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Difficult weaning

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For the majority of ICU patients, resumption of spontaneous ventilation is easily obtained. Depending on the case mix and referrals of any individual ICU, the weaning success rate is usually higher than 70%. A patient is considered a "weaner" when he is still breathing spontaneously, without any form of mechanical respiratory assistance, 2 days after he was disconnected from the ventilator. A "non-weaner" is defined as a patient who still requires some ventilatory support, total or partial, via a tracheal tube or even using a face mask [1]. This situation of non-weaning, or difficult weaning, has to be dissociated from the persisting need for a tracheal tube for other reasons, such as airway protection in neurological patients, for instance. A prospective study made in our medical ICU in 1987 (Fig. 1) showed that 95 of 500 patients (19%) who were mechanically ventilated for more than 24 h (half of our total admissions during that period) had a weaning time longer than 2 days [2]. Table 1 gives the rate of weaning failure in published series. In some ICUs, corresponding to specific referrals, weaning failure can be as high as 60–70%.

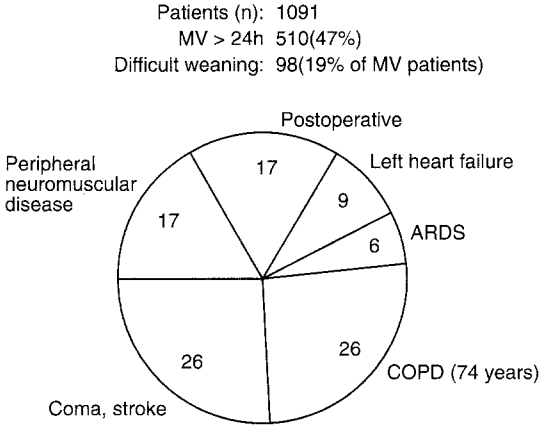

Fig. 1. Difficult to wean patients – a prospective study (Jan 1987–March 1988)

Table 1. Rate of weaning failure

Authors, year	Failure/total (%)	Patients
Sahn, 1973	17/100 (17)	Postoperative, ARDS, COPD
Tahvanainen, 1983	9/47 (19)	ARDS, LVF, Guillain-Barré
Pourriat, 1986	19/37 (51)	COPD
Fernandes, 1987	4/16 (25)	COPD
Kemper, 1987	17/35 (48)	Postoperative
Kline, 1987	21/50 (42)	Miscellaneous
Montgomery, 1987	5/11 (45)	ARDS, COPD
Sassoon, 1987	4/16 (25)	COPD
Tobin, 1987	7/17 (41)	COPD, LVF, flail chest
Fiastro, 1988	6/17 (35)	Postoperative
Murciano, 1988	5/16 (31)	COPD
Tassin, 1988	98/510 (19)	COPD, CHF, pneumonia, postoperative
Kriger, 1989	28/269 (10)	Aged >70 years, miscellaneous
Tomlinson, 1989	10/165 (6)	Medical and chir (3% COPD)
Shikora, 1990	15/20 (75)	Postoperative (10 cardiac)
Brochard, 1991	28/114 (24)	Miscellaneous
Jabour, 1991	22/38 (42)	Miscellaneous, medical
Yang, 1991	40/100 (40)	Miscellaneous
Conti, 1992	7/13 (53)	COPD

Strategy of weaning

Weaning procedures are usually started only after a series of conditions are fulfilled, as listed in Table 2. In particular, the following must apply:

1) The underlying disease process responsible for the acute respiratory failure and mechanical ventilation (MV) is cured
2) The patient must be in good clinical condition, and psychologically stable
3) The patient must be capable of spontaneous respiration.

Disconnecting the patient from the ventilator, and observing respiratory rate, tidal volume, abdominal paradox, and activity of accessory inspiratory muscles may be a useful guide.

Table 2. Requirements for initiation of weaning.

Start weaning only after correction of:

- Metabolic alkalosis (diuretics, bicarbonate infusion, gastrointestinal suctioning)
- Sedation (ongoing or recently interrupted)
- Encephalopathy, agitation, coma
- Extreme and/or chronic malnutrition
- Fever, sepsis, septic shock
- Haemodynamic instability (shock from any cause, arrythmia, cardiac failure)
- Excessive caloric intake (>3,000 Kcal/day)
- Untreated (or uncured) acute respiratory disease (mainly bacterial pneumonia, bronchospasm, pulmonary oedema)

More reproducible and objective measurements are available to help clinicians choose the right moment to initiate weaning. Table 3 gives the more commonly used indices. Besides classical – and still used – measurements such as blood gases, maximum inspiratory force [3], respiratory frequency and tidal volume, recently analysed by Yang and Tobin [4], an index of breathing control – the occlusion airway pressure ($P_{0.1}$) – has recently and repeatedly been shown to have a high predictive value [5–7]. Other indices such as oxygen consumption [8] or work of breathing (WOB) [9], despite providing valuable insights into the pathophysiology of difficult weaning, are not available at the bedside, and therefore cannot be recommended as routine predictive tools.

These various indices are usually measured a few minutes after disconnection from the ventilator. In many patients, despite positive tests obtained shortly after disconnection, spontaneous breathing gradually becomes less effective as time passes, suggesting the development of respiratory muscle fatigue. To predict such secondary occurrence of weaning failure before extubation, we now systematically test the patient during a 2 h T-piece trial. Extubation is only performed if the patient is still well after this 2 h "endurance" test. However, in some patients, at the end of a long period of partial support, a small level of pressure support (PS) (8 cmH_2O) is maintained until extubation, to eliminate the extra work caused by the tracheal tube.

When a patient has positive or borderline weaning criteria, and if he cannot sustain longer periods of spontaneous ventilation (SV), he is placed on a partial mode of ventilatory support such as pressure support ventilation [10] until he is ready for extubation. This may take days, weeks or even months.

Table 3. Weaning criteria during a T-piece trial.

1. No diaphragmatic rib cage disco-ordination (abdominal paradox)
2. Maximum inspiratory pressure <–20 cmH_2O
3. Respiratory rate (RR) <35/min
4. Tidal volume (Vt) >5 ml/kg
5. RR/Vt ≤105
6. Vital capacity >10 ml/kg
7. Minute ventilation ≤10 l/min and can be doubled voluntarily
8. Occlusion pressure <6 cmH_2O
9. Blood gases: PaO_2 maintained (but FiO_2 may be increased), $PaCO_2$ does not increase >8 mmHg
10. Endurance: spontaneous breathing via a T-piece >2 h

Causes of weaning failure

Mechanisms and diseases responsible for weaning failure are numerous (see Table 4) but the underlying mechanism is always the same: an imbalance between the increased work of ventilation and the limitation of the respiratory system to perform that work (or inequality between respiratory muscles' energy demand and supply). Most of the factors explaining the increase in energy demand (see Table 4.3b) are expressed as an increased WOB. They are mostly present in patients with chronic obstructive pulmonary disease (COPD), and explain why these patients represent one-half to two-thirds of cases of weaning failures listed in Table 1.

Recognition of imbalance between energy demand and supply has given rise to the concept of respiratory muscle fatigue, developed by the Montreal group for the last 15 years [11]. In a number of studies of patients assessed during weaning failure, measurements suggestive of respiratory muscle fatigue have been obtained [5,10,12,13]. In eight difficult-to-wean patients, mechanically ventilated with increasing levels of pressure support, Brochard et al. [10] demonstrated a clear relationship

Table 4. Causes for weaning failure.

1. Lung failure:
   - Cause(s) for ARF not cured (lung infections, pneumothorax, asthma, . . .)
2. General:
   - Fever, ongoing sepsis
   - Cardiac failure, haemodynamic instability
   - pH and electrolyte disturbances
   - Co-operation is not possible (agitation, confusion, pain)
3. Respiratory pump failure:

   a) Respiratory drive insufficiency
   - sleep deprivation
   - encephalopathy
   - sedation
   - recent intracerebral accident
   - metabolic alkalosis

   b) Increased respiratory workload
   - excessive caloric intake (>4,000 Kcal/day)
   - increased $\dot{V}E$ (high VD/Vt, high respiratory drive)
   - airflow limitation:
     - patient: COPD, asthma, tracheal stenosis, auto-PEEP
     - machine (partial support mode): high circuit impedance (demand-valve, humidifier), inadequate use of IMV or AC

   c) Respiratory muscle weakness or fatigue
   - incomplete recovery from neuromuscular paralysis (Guillain-Barré, polio, myasthenia)
   - malnutrition (diaphragmatic "cannibalisation" or disuse atrophy)
   - flattening of diaphragm (emphysema, gas trapping)
   - insufficient diaphragmatic blood flow (shock, LVF)
   - diaphragmatic paralysis (polio, phrenic nerve injury, complication of open heart surgery)
   - critically ill polyneuritis and/or myopathy, prolonged or high doses of corticosteroids, and/or neuromuscular blocking agents

between the WOB expressed in joules and an index of diaphragmatic fatigue, the shift of the high-low (H/L) ratio of the spectral power of the diaphragmatic electromyogram (Fig. 2). All patients with a WOB higher than 10 J/min had signs of respiratory muscle fatigue, and required higher levels of PS.

However, this concept of respiratory muscle fatigue has been recently challenged, several authors arguing that respiratory drive and muscular performance are reduced before exhaustion occurs, explaining the shallow breathing pattern, intended to spare respiratory muscles [14]. Clinically, it is also difficult to distinguish between fatigue and weakness. Most of the causes listed in Table 4 (3c) can be defined as causing weakness of the respiratory muscle.

Chronic airflow limitation increases the WOB. But during the weaning phase, when the patient is still intubated and connected to the ventilator, he has major additional causes of increased resistance: the tracheal tube itself, the circuitry and humidifier (if used), the demand valves, with frequent inspiratory gas flow limitation. Brochard et al. [15] measured the WOB developed by patients before and after extubation, during a T-piece trial, at different levels of PS (Fig. 3). Breathing via the tracheal tube and ventilator circuitry (PS=0) increased nearly by half the WOB. This extra work was only at a PS level of 8 cmH_2O in non-COPD, and of 12 for COPD patients. In addition to resistance due to "circuitry", another factor of increased resistance is the way inspiratory gas flow is delivered to patients, whatever the mode of assistance: demand-valves or flow-by for continuous positive airway pressure (CPAP) and IMV systems, mechanical tidal breaths for the assisted modes of ventilation.

It has been shown that many supportive modes of MV (assist-control, IMV), when poorly titrated for a specific patient, may actually increase his inspiratory workload [16,17], induce chronic respiratory fatigue, and probably delay extubation. However, demand-valves in the newer generation of electronically driven ventilators are less resistive [18].

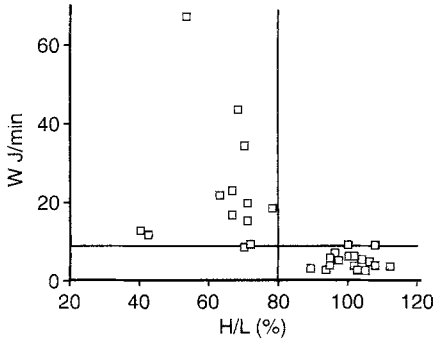

Fig. 2. Relationship between the work of breathing (W) expressed in J/min and the high/low ratio of the power spectrum of the diaphragmatic electromyogram, expressed in percent of control value (from [10]). See text for explanation

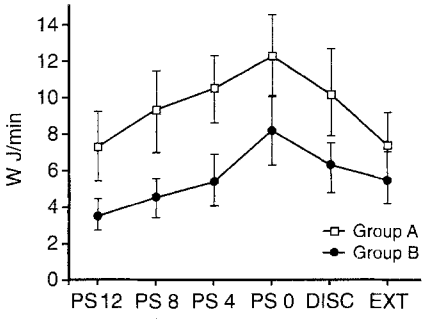

Fig. 3. Work of breathing (W), in J/min, before and after extubation. Group A: COPD patients; Group B: non-COPD. PS 12, 8, 4 pressure support 12, 8, 4 cmH_2O; PSO patients intubated, with the ventilator connected, using a CPAP mode with no PEEP; DISC, disconnection from the ventilator, tracheal tube still there. EXT extubation (from [15])

Auto-PEEP

Some degree of expiratory flow limitation has been demonstrated in many patients during the weaning phase, at a period when their respiratory rate is high and the expiratory time critically short. Dynamic hyperinflation results, with alveolar pressure above atmospheric pressure, yielding an increased inspiratory (elastic) WOB. Petrof et al. [19], in 7 COPD patients, breathing spontaneously during the weaning phase, demonstrated that incremental levels of CPAP reduced the inspiratory WOB and transdiaphragmatic pressure (Pdi). Only at the highest level of CPAP (15 cmH_2O) was in some patients the end-expiratory lung volume significantly increased. This study confirmed earlier recommendations that some level of external positive end-expiratory pressure (PEEP), but lower than auto-PEEP, should be used during weaning trials in spontaneously breathing patients, to reduce the inspiratory workload and possibly retard or suppress the occurrence of muscle fatigue [20].

However, expiratory pressure should not necessarily be applied indiscriminately to all patients in whom some levels of auto-PEEP is measured [21,22]. Tuxen [23] and Gay [24], in obstructive patients with no airflow limitation, demonstrated an increase in lung volume at each step of applied PEEP (external). Obviously, this would worsen inspiratory workload if applied in such patients during a weaning trial.

Another way to reduce the level of auto-PEEP is to reduce the respiratory rate of these (tachypneic) patients, thus lengthening the expiratory time, and leaving time for the lung volume to reach the elastic recoil equilibrium. This can also be achieved with PS ventilation, which usually reduces the respiratory rate and the level of auto-PEEP.

Critical illness polyneuropathy (CIP)

Failure to wean is usually the first and major manifestation of CIP. Limb weakness or paralysis develop either simultaneously or later. In the 15 patients with CIP reported by Bolton et al. [21], seen between 1977 and 1982, unexplained difficulty in weaning was the first sign, present within one month of admission to the CCU. All patients were septic, most of them having one or several episodes of septic shock. Electrophysiological studies revealed that CIP abnormalities were typical of a primary axonal degeneration of motor and sensory nerves, suggesting a toxic or metabolic disturbance, rather than an inflammatory or immune-mediated demyelination. Nine of these 15 patients died. In 8 patients, polyneuropathy improved, but of the 5 who did not improve and the 2 who worsened, mortality rate was the highest: 6/7.

Since then, several reports have emphasised the severity and frequency of the syndrome [26]. Aetiology is still unknown. In addition to sepsis and multiple organ failure (MOF), shock, hypoxia and medications have been implicated, as has the prolonged use of neuromuscular blocking agents [27]. This complication of neuromuscular blockade may be compared with the neuropathy of severe asthma, where the toxic role of corticosteroids has been stressed [27,28]. However, distinction between the different causative factors is not so easy, as patients frequently have several possible deleterious factors concurrently.

The diagnosis of neuromuscular disease as an explanation for weaning failure is probably underestimated. Witt et al. [30] studied prospectively 43 patients with sepsis and MOF. Electrophysiological signs of axonal degeneration were present in 70% of them, and 30% had a "difficult" weaning. Spitzer et al. [31] performed electrophysiological studies prospectively in 21 patients with inability to wean, over an 18-month period, none of whom had pre-existing neuromuscular disease. Electrophysiological evidence of neuromuscular disease severe enough to account for ventilator dependency was found in 62% of these patients.

Left ventricular (LV) failure during weaning failure

In 1988, we reported 19 COPD patients, whose unsuccessful weaning was attributed to acute LV dysfunction when spontaneous breathing was resumed [32]. Acute respiratory distress ($PaCO_2$ increasing to 42–58 mmHg in 10 min) and weaning failure were accompanied by an abrupt increase in transmural pulmonary artery occluded pressure (PAOP) from 7.5–24.5 mmHg. In some patients, acute pulmonary oedema developed before MV resumed. Fig. 4 shows a typical example of a PAOP rise during a weaning attempt. Many factors are involved, explaining the LV filling pressure increase, which are listed in Table 5.

In our series, all patients had a history of coronary artery disease (CAD), or exhibited during heart nuclear imaging unequivocal signs of acute coronary ischaemia, revealed or aggravated by spontaneous breathing. Similar results were obtained by Hurford et al. [33] in 14 patients during a weaning trial. Thallium-201 myocardial scintigraphy revealed significant alterations of myocardial perfusion or LV dilatation. All these patients had a history or recent evidence of CAD.

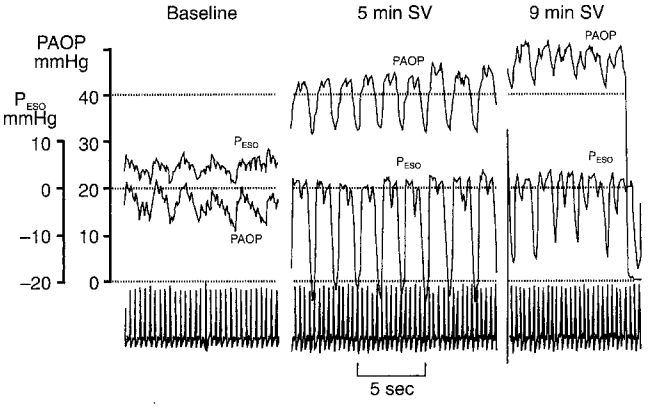

Fig. 4. Oesophageal (P_{eso}) and pulmonary artery occluded pressure (PAOP) during a weaning trial. Baseline: mechanical controlled ventilation. SV spontaneous ventilation after 5 and 9 min following disconnection

Table 5. Factors increasing pulmonary artery occluded pressure during unsuccessful weaning from MV.

1. Increased preload:
   a) Increased venous return
      - Decreased pleural pressure
      - Sympathetic discharge (stress, hypercapnia)
      - Increased abdominal pressure

   b) Reduced LV compliance
      - Myocardial ischaemia
        - Oxygen supply reduced
        - PaO_2 and SaO_2 reduced
        - LVEDP and HR increase, reducing coronary blood flow
      - Oxygen demand increased
        - catecholamines
        - HR and systolic BP increase
        - WOB increase
      - LV enlargement
      - RV enlargement (ventricular interdependence)
      - Compression of heart chambers by regionally hyperinflated lung
2. Reduced contractibility:
   Ischaemia
3. Increased afterload:
   Systolic BP increased (hypercapnia, catecholamine discharge)
   Pleural pressure reduced

Patients, in our series, were given diuretics and vasodilators [32]. Subsequently, 9 of these 25 patients weaned successfully, while measurement of PAOP during disconnection did not show any increase. Enoximone, a phosphodiesterase inhibitor, was used in a subsequent series of 5 patients with stable CAD to facilitate weaning [34]. After enoximone infusion, PAOP increase was less (9.6–16 compared with 15–27 mmHg), cardiac index greater (4.4 compared with 3.4) and the oxygen delivery much higher (611 compared with 455 ml/min/m^2).

That ischaemic hearts should fail following an acute fall in intrathoracic pressure is not actually surprising. However, Richard et al. [35] studied 5 COPD patients during weaning, also using Thallium-201 myocardial perfusion scanning. Spontaneous ventilation induced a significant decrease of LV ejection fraction from 56% to 44%, with no regional asynchrony. LV function impairment is probably the consequence of the acute LV afterload increase, induced by the fall in intrathoracic pressure.

LV function should be systematically explored when faced with an otherwise unexplained weaning failure. The easiest way to prove it is to place a Swan-Ganz catheter and to monitor PAOP during the weaning phase. Once documented, this phenomenon must be treated actively with diuretics, inotropes and/or vasodilators.

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