). The study concluded that an SBT conducted on PS of 10 cm H<sub>2</sub>O was as effective as an SBT using a T-piece. In 2002, the same authors (61) studied 418 patients intubated for at least 48 hrs using a SBT for 2 hrs by either T-piece or PS of 10 cm H<sub>2</sub>O. Of the 323 patients (77%) who passed the SBT and were extubated, 14% were reintubated within 48 hrs. Respiratory rate, tidal volume, RSBI, and maximal negative inspiratory pressure (PI<sub>max</sub>) were all poor predictors of extubation outcome. In both studies, patients underwent a SBT only when the primary physician deemed them ready, and this may not have been the earliest point at which a SBT could have been performed. In adults, Esteban found that two thirds of patients passed an SBT before weaning had even begun (3). If the SBT had been performed earlier in the Farias study, there might have been an increase in the SBT failure rate in the T-piece group when compared with the PS group.

Mean LMV = 4.8 days

Mean FE rate = 6.2%

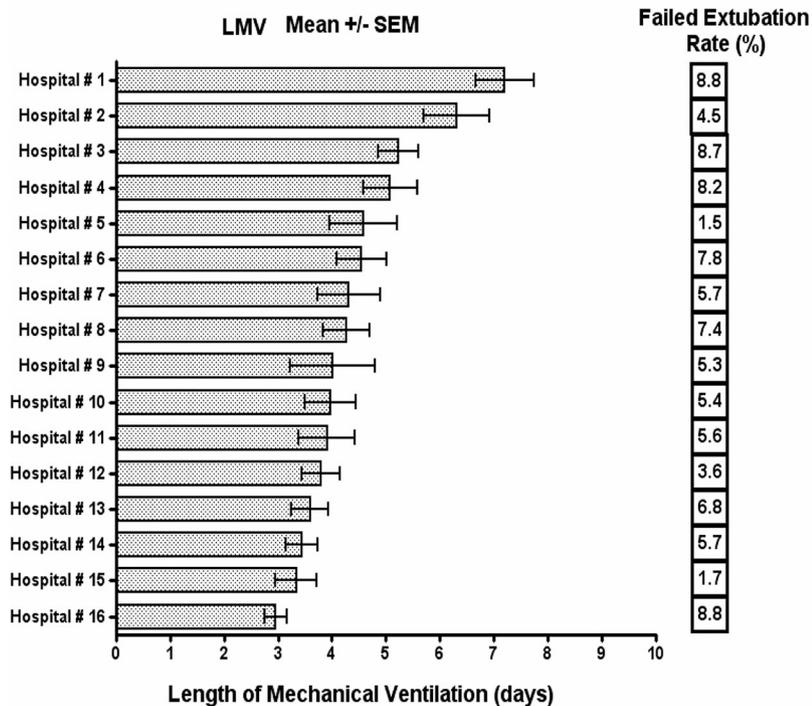


Figure 3. The rates of failed extubation in 16 pediatric intensive care units across the United States along with their average number of days of mechanical ventilation. There are marked variations in the lengths of ventilation and also the failed extubation (FE) rates, with no relationship between the two, i.e., longer ventilation does not result in fewer FEs and vice versa. This presents previously unpublished data from the report of Kurachek et al (7). LMV, length of mechanical ventilation.

Chavez et al (65) used a 15-min SBT to determine extubation readiness in pediatric patients. The SBT was performed when the attending intensivist deemed the patient ready for extubation and consisted of providing a continuous flow rate (3 L/min for infants and 10 L/min for older children) via an anesthesia bag adjusted to provide a CPAP of 5 cm H<sub>2</sub>O. Of the 70 patients, 64 passed (91%) and, of those, 5 subsequently failed extubation (7.8%) (one reintubation, four required noninvasive ventilation). The failed extubation rate was no better than historical rates where extubation was based on clinical decision alone. Although the SBT had high sensitivity (95%) and positive predictive value (92%), the high success rate could have been simply because all the patients enrolled in the study were deemed ready for extubation by the clinicians. In essence, the SBT did not contribute to predicting a successful extubation compared to clinical decision alone.

el-Khatib et al (66) evaluated the accuracy of the initial negative inspiratory pressure (PI) to PI<sub>max</sub> ratio in predicting extubation outcome for 50 infants and children. They concluded that the PI/

PI<sub>max</sub> ratio could not be used to predict extubation outcome in pediatric patients, and further stated that indices predicting extubation outcome in adults should not be extrapolated to infants and children before testing and validation.

Venkataraman and coworkers (60) prospectively evaluated predictors of successful extubation in infants and children. In 1996, they examined 208 infants and children on MV for at least 24 hrs. They excluded premature infants and those with neuromuscular disease and defined extubation failure as reintubation within 48 hrs. Factors associated with extubation failure included decreased tidal volume to inspiratory time ( $V_T/T_i$ ), signifying a decreased central drive possibly related to sedation; decreased spontaneous  $V_T$ , signifying a decreased effort of breathing; and a higher positive inspiratory pressure associated with a low dynamic compliance, signifying an increased load on the respiratory muscles. Additional parameters included higher  $F_{IO_2}$ , mean airway pressure, oxygenation index ( $OI = \text{mean airway pressure} \times F_{IO_2}/Pa_{O_2}$ ), and fraction of the total minute ventilation provided by the venti-

lator (FrVe). The overall extubation failure rate was 16.3%. Dividing patients into low-risk (<10%) and high-risk groups (>25%), the FrVe for the low-risk group was <20% and was >30% for the high-risk group. The RSBI and CROP index were not good predictors of extubation outcome in this study. Venkataraman et al (33) validated their earlier study with 312 patients who had a similar extubation failure rate of 16%.

There has been only one prospective study evaluating weaning protocols and an ERT (19). In 2002, Randolph et al examined the effect of weaning protocols on extubation outcome in 313 patients intubated for at least 24 hrs from 10 PICUs. Of 313 subjects, 183 failed an initial ERT (58%) consisting of a 2-hr SBT on PEEP of 5 cm H<sub>2</sub>O and  $F_{IO_2} \leq 0.5$ . Failure was defined as a  $Sp_{O_2} < 95\%$ , an exhaled tidal volume <5 mL/kg ideal body weight, or a respiratory rate outside the normal range for age. Patients passing the initial ERT were switched to PS and the PS adjusted for ETT size (ETT size 3.0–3.5 = PS of 10 cm H<sub>2</sub>O; ETT size 4.0–4.5 = PS of 8 cm H<sub>2</sub>O; ETT size  $\geq 5.0$  = PS of 6 cm H<sub>2</sub>O). Patients who failed were randomized to three groups for subsequent weaning: PS, volume support, and no protocol. There were no significant differences in the extubation failure rate or duration of weaning among the three groups. Increased sedative use in the first 24 hrs of weaning predicted failure. This study was important for several reasons. Although it defined an ERT, it failed to consider previously described predictors of extubation success. Similar to other studies looking at predictors of extubation success, the failed extubation rate was in the 14%–20% range—significantly higher than the range found with clinical determination of extubation readiness (2%–9%) (7, 58, 59). The protocol also used high amounts of PS, ostensibly to overcome the resistance imposed by the ETT. This likely amounted to continuing MV and may have led to an overestimation of readiness for extubation.

### Criteria for Readiness for Extubation

Readiness for extubation implies that weaning is completed, the patient is sufficiently awake with intact airway reflexes, is hemodynamically stable, and has manageable secretions. Extubation failure has been variably defined as rein-

Table 3. Criteria for extubation readiness test failure

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Proposed criteria for failure during 2 hrs on
Continuous positive airway pressure $\leq 5$ cm H <sub>2</sub> O or T-piece (zero end-expiratory pressure)
Clinical criteria
Diaphoresis
Nasal flaring
Increasing respiratory effort
Tachycardia (increase in HR $>40$ bpm)
Cardiac arrhythmias
Hypotension
Apnea
Laboratory criteria
Increase of PETCO <sub>2</sub> $>10$ mm Hg
Decrease of arterial pH $<7.32$
Decline in arterial pH $>0.07$
Pao <sub>2</sub> $<60$ mm Hg with an Fio <sub>2</sub> $>0.40$ (P/F O <sub>2</sub> ratio $<150$ )
Spo <sub>2</sub> declines $>5\%$

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tubation within 24–72 hrs. Clinical and laboratory signs predictive of extubation failure are given in Table 3. Tests commonly used to assess extubation readiness include testing for a leak around the ETT (“leak test”) and assessing respiratory muscle strength by measuring negative inspiratory force (NIF). In some cases, it may be desirable to extubate a patient who has not completed weaning and subsequently support them with noninvasive ventilation.

### Leak Test

UAO has been stated as a cause of up to 37% of failed extubations in children (7). UAO is infrequently reported as a cause of extubation failure in adults but a recent investigation suggests that it may be as common in adults as in children (66). Cuffed ETTs have been cited as a cause of increased UAO on extubation but Newth et al (68) found no difference in the incidence of failed extubations over all age groups between those intubated with appropriately sized cuffed or uncuffed tubes.

The leak test (69–72), whereby air is heard to leak around the ETT at low pressure, usually  $<20$ – $25$  cm H<sub>2</sub>O, is commonly used to predict UAO after extubation. Finholt et al (73) showed the leak test was reproducible only under conditions of neuromuscular blockade with the head in a neutral position—hardly the condition for imminent extubation of a child. In a survey of Pediatric Critical Care Fellowship Directors in North America, 76% of the responders taught and performed the leak test and would

recommend delay of extubation (and prescription of steroids) if there was no leak under 30 cm H<sub>2</sub>O (71). Steroids are a confounding factor in that they seem to reduce stridor, but their effect on reducing extubation failure is controversial (25, 26). In a recent study, Mhanna et al (74) demonstrated that a leak test of  $<20$  mm Hg (27.2 cm H<sub>2</sub>O) was better at predicting stridor in children older than 7 yrs of age than those younger, but in neither case had very good sensitivity. In a prospective, blinded study of 50 pediatric patients, Wratney et al analyzed the change in airway leak as measured at the time of intubation and extubation as a predictor of extubation outcome. They found that measuring the leak serially over time was a better predictor of extubation success than of extubation failure (75).

From these data, one can conclude that if an audible leak (to the ear, not the stethoscope) can be heard at  $<25$  cm H<sub>2</sub>O in a patient with the head in neutral position this is probably good news. However, extubation should not be delayed if the test is negative and all other conditions for extubation are favorable. Many patients, particularly those with numerous secretions and/or prolonged intubated, will have a “seal” around their ETT which will be coughed out once the ETT is removed.

### Negative Inspiratory Force

Common procedures used to evaluate the respiratory muscles are maximum inspiratory pressure and maximum expiratory pressure. However, there is little consensus concerning these methods. Measurement of maximum inspiratory pressure is the most clinically relevant because the inspiratory muscles (the major one of which is the diaphragm) carry the largest burden of ventilatory work, even when the patient’s primary problem is air flow obstruction. The measurement of maximum expiratory pressure is also useful, however, for differentiating generalized neuromuscular weakness from specific weakness of the diaphragm or other inspiratory muscles. In the PICU, maximum inspiratory pressure is sometimes referred to as *NIF*. This is inappropriate in that it removes the essential elements of “maximal” and “low-lung volume” from the intent of the procedure. True maximal NIF can be produced only when the subject in-

spires from residual volume—a condition rarely met in intubated patients. NIF of at least  $-30$  cm H<sub>2</sub>O has been found predictive of extubation success in adults (76, 77) and also in children as part of the CROP index (18, 31) or as a stand-alone test under rigorous conditions with CO<sub>2</sub> stimulation (78). However, Venkataraman et al (60) did not find this test useful for prediction as part of the CROP index or as a single test. In the PICU, the test is usually performed quickly at the bedside with an uncalibrated manometer and with both inspiration and exhalation obstructed, i.e., an unvalidated technique.

From these data, one can conclude that it is probably reassuring if a spontaneously breathing patient has a routinely obtained NIF of at least  $-30$  cm H<sub>2</sub>O, but it is unreliable and not validated in children as a test of extubation readiness. Although the measurement of a true maximum inspiratory pressure in critically ill patients should be a useful indicator of global respiratory muscle function, it is highly dependent on numerous variables, and there is no accepted, standardized approach. Consistently low values (i.e., above  $-15$  cm H<sub>2</sub>O), irrespective of technique, are unlikely to be associated with successful weaning.

### Misperceptions About the Impact of Endotracheal Tubes on Weaning and Spontaneous Breathing Trials

Many clinicians believe that, for an infant or young child, respiring through a small ETT is akin to breathing through a straw, thereby imposing an unacceptable work of breathing. This notion is contrary to both clinical observation and physiology. Data from Keidan et al (79) show the work of breathing through an ETT (without PEEP) to be half the effort required for the mask and oropharyngeal airway. They also found that breathing spontaneously with a face mask in place was even more work when there was no oropharyngeal airway (79). A 3 kg infant accepts a 3.0 mm ID ETT, whereas an adult of 60 kg can tolerate a 9.0 mm ID ETT—a 20 times increase in body size, but only a three times increase in ETT size. The subglottic area of the infant is also 20 times greater in proportion to body size than that of an adult (80). Nonetheless, the inverse fourth power relationship of air flow resistance to radius

dictates that the infant ETT has a much higher “resting” resistance, but it is irrelevant because of the shorter ETT and low flows generated by the infant compared with the adult (*vide infra*). The net effect is that the infant is breathing through a hose rather than a straw when compared with the adult.

The main determinants of ETT resistance are internal diameter and length. However, the resistance of a tube to air flow must incorporate the notion of resistance at a flow that is physiologically relevant. This is sometimes ignored in clinically relevant articles (81). Peak and mid-inspiratory flows in humans are approximately 0.5 L/kg/min (31). When related to a 60 kg adult, this gives flows of about 30 L/min with a resistance of 10 cm H<sub>2</sub>O/L/sec in even a 6.5 mm ID ETT (Fig. 4). By comparison, a 3 kg infant breathing through a 3.0 mm ID ETT has inspiratory flows of about 1.5 L/min and a resistance of 15–20 cm H<sub>2</sub>O/L/sec, almost double that of the adult but clinically and physiologically irrelevant when considering the inspiratory resistance in the normal infant is already 80–90 cm H<sub>2</sub>O/L/sec (31).

The notion that resistance increases in smaller ETTs because of conversion from laminar to turbulent flow was investigated by Jarreau et al (82). They found that flow in smaller ETTs of 2.5–3.5 mm ID was laminar, not turbulent. Flow limitation in ETTs was studied by Hammer and Newth (83) in Rhesus monkeys about the size of human infants. They showed that even in the smallest ETT studied (3.0 mm ID), limitation of flow occurred only at about 400 mL/sec over most of vital capacity. This is the equivalent of 24 L/min or 8 L/kg/min in a 3 kg infant—well above the 1.5 L/min peak and mid-inspiratory flows normally achieved by infants of this size (*vide infra*).

Willis et al (84) quantified the work of breathing (as measured by a surrogate, the pressure-rate product) of 17 patients. They found no difference between CPAP and PS of 5 cm H<sub>2</sub>O. Both provided a decreased work of breathing from that of either T-piece (with or without heliox) or the extubated patient (Fig. 5). Patients on T-piece had less work of breathing than when extubated. Takeuchi et al (85) showed that the work of breathing through an ETT for infants was only marginally higher than that after extubation. They also showed that 4 cm H<sub>2</sub>O PS was more than enough to offset the marginal increases in work of breathing through a

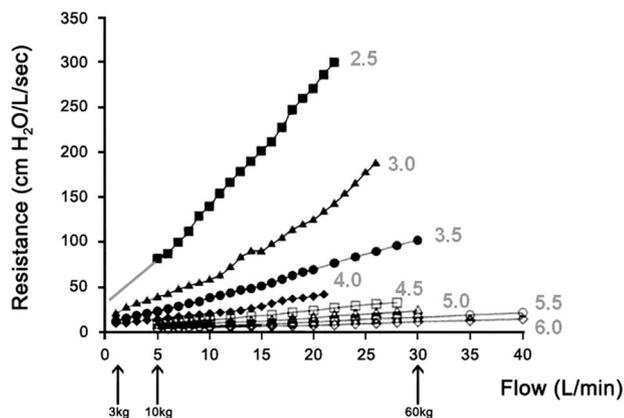


Figure 4. The resistance of air flow through an endotracheal tube, modified from the work of Manczur et al (81). The various endotracheal tube (ETT) sizes are identified by lighter lettering, representing the internal diameters of the tubes in millimeters (mm ID). As flow rates (in liters/minute) are increased there is an increase in resistance, which becomes greater the smaller the internal diameter of the ETT. Thus, small diameter (i.e., pediatric) ETT has become associated with high air flow resistances and the notion of “breathing through a straw” was (wrongly) conceived. Peak inspiratory flow rates are approximately 0.5 L/kg ideal body weight/min at all ages in humans. On the abscissa, the three arrows (from right) represent the peak flows for a 60 kg adult (intubated with a 6.5–8.5 mm ID ETT), a 10 kg child (using a 4–4.5 mm ID ETT), and a newborn infant of 3 kg (with a 3 mm ID ETT), respectively. All resistances generated at these flows are well within normal limits and are, in fact, all <50 cm H<sub>2</sub>O/L/sec). Note, for simplicity of interpretation, the linear data for the 2.5 mm ID ETT have been extended into the lower flow range where it had not been measured by the authors of the original article. Reproduced with permission from Manczur et al (33).

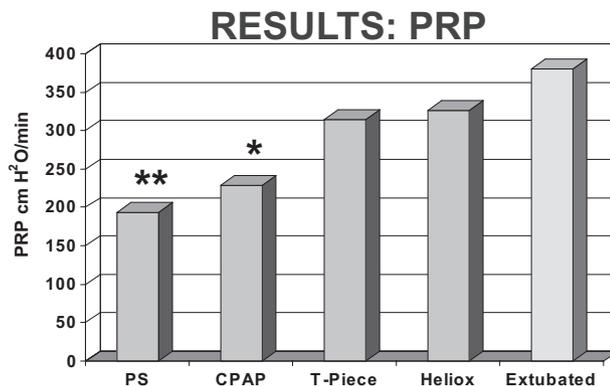


Figure 5. The work of breathing (as approximated using pressure-rate product by Willis et al [84]) measured in 17 infants and young children under the various randomly applied conditions (from left to right) of: Pressure supported breaths (5 cm H<sub>2</sub>O), continuous positive airway pressure (4 cm H<sub>2</sub>O), T-piece with oxygen, T-piece with Heliox, and postextubation. As demonstrated, the work of breathing rose slightly for each condition, but always remained low and was statistically significantly lower only for breaths supported with pressure support and CPAP. Reproduced with permission from Willis et al (84).

3.5–4.5 mm ID ETT and was equivalent to breathing without the ETT (85). Farias et al (4, 61, 64) in a series of studies involving 634 infants and children demonstrated that for an ERT a trial of spontaneous breathing lasting up to 2 hrs could be safely undertaken on a T-piece.

Although it has become fashionable to use PS with PEEP rather than CPAP or T-piece breathing to overcome ETT resistance, it is clear the evidence shows the increased resistance is minimal and the additional work of breathing negligible. If an infant or young child cannot sustain a

SBT on CPAP or a T-piece for several hours, they are as likely to fail extubation as with PS applied. Additionally, adding PS is likely to mask respiratory insufficiency and contribute to a higher failed extubation rate.

### Future Research in Pediatric Weaning and Extubation

Despite better understanding of how to avoid lung injury with positive pressure ventilation, the goal remains to minimize time on MV. Optimized wean-

ing strategies and tools to predict extubation readiness are means to that goal. Several areas of investigation are suggested.

*Extubation predictors in the PICU.* To promote research in weaning, SBTs and ERTs, a score could be devised similar to the Pediatric Risk of Mortality III for predicted mortality that would instead give case-mix adjusted extubation failure rates. Failed planned extubation (or, conversely, successful planned extubation) predictors could be developed as quality indicators for ventilation outcomes. Once case-mix adjusted extubation failure rates were validated, if there prove to be differences among PICUs (as preliminary data suggest; A. Wratney and M. Pollack, personal communication), then practice patterns could be investigated to identify those that are successful and those that are not.

*Spontaneous Breathing Trials.* Given that even a CPAP trial gives more support to a weaning infant than he or she needs if ready for extubation, SBTs utilizing T-piece trials vs. CPAP with and without “minimal PS” should be rigorously undertaken. Such trials should comply with the canons of diagnostic test evaluation grounded on Bayes’ Theorem (conditional independence, pretest probability, test-referral bias and spectrum bias) (28, 86).

*Postextubation Incidence of Acute Upper Airway Obstruction.* The incidence of postextubation UAO as a cause of extubation failure seems to be very high, approximately 40% of cases in the Kurachek study (7). Thus, it is appropriate to determine the true incidence of UAO in pediatric practice after extubation using objective measuring methods such as esophageal flow-pressure loops for evidence of flow-limitation using noninvasive respiratory inductance technology for the flow component. This would allow not only further evaluation of case-mix adjusted extubation failure rates (*vide supra*), but also a firm, objective basis for the application of innovative therapies for reducing subglottic edema such as continuous vaporization of alpha-agonists and the respective roles of heliox and CPAP in lessening intrinsic PEEP.

*The Role of Corticosteroids in Extubation Success or Failure.* Steroids are widely used but their role in extubation is ill-understood (*vide infra*).

## Summary of Relevant Pediatric and Adult Patient Studies

MV is often life saving but is associated with risks. Risks can be reduced by weaning and extubation as soon as the patient is able to support his/her breathing. Key points include the following:

- Not all patients require gradual weaning. Both adult (36, 50) and pediatric (19, 61) studies have shown that when patients pass a SBT and are subjected to an ERT, 50%–75% of the patients are deemed ready to extubate.
- There are no infallible predictive tests for successful extubation. The RSBI has become moderately popular but since there is a wide range of age groups with different respiratory rates it may not be a good predictor of extubation success or failure in the pediatric population (34). Whether age-specific  $f/V_T$  ratio is better is currently unknown. This area is fertile ground for future research. Identifying predictors of successful weaning and extubation would likely shorten the duration of ventilation and prove not only to decrease lengths of stay, but potentially reduce ventilator associated lung injury.
- Adult studies show that T-piece or PS trials for an ERT are equally effective; IMV or SIMV are not deemed as useful. Pediatric studies have led to similar conclusions (4, 61, 64).
- Use of a weaning protocol results in faster weaning in adults. Although the data are less clear in children, it is likely a consistent approach to ventilator weaning will shorten ventilator time and result in better outcomes.
- A recent Cochrane Review on the role of steroids concludes “Using corticosteroids to prevent (or treat) stridor after extubation has not proven effective for neonates, children or adults. However, given the consistent trend toward benefit, this intervention does merit further study” (87).

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