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Weaning from mechanical ventilation

J. Mancebo

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ABSTRACT: Weaning from mechanical ventilation is a period of transition from total ventilatory support to spontaneous breathing. It represents a relevant clinical problem because as many as 25% of intubated and mechanically-ventilated critically ill patients will need a progressive withdrawal from artificial ventilatory support.

From a clinical standpoint, it is very important to recognize as soon as possible when a patient is ready to be weaned. Accordingly, a daily routine follow-up should be performed in every patient in order to verify whether patients meet clinical criteria to be disconnected from the ventilator. Several physiological indices have been used to predict the outcome of weaning trials. However, an adequate clinical tolerance to spontaneous breathing during a 2 h T-piece trial is very useful to predict a successful extubation.

A number of physiopathological mechanisms explain why some patients fail the weaning trials; particularly important from a clinical point of view are those related to respiratory pump failure and cardiovascular instability, which are usually accompanied by an abnormal gas exchange.

Different ventilatory techniques can be used to wean these patients from mechanical ventilation. Up to now, the most efficient techniques seem to be pressure support ventilation and once daily trials of T-piece interspersed with conventional volume assist-control ventilation.

Finally, knowledge-based system applied to modern microprocessor mechanical ventilators can help in the process of weaning by automatically reducing the ventilatory assistance and indicating the optimal time to perform extubation.
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Servei de Medicina Intensiva, Hospital de Sant Pau, U.A.B., Av. S.A.M. Claret 167, 08025 Barcelona, Spain.

Correspondence: J. Mancebo
Servei de Medicine Intensiva
Hospital de Sant Pau
Av. S.A.M. Claret 167
08025 Barcelona
Spain

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Weaning from mechanical ventilation represents the period of transition from total ventilatory support to spontaneous breathing. Recently published data [1, 2] confirm that the majority, about 75%, of intubated mechanically-ventilated patients are extubated after disconnection from the ventilator: after letting them breathe spontaneously for a short period of time, the endotracheal tube is successfully withdrawn when no clinical signs and symptoms of poor tolerance are observed. The remaining patients, about 25%, need progressive withdrawal from artificial ventilatory support.

Patients who are difficult to wean represent a crucial clinical problem for a number of reasons. Firstly, they usually require a longer hospital stay. Indeed, it has been reported that the weaning period represents 40% of the total duration of mechanical ventilatory support [3]. Furthermore, morbidity and even mortality may be higher in these patients. Accordingly, both for clinical and economical reasons, every effort should be made to determine as soon as possible which patients can be rapidly extubated, and to keep the weaning period to a minimum.

Physiological and clinical approach to weaning

The first step is to recognize when a patient is ready to be weaned. This is still an important part of our clinical practice, and a daily routine follow-up should be performed in every intubated, mechanically-ventilated patient in order to verify if those conditions required for withdrawal of mechanical ventilatory support have been achieved [4, 5]. Table 1 shows the clinical criteria which should be met before disconnecting the patient from the ventilator; points 1 and 2 are mandatory criteria to be met before weaning is attempted.

Classically, when patients meet these criteria they are allowed to breathe spontaneously for a period of time, which may range from several minutes to several hours, before the decision to extubate them is made. In order

Table 1. – General clinical parameters to be met before initiating weaning

1.	Cause for instituting mechanical ventilation is resolved or is significantly improved
2.	Adequate gas exchange, usually S_{a,O_2} >90% with F_{I,O_2} <0.4 or $P_{a,O_2}/F_{I,O_2}$ >200 with PEEP <5 cmH_2O
3.	Absence of fever
4.	Adequate haemoglobin levels
5.	Appropriate neurological and muscular status
6.	Stable cardiovascular function
7.	Correction of metabolic and/or electrolyte disorders, if any
8.	Adequacy of sleep

S_{a,O_2}: arterial oxygen saturation; F_{I,O_2}: inspiratory oxygen fraction; P_{a,O_2}: arterial oxygen tension; PEEP: positive end-expiratory pressure. (Taken, in part, from [1, 2]).

Table 2. – Some physiological indices predicting weaning outcome

1.	f_R <35 breaths·min^{-1}
2.	Spontaneous ventilation <15 L·min^{-1}
3.	Maximal inspiratory pressure lower than -30 cmH_2O
4.	Ratio f_R/V_T <105
5.	$P_{0.1}$ <6 cmH_2O, or $P_{0.1} \cdot f_R/V_T$ <450
6.	Vital capacity >10–15 mL·kg^{-1}

f_R: respiratory frequency; V_T: tidal volume; $P_{0.1}$: mouth occlusion pressure. (Taken, in part, from [1, 2, 6, 7].

to make an objective decision regarding extubation, several physiological indices have been proposed. Table 2 shows some physiological indices suggesting an adequate capacity of the ventilatory pump, which should be met before attempting to wean.

For different reasons, many of these indices are not accurate in predicting the outcome of a weaning trial. The lack of sensitivity and specificity can be explained by a number of methodological problems regarding study design, such as: inappropriate definition of predictive index (*i.e.* its objective measurement is not adequately explained or the index itself is not a true determinant of outcome); outcome events not clearly defined; study population not including a wide spectrum of patients; and statistical methods not carefully described. Of these indices, one has been described which adheres to high quality methodological standards [6]: this is the respiratory frequency/tidal volume (f_R/V_T) ratio. This index of rapid shallow breathing showed the highest positive and negative predictive values (78 and 95%, respectively) among those analysed in this investigation, and the area under the curve plotting the proportions of true-positive and false-positive results against each other for a threshold value (the receiver-operating-characteristic curve) was 89%, higher than that for any other index. The combination of this index of rapid and shallow breathing with $P_{0.1}$ seems to increase its specificity [7]. The respiratory centre output is usually estimated by measuring the airway occlusion pressure, $P_{0.1}$, (the airway pressure generated at the mouth at 0.1 s after initiating an inspiration against an occluded airway). In a study by SASSOON and co-workers [8] performed in 12 chronic obstructive pulmonary disease (COPD) patients, the authors observed that the seven patients who were successfully weaned had $P_{0.1}$ values lower than 6 cmH_2O. Maximum inspiratory pressure reflects the global strength of inspiratory muscles. However, a value lower than -30 cmH_2O is a poor predictor of weaning outcome, as recently assessed [6]. Its lack of predictive power may be due, at least in part, to the fact that this parameter depends on the strength rather than on the endurance of respiratory muscles. A high respiratory rate is a very sensitive parameter indicating respiratory dysfunction, and patients who subsequently fail a weaning trial present an immediate increase in respiratory rate when they are disconnected from the ventilator [9].

Another test which seems very useful is the clinical tolerance exhibited during a 2 h T-piece trial. In a prospective evaluation made in 169 patients, only 21 of them (12%) were poorly predicted by the 2 h T-piece trial and needed reintubation [1]. More recent data obtained in another multicentre study confirm the clinical interest of the tolerance of a 2 h T-piece trial in predicting the weaning outcome [2]. The evaluation of clinical tolerance to spontaneous breathing during a T-piece trial should take into account signs of increased patient effort, such as an increase in the respiratory rate, accessory muscle recruitment, paradoxical motion of the rib cage and abdomen, inappropriate recruitment of expiratory muscles, recession of suprasternal and intercostal spaces, nasal flaring, diaphoresis, cardiovascular instability (increase in heart rate, changes in blood pressure, cardiac arrhythmias), and abnormal mental status (agitation and/or anxiety).

When a patient fails a weaning trial, we should look for the physiopathological mechanisms explaining such a failure. Inability to sustain spontaneous breathing is usually of multifactorial origin, and a complete clinical appraisal is then mandatory before using a ventilatory method to progressively withdraw the patient from mechanical ventilation.

Physiopathological mechanisms to explain difficult weaning

The main reasons for weaning failure are usually abnormal gas exchange, cardiovascular instability, psychological dependence on the ventilator and respiratory pump failure. The latter is probably the most common mechanism, and is typically viewed as an imbalance between capabilities and demands [10].

Left ventricular failure can be a relevant clinical problem during weaning, and is mainly explained by the physiological changes which occur during the resumption of spontaneous ventilation [11]. At least three factors contribute to this phenomenon [12]: the switch from a positive to a negative intrathoracic pressure state; the increase in catecholamine release; and the increase in the work of breathing, particularly in patients with airway obstruction and pulmonary dynamic hyperinflation.

The decrease in pleural pressure occurring during spontaneous breathing increases both left ventricular afterload and left ventricular end-diastolic pressure, and these two mechanisms can precipitate a myocardial ischaemic event as they have the potential to increase myocardial oxygen consumption [13]. Myocardial ischaemia then leads to an overt left ventricular dysfunction with acute pulmonary oedema and arterial hypoxaemia [12]. The increase both in catecholamine release and the work of breathing contributes to the overall and myocardial increase in oxygen consumption, thus creating a vicious circle leading to further deterioration of myocardial ischaemia, which is fuelled by arterial hypoxaemia, and development of pulmonary oedema.

From a clinical point of view, it is frequent to observe patients suffering both from COPD and coronary artery disease, thus creating a clear set-up for weaning failure. A significant decrease in left ventricular ejection fraction [13] has also been described during spontaneous breathing in COPD patients without coronary artery disease while they are being weaned.

The general mechanisms leading to respiratory pump failure are shown in table 3.

The decreased output of respiratory centres occurs after the administration of sedative, narcotic and/or anaesthetic agents. Some sedatives or their metabolites can exhibit long-acting effects, and these problems are usually enhanced

Table 3. – General mechanisms explaining respiratory pump failure

Decrease in capabilities:
1. Decreased output of the respiratory centres
2. Phrenic dysfunction and other peripheral neurological disorders
3. Decrease in the strength and/or endurance of the respiratory muscles
4. Chest wall mechanical defects:

Increase in demands:
1. Increase in the ventilatory needs
2. Increase in the work of breathing due to abnormalities in respiratory system mechanics

in the presence of renal and/or hepatic failure [14, 15]. Central nervous system disorders (stroke, bleeding, post-neurosurgical status, infectious diseases, such as meningitis or encephalitis, *etc.*) and brain-stem diseases are accompanied by an altered level of consciousness (often associated with the inability to protect upper airways and inefficient cough mechanisms) and/or depressed respiratory drive, thus making weaning very difficult. Finally, severe metabolic alkalosis decreases the output of the respiratory centres.

Phrenic dysfunction can occur after traumatic injuries (high cervical spine lesions) and is also rather common after cardiac surgery, especially when iced topical cardioplegic solution is used or when internal mammary arteries have been dissected [16, 17]. Diaphragmatic dysfunction is also frequent after upper abdominal surgery [18]. Other peripheral neuromuscular disorders can be associated with the inability to tolerate weaning, especially the critical illness, polyneuropathy or myopathy, which are frequent complications of sepsis and multiple organ system failure [19, 20]. Finally, the toxic effects of some neuromuscular blocking agents, associated or not with corticosteroids and/or aminoglycosides, which can also be potentiated by hepatic and/or renal dysfunction, may be the cause of weaning failure in a number of patients [21–26].

The strength and/or endurance of respiratory muscles decreases in many clinical conditions. Dynamic pulmonary hyperinflation, apart from generating an elastic threshold load, places the diaphragm at a disadvantageous position according to Laplace's law [27]. In fact, the pressure generated by the diaphragm is greatly affected not only by its length but also by its geometry. Thus, if lung volume is increased above its passive functional residual capacity, the diaphragm flattens and its radius of curvature increases. Consequently, for the same tension development, the transdiaphragmatic pressure which can be generated decreases. Malnutrition, detraining and disuse due to prolonged bed rest, and increased muscular catabolism can induce severe muscle dysfunction [28]. Additionally, immobilization leads to a dramatic atrophy of skeletal muscles, and diaphragmatic dysfunction can occur because this muscle is at rest during full mechanical ventilatory support, thus promoting disuse atrophy. Moreover, at least in animals, it seems that the diaphragm is more sensitive to disuse atrophy than other peripheral skeletal muscles [29]. Patients with a poor muscular mass, and those with chronic heart failure [30], chronic renal failure or severe emphysema also present with muscle dysfunction. Finally, the abnormalities in muscle function are exacerbated by a decrease in oxygen supply to these muscles [31], metabolic acidosis and by certain electrolytic (hypokalaemia, hypocalcaemia, hypomagnesaemia, hypophosphataemia) and endocrinological disorders, such as hypothyroidism.

Chest wall abnormalities severe enough to cause weaning failure are uncommon. However, in certain cases of flail chest, muscle contraction can be completely inefficient because the decrease in pleural pressure induced by the diaphragmatic contraction leads to a paradoxical inward movement of the chest wall.

An increase in ventilatory needs is quite common in intensive care patients, particularly during the episodes of fever, when carbon dioxide production is augmented because of an increase in metabolic needs. In fact, when accompanied by fever and metabolic acidosis, septic states can impose a very substantial increment in respiratory system demands. Furthermore, a nutritional overload can increase carbon dioxide production and induce an augmentation in alveolar ventilation in order to maintain a constant arterial carbon dioxide tension (P_{a,CO_2}). Hyperventilation is also common during episodes of anxiety and pain, and the concomitant catecholamine release also enhances the oxygen consumption and carbon dioxide production. Finally, an increase in the dead space/tidal volume ratio, which can be induced by a number of diseases, is another source of increase in ventilatory needs.

The increase in work of breathing may be due to an increase in elastic or resistive loads, or both. Essentially, the augmentation in elastic workload occurs when there is a reduction in compliance of the lungs (pulmonary oedema, extreme hyperinflation during an acute asthmatic attack, pulmonary fibrosis) and/or a reduction in the compliance of the chest wall (abdominal distension, obesity, trauma, thoracic deformities). Pulmonary dynamic hyperinflation with intrinsic PEEP is another example of increased elastic workload and is a relatively common phenomenon, especially in COPD patients. It implies that at the end of an expiration there is still a positive pressure at the alveolar level. Consequently, to initiate the next inspiration, the respiratory muscles should first overcome this level of intrinsic positive pressure (by generating an equal amount of negative pleural pressure) in order to counterbalance this intrinsic PEEP and then generate a pressure gradient between the mouth and the alveolus so as to produce an inspiratory flow [27]. The increase in the resistive component of work is essentially related to an augmented airway resistance, excessive secretions, decrease in endotracheal tube diameter because of kinking and/or mucous plugging, and ventilator circuits and humidifiers.

Methods of progressive withdrawal of mechanical ventilation

Different ventilatory techniques can be used during weaning from artificial ventilation. The most common are pressure support ventilation (PSV), synchronized intermittent mandatory ventilation (SIMV), continuous positive airway pressure (CPAP) and spontaneous breathing with a T-tube. Although two recent prospective, multicentre, randomized trials [1, 2] have shown that SIMV does not seem as successful as the other techniques, the respective advantages and disadvantages of each technique are explained here.

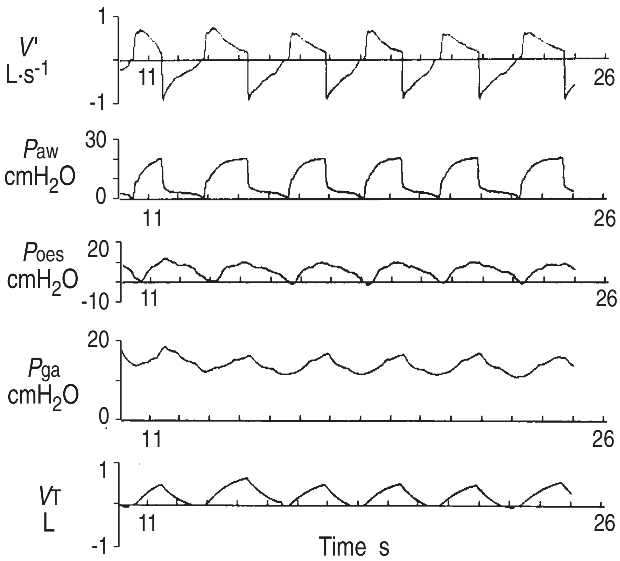

Fig. 1. – From top to bottom: tracings of airflow (V'), airway pressure (P_{aw}), oesophageal pressure (P_{oes}), gastric pressure (P_{ga}) and tidal volume (V_T) recorded in a patient breathing with pressure support ventilation (PSV) mode. From the P_{ga} tracing it is observed that expiration is passive, without expiratory muscle activity. (Taken from [69], with permission).

Pressure support ventilation

Pressure support is a patient-triggered, pressure-limited, flow-cycled mode in which airway pressure is maintained almost constant during the whole inspiration. When inspiratory flow reaches a certain threshold level, the cycling from inspiration to expiration occurs (fig. 1). This method of ventilatory assistance allows the patients to retain a near complete control over respiratory rate and timing, inspiratory flow rate and tidal volume. The level of pressure support, the mechanical properties of the respiratory system (resistance and compliance) and the magnitude of the inspiratory effort made by the patient will modulate the size of V_T. These characteristics probably provide a good synchrony between the patient and the ventilator, although in a recent study [32] which compared SIMV and PSV, the levels of dyspnoea and anxiety reported by the patients were similar with these two modes. Interestingly, the levels of dyspnoea did not seem to differ at various levels of support from 100% (PSV adjusted to achieve a V_T of 10 $mL \cdot kg^{-1}$, SIMV adjusted with a V_T of 10 $mL \cdot kg^{-1}$, constant inspiratory flow (V'_I) at 1 $L \cdot s^{-1}$ and minute ventilation equal to that observed during baseline assist-control ventilation) to 0% support (CPAP 5 cmH_2O in both modes).

One of the most important features of PSV is that it improves the efficacy of spontaneous breathing and reduces external respiratory work and oxygen consumption by respiratory muscles during weaning [33], thus helping to prevent the appearance of electromyographic signs of impending diaphragmatic fatigue. The addition of external PEEP in patients who have dynamic pulmonary hyperinflation with dynamic airway collapse is beneficial in terms of energy consumption of the respiratory muscles [34]. This strategy, the combination of pressure support and PEEP, may be very useful in the weaning of COPD patients with expiratory flow limitation.

The pressure level which should be adjusted to begin weaning is usually determined by letting the patient breathe in a "comfortable" way. This is usually still done in an empirical way. However, both previous clinical experience [1, 2] and clinical investigative data [33, 35] suggest that "optimal" initial levels are those providing a f_R 25–30 $breaths \cdot min^{-1}$. Again, the level of external PEEP to be used in patients with clinically suspected dynamic hyperinflation and dynamic airway collapse should be adjusted with great caution, since measurement of dynamic intrinsic PEEP in spontaneously breathing patients is not easy without specific equipment. To the extent that each ventilatory cycle should be initiated by the patient, those patients who have an unstable respiratory drive may be inadequately ventilated and develop hypercapnia and secondary hypoxaemia. In some patients with very high inspiratory rates, or with inappropriate inspiratory pressure output, or in those who have a COPD with the presence of significant dynamic hyperinflation, a lack of synchrony may be observed between the inspiratory efforts of the patient and ventilator breaths, especially at high preset levels of pressure support and when external PEEP is not used [36–38].

Another interesting effect of PSV is that it is useful to overcome the extra work of breathing imposed by the endotracheal tube and the inspiratory valve and circuit of the ventilator [39, 40]. The level of pressure support necessary to eliminate this extra work, which is induced by a flow-dependent pressure drop across the endotracheal tube, depends on various factors: the diameter of the endotracheal tube; the patients' inspiratory drive; and the presence or absence of a severe underlying lung disease. During weaning, the levels of pressure support are decreased according to the clinical tolerance of the patients, usually by steps of 2–4 cmH_2O twice a day. In general, an adequate clinical tolerance to a level of PSV equal to or lower than 8 cmH_2O is required before performing extubation.

The efficacy of pressure support to wean patients from mechanical ventilation has been evaluated in two recent studies using similar methodology [1, 2], and conflicting results have been reported. In the study by BROCHARD *et al.* [1], the number of patients successfully weaned 3 weeks after beginning weaning (primary end-point of this investigation) was higher with PSV than with SIMV or T-piece trials (fig. 2), and the mean weaning duration was significantly shorter with PSV (5.7 days) than with SIMV and T-piece pooled together (9.3 days). In the study by ESTEBAN *et al.* [2], the rate of successful weaning 2 weeks after its initiation was significantly higher with a once daily trial of T-piece than with PSV or SIMV (fig. 3), and the median weaning duration was shorter with once daily trial of spontaneous breathing with T-piece (3 days) than with PSV (4 days) or SIMV (5 days). Despite these different results, in part explained by the different criteria used to evaluate the clinical tolerance with PSV and T-piece in the study by ESTEBAN *et al.* [2] (during PSV a f_R >25 $breaths \cdot min^{-1}$ was considered a sign of distress, thus increasing the level of PSV, whereas during T-piece the signs of distress were considered when the f_R was >35 $breaths \cdot min^{-1}$), these studies show that if the criteria for extubation are too rigid the period under mechanical ventilation is probably lengthened. Also, it is important to keep in mind that the way the different ventilatory techniques are used is as important as the technique itself.

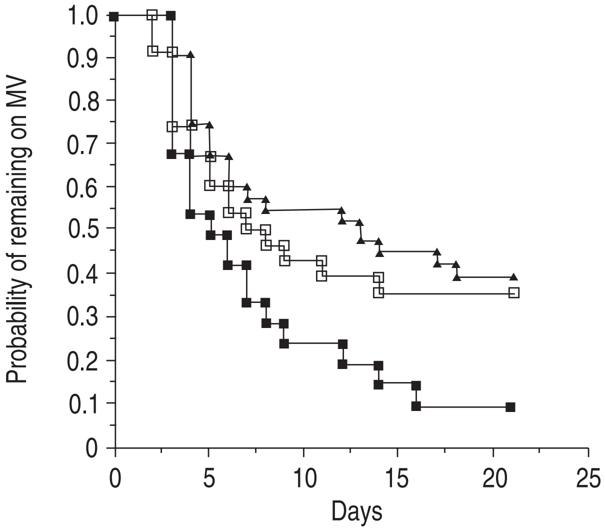

Fig. 2. – Probability of remaining on mechanical ventilation (MV) over three weeks from the start of weaning according to three different techniques. $p<0.03$ between PSV and T-piece and SIMV. —▲— : SIMV; —□— : T-piece; —■—: PSV. PSV: pressure support ventilation; SIMV: synchronized intermittent mandatory ventilation. (Taken from [1], with permission).

Synchronized intermittent mandatory ventilation

This mode of mechanical ventilation delivers a certain number of mandatory breaths every minute, whilst spontaneous breaths are allowed between machine breaths (fig. 4). Mandatory breaths may be pressure-limited or flow-limited. The main advantages include its versatility to provide a wide range of ventilatory support: from total assistance to partial support or even no support at all. This feature has the theoretical advantage of allowing a very smooth transition from full ventilatory assistance to spontaneous breathing.

Weaning with SIMV provides a readily available apnoea back-up, may reduce the likelihood of respiratory alkalosis, and when the mandatory rate is low, each of these breaths may provide a sort of sigh [41].

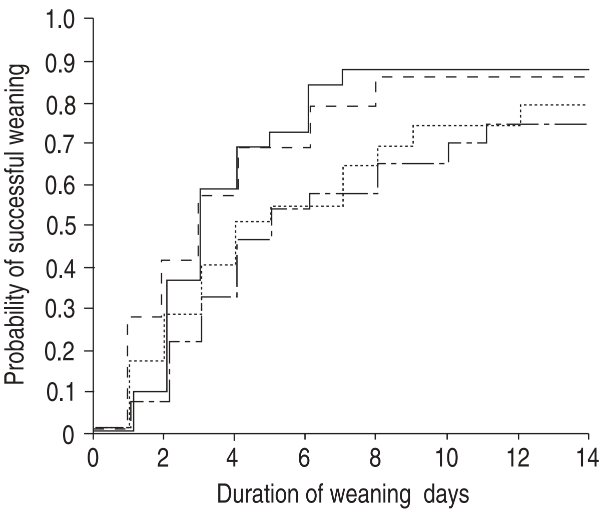

Fig. 3. – Probability of successful weaning with four different techniques over 2 weeks. $p<0.04$ between pressure support ventilation (PSV) and once daily trial of T-piece. ——— : intermittent trials of T-piece; ············ : once daily trial; ············ : PSV; — - —: synchronized intermittent mandatory ventilation. (Taken from reference [2], with permission).

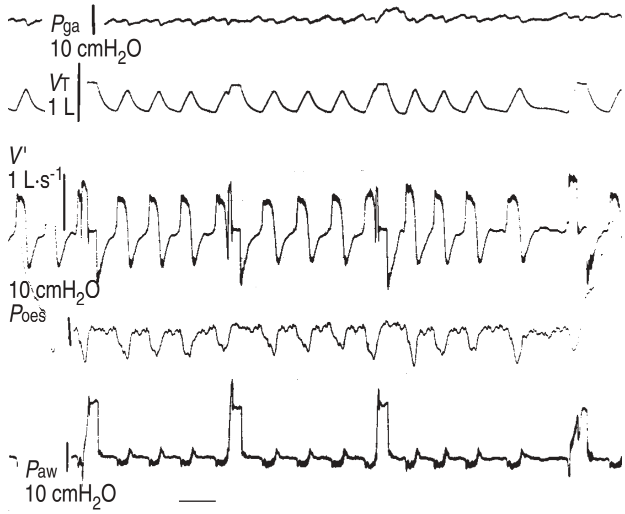

Fig. 4. – From top to bottom: tracings of gastric pressure (P_{ga}), tidal volume (V_T), airflow (V'), oesophageal pressure (P_{oes}) and airway pressure (P_{aw}) recorded in a patient breathing with SIMV mode, showing spontaneous and mandatory cycles. It can be seen that inspiratory efforts (oesophageal pressure swings) are almost identical both in spontaneous and mandatory breaths. The horizontal bar (bottom) represents 2 s. SIMV: synchronized intermittent mandatory ventilation.

One of the problems related to SIMV concerns the extra work of breathing imposed by certain demand valve systems, and the resistance of external ventilator circuits and the humidifiers. Another important shortcoming of this ventilatory mode is that patients do not exhibit a good breath-to-breath adaptation to mechanical assistance [42, 43]. In fact, these studies have shown that a significant amount of external work of breathing is performed at any level of ventilatory assistance, perhaps because the central respiratory drive is preprogrammed and cannot be modified on a breath-by-breath basis. Additionally, when reduction in SIMV assistance is compared to similar reductions in PSV levels, the electromyographic patterns of diaphragmatic activity are different, showing that SIMV reloads early and PSV reloads late [44, 45].

SIMV has the potential to increase the duration of weaning if the mandatory rate is not carefully reduced. Two recently published studies [1, 2] analysing the efficacy of different weaning techniques have shown that SIMV performs worse than PSV or T-piece in terms of weaning duration and probability of successful weaning after 14 or 21 days. In these studies, weaning with SIMV was performed in a very similar way: the initial ventilator rate was set at half the frequency used during assist-control ventilation, without changing inspiratory flow and tidal volume. The ventilator rate was then subsequently reduced, according to the patients' clinical tolerance, by 2–4 breaths·min^{-1} at least two times per day. Patients were extubated once they tolerated mechanical rates of 4–5 breaths·min^{-1} without signs of clinical intolerance for periods ranging 2–24 h. The possibility of improving SIMV performance, for example with low PSV levels during spontaneous breaths, has not yet been tested.

Spontaneous breathing with T-tube

The essential advantage of T-tube is that it allows periods of respiratory effort to be alternated with periods of rest, or at least of reduced muscular activity, when patients are reconnected to the mechanical ventilator between the periods of spontaneous breathing. This is conceptually interesting because if it is accepted that respiratory muscles can be fatigued, rest is needed to relieve this. It has recently been shown that in healthy subjects submitted to a fatigue protocol with inspiratory resistive loading, the rate of recovery from diaphragmatic fatigue may last at least 24 h [46]. Accordingly, a better outcome of weaning trials could be expected if more support was given between these spontaneous breathing trials with T-piece. This is, in fact, one reason to explain the findings observed in the study by ESTEBAN *et al.* [2].

The T-tube system offers very little resistance to gas flow. There is no additional imposed work of breathing because neither ventilator valves nor circuits are involved. The only factor which can still increase the patient's work of breathing, its resistive component, is the endotracheal tube itself. Tolerance to T-tube represents a good test to evaluate a patient's capacity to maintain autonomous spontaneous breathing [47]. Its optimal duration has not been established and, although 2 h appears to be a good balance between optimal extubation rate and low reintubation rate [1], some recent data obtained in a multicentre Spanish study [48] show that the clinical profile of patients during this 2 h period begins to diverge after approximately 30 min, and an increase in respiratory rate is the most sensitive parameter to indicate whether or not a patient can be extubated. These data, however, are still to be tested in a prospective and randomized way, and of course this method of extubating after 30 min of adequate clinical tolerance should be very well balanced with the more conservative approach of 120 min, particularly if the 90 min difference (over a total duration of mechanical ventilation of days or weeks) can lead to a higher reintubation rate and its associated complications [49, 50].

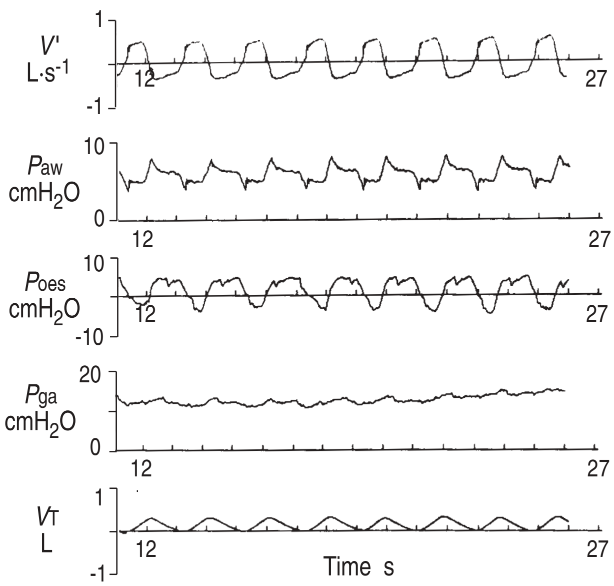

Fig. 5. – From top to bottom: tracings of airflow (*V'*), airway pressure (P_{aw}), oesophageal pressure (P_{oes}), gastric pressure (P_{ga}) and tidal volume (V_T) recorded in a patient breathing with the CPAP mode. (Taken from [69], with permission). CPAP: continuous positive airway pressure.

The main disadvantage of the T-piece trial is related to the absense of a connection to a mechanical ventilator: the patient is not monitored, and no apnoea backup is available. Therefore, patients should be closely supervised, and this is highly demanding for the nursing staff. These disadvantages are overcome if the CPAP (fig. 5) option available in the majority of mechanical ventilators is used. Additionally, the transition between the periods of muscular rest and the periods of spontaneous unassisted breathing can be excessively abrupt for some patients, especially those who have panic reactions after disconnecting from the ventilator and those with latent left ventricular failure and myocardial ischaemia.

Another problem associated with the T-tube technique is the abolition of glottic function during intubation: the glottis acts as an expiratory brake, facilitates the cough mechanism and helps to maintain a certain intrapulmonary volume [51]. This is one of the reasons for using low levels of CPAP (5 cmH_2O) if possible. Furthermore, in patients with a reduced functional residual capacity and those with intrinsic PEEP due to dynamic airway collapse, the use of low levels of CPAP is advisable because it reduces the work of breathing in comparison with the T-tube technique: in the former because CPAP improves pulmonary compliance and reduces the inspiratory work of breathing [52], and in the latter because the extra load which intrinsic PEEP represents is counter-balanced with external PEEP and, thus, reduces the mechanical work of breathing [53].

One of the major problems of the CPAP systems is that related to the extra work of breathing induced by the demand valves [54, 55]. Expiratory circuits and PEEP valves are another source of increased expiratory resistance, particularly when airflow is high [56]. An increase in expiratory resistance may enhance the sensation of dyspnoea and this, in turn, generates discomfort and an increase in the inspiratory work of breathing because of high fluctuations in airway pressure between inspiration and expiration [56, 57].

To obviate the problems related to the conventional demand valves, some ventilators have modified continuous flow systems. These "flow-by" or flow-triggered mechanisms have been compared to conventional demand-valve systems, and recent studies [58–60] have reported that flow-by systems, used either in CPAP or SIMV, are able to produce a significant decrease in respiratory work and other indices of inspiratory muscle effort when compared to the conventional demand-valve.

Withdrawal of mechanical ventilation in COPD patients

Weaning COPD patients from mechanical ventilation is a particularly difficult issue. The reasons explaining these difficulties are mainly related to respiratory muscle weakness (which can be enhanced by treatment with corticosteroids), abnormalities in arterial blood gases, malnutrition, derangements in respiratory system mechanics, and eventually other co-morbidities, such as renal failure or coronary artery disease [25, 26, 61]. In one study [1], it has been shown that COPD is one of the main factors explaining weaning duration: these patients are more difficult to be weaned than those who had an acute respiratory failure without COPD or those who needed mechanical ventilation for a neurological disease.

In a recent study by NAVA *et al.* [61], including 42 COPD patients requiring more than 3 weeks of mechanical ventilation, it was observed that 23 patients were weaned after an average period of 44 days. The weaning technique was pressure support. The factors which allowed the best discrimination between successfully and unsuccessfully weaned patients were P_{a,CO_2} and maximal inspiratory pressure. Additionally, the 2 year survival rate of successfully weaned patients was 68%.

An alternative method to facilitate weaning in patients with chronic respiratory failure is the use of noninvasive ventilation. Indeed, UDWADIA *et al.* [62] studied 22 patients with chronic respiratory insufficiency who underwent nasal intermittent positive pressure ventilation (NIPPV) (20 patients with volume-cycled ventilators and two patients with pressure support) after being conventionally ventilated for a median of 31 days. Only two patients were unable to tolerate the noninvasive ventilation, and 18 patients were discharged from the hospital (10 with nocturnal noninvasive ventilation). These encouraging results have been reported by other authors [63, 64]. The study by RESTRICK *et al*. [64] included 14 patients, eight of whom had a COPD and six chest wall or neuromuscular disease. Again, NIPPV allowed successful weaning from invasive mechanical ventilation in 13 patients (including the eight with COPD).

All these studies suggest that NIPPV may be a useful tool to improve the weaning rate in patients with severe underlying respiratory diseases, and may even avoid tracheotomy in some of these patients. It should be stressed, however, that none of the studies were controlled, so that randomized trials comparing NIPPV with conventional weaning techniques are urgently needed in this group of patients.

Other methods to reduce weaning time from mechanical ventilation include tidal volume and electromyographic relaxation feedback. HOLLIDAY and HYERS [65] studied a group of 40 patients who were submitted to mechanical ventilation for at least 7 days. Twenty patients were assigned to the biofeedback group, and these patients showed a significant reduction in mean ventilator days (20.6±8.9 days) in comparison with the 20 patients who underwent conventional weaning with T-piece or SIMV (32.6±17.6 days). These beneficial effects were related to an improvement in respiratory drive and respiratory muscle efficiency.

Finally, some difficult-to-wean patients may benefit from a tracheotomy. Nevertheless, the precise time at which to perform tracheotomy is subject to debate and a consensus has not been reached [66]. The policy in our institution for performing tracheotomies is as follows: patients with an expected long duration of mechanical ventilation; some patients who cannot be successfully weaned after 3 weeks of mechanical ventilation; and patients in whom the provision of a more secure airway is mandatory, such as those with anticipated difficulties with reintubation.

Summary

Every intubated and mechanically-ventilated patient should be clinically evaluated, at least on a daily basis, by a skilled team in order to speed up the weaning process as much as possible. In one study performed in Spain analysing the prevalence of mechanical ventilation in intensive care units [3], it was reported that the mean number of days that patients spent under mechanical ventilation was 27 days. In a more recent intervention study, in which a specific protocol was followed each day [2], the mean number of days under mechanical ventilation was only 12 days. These results not only have important clinical implications but also a direct economic impact, because while the quality of care is maintained such patients are now less costly.

Despite all the efforts made to promote weaning from invasive mechanical ventilation, some patients remain completely dependent on the ventilator in the intensive care unit. These patients pose not only clinical but also economic problems, as mentioned above. For these reasons, the transfer of selected patients to specialized weaning centres may be advisable. In fact, one study has shown a survival rate of 68% (287 out of 421 patients); and 74% of survivors (212 of the 287) were discharged free of ventilatory support. Moreover, the economic cost of this approach seems to be lower than the conventional treatment in the intensive care unit [67], thus indicating that this alternative may be a valuable resource.

Despite the considerable amount of knowledge acquired in recent years, the problem of weaning is far from being definitively resolved. Although we now have the answer to some questions, others have arisen. The optimal duration of T-piece trials before extubation is still under debate. Indices to predict the outcome of weaning trials may differ depending on the characteristics of the patients. Thus, those with neurological diseases may behave in a different way from COPD patients [68]. The same may occur with the different weaning techniques, and it can eventually be shown that a particular technique is best suited for a specific disease [69]. Moreover, about 15% of patients will need reintubation in the first 48 h after extubation despite meeting the usual criteria for removal of the endotracheal tube. The reasons for failure in these cases are poorly understood, and specific data concerning different patient groups are still lacking.

Finally, very recent advances in technological areas not specifically related to intensive care medicine, such as artificial intelligence and the use of knowledge-based systems, are proving to be useful in the management of the weaning process [70]. When such systems are applied to modern microprocessor mechanical ventilators, they can provide significant help in the process of weaning [71] by automatically reducing the ventilatory assistance and by indicating the optimal time to withdraw the patient from the ventilator and proceed with extubation.

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