

## Weaning from mechanical ventilation

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The capacity to ventilate the lungs has led to the widespread application of this technique in the intensive care unit, where the number of patients ventilated and surviving has been increasing since the early 1950s.<sup>1</sup> The indications for ventilatory support are now broad and include postoperative ventilation, cardiac failure, trauma, and ventilatory support in multiorgan failure in addition to ventilation for respiratory failure.<sup>2</sup> During recovery the transition from a positive pressure system (on the ventilator) to spontaneous, negative pressure breathing is in general accomplished without difficulty. Drugs are withdrawn, and the patient is allowed to make spontaneous efforts to breathe, either through the ventilator or from a simple breathing circuit. After a trial of unassisted breathing extubation usually follows, with or without supplemental oxygen.

The ability of a patient to breathe spontaneously after mechanical ventilation depends on many factors, including the diagnosis on admission and the length of time spent on the ventilator. In patients receiving short term ventilation as many as 20% of initial trials of spontaneous respiration may not be successful,<sup>3</sup> and further ventilation<sup>4</sup> or reintubation is required.<sup>5</sup> The incidence of weaning failure varies considerably, however; in a study of patients ventilated after cardiac surgery, where the period of elective ventilation had been a few hours, the overall incidence of initial failure to extubate was as low as 4%.<sup>6</sup>

Although 20% of patients ventilated acutely fail to be weaned initially, their progress and subsequent weaning is usually successful and rapid. Nett and coworkers showed that in such patients over 91% were able to breathe spontaneously after seven days.<sup>7</sup> In patients in whom weaning was still being attempted at one week the problems were complex. This group consists of patients with pre-existing lung disease as well as those patients surviving after severe multiorgan failure or neuromuscular disease, who tend to require ventilation for several days. Patients who have prolonged ventilation are more likely to require many days for weaning, and may take days or months to achieve spontaneous respiration by day and night.<sup>8</sup>

How then can we decide whether or not a patient is ready to be weaned successfully? The possibility of judging when a patient is able to breathe spontaneously has been examined largely in patients ventilated acutely, where investigators have documented various res-

piratory measurements before and during a trial of spontaneous respiration and compared the results with outcome (table 1). Unfortunately, there is little agreement in published reports about the power of these measurements to predict patients who will be unable to sustain spontaneous ventilation. For example, Tahvanainen and colleagues measured a battery of physiological parameters before extubation in a group of patients ventilated for either the adult respiratory distress syndrome, left ventricular failure, or neuromuscular disorders.<sup>5</sup> None of the conventional tests, including measurements of vital capacity, minute ventilation, respiratory rate, maximum voluntary ventilation (MVV), or maximum inspiratory pressure, distinguished patients that eventually required reventilation.

It has been suggested that simple clinical signs will detect patients who will fail to be weaned, including rapid shallow breathing<sup>15</sup> and respiratory paradox and alternans.<sup>16</sup> Although such clinical assessment is widely practised, published evidence to corroborate these signs is scarce. For example, in only about half of the studies is failure of weaning associated with increasing tachypnoea.<sup>5 8 14 20 59</sup> In some patients, although the tachypnoea is a sign of eventual weaning failure, the high respiratory rate does not indicate the exact point when reventilation is appropriate. In other studies there has been no difference between the respiratory rate in those who were weaned successfully and those who were not.<sup>5 17 18</sup>

The absence of a consensus on the value of signs and measurements predicting an individual patient's ability to be weaned successfully is reflected in clinical practice within the United Kingdom. In a survey of weaning practices in which 72% of 235 intensive care units in the United Kingdom responded the most common measures used were fractional inspired oxygen (FIO<sub>2</sub>) and arterial oxygen tension (PaO<sub>2</sub>); vital capacity was measured by only 35%, and maximum inspiratory pressure

Table 1 Physiological measures conventionally associated with weaning failure

Tidal volume	< 5 ml/kg <sup>9</sup>
Vital capacity	< 10 ml/kg <sup>10</sup>
Minute ventilation (MV)	> 10 l/min <sup>11 12</sup>
Maximum voluntary ventilation	< 2 × MV <sup>4 13</sup>
Maximum inspiratory pressure	> -20 cm H <sub>2</sub> O <sup>4</sup>
Alveolar-arterial oxygen tension difference	> 300 mm Hg <sup>14</sup>
Dead space/tidal volume	> 0.6 <sup>14</sup>

Conversion to SI units: 1 mm Hg = 0.133 kPa; 1 cm H<sub>2</sub>O = 0.098 kPa.

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( $P_{\text{imax}}$ ), maximum voluntary ventilation (MVV), compliance of the respiratory system, and the alveolar-arterial oxygen tension difference ( $A-a\text{D}\text{O}_2$ ) were measured in less than a quarter of the units (J C Goldstone, unpublished findings). The deadspace-tidal volume ratio ( $V_D/V_T$ ) and the pressure generated during the first 0.1 second of inspiration ( $P_{0.1}$ ) were assessed by 6% of units. Most respondents stated that "clinical assessment," rather than tests, before and during periods of spontaneous breathing formed the basis for decisions on weaning.

### Mechanisms of ventilatory failure

The ability to breathe spontaneously depends on three factors: central respiratory drive, the capacity of the respiratory muscles, and the load placed on the respiratory muscle pump. Hypercapnic respiratory failure will ensue when the balance between these factors is disrupted, either by a decrease in capacity (for example, in neuromuscular disease), an increase in load (for example, increased airway obstruction), or depression of central drive (for example, after a drug overdose). An approach towards answering the questions of when to withdraw mechanical ventilation and for how long and when to reinstitute support rests on the assessment of these three components—capacity, load, and drive.

#### CAPACITY OF THE RESPIRATORY MUSCLES IN THE INTENSIVE CARE UNIT

Measurement of the capacity of the respiratory muscles centres around their ability to generate pressure. For the inspiratory muscles strength can be measured during a static effort against a closed airway, pressure being recorded at the mouth or in the endotracheal tube. Although methods may differ, most reports of maximum pressure generation in the intensive care unit show a 75% reduction in capacity.<sup>4 19 20</sup>

Before admission to the intensive care unit, the patient may have reduced strength of the respiratory muscles. Systemic disease may affect the respiratory muscles, at the level of the nerves,<sup>21 22</sup> the neuromuscular junction,<sup>23</sup> or the muscle itself.<sup>24</sup> This may exacerbate or precipitate respiratory failure. Pulmonary disease may adversely affect the mechanical performance of the respiratory muscles. With airways obstruction there is hyperinflation, muscle shortening, and a reduced capacity to generate inspiratory pressures. When low and flat the diaphragm is less effective at reducing pleural pressure and less able to raise gastric pressure and displace the abdominal contents to achieve a change in volume.

Respiratory muscle strength may diminish after admission to the intensive care unit (table 2). Metabolic abnormalities such as hypophosphataemia,<sup>25</sup> hypomagnesaemia,<sup>26</sup> and hypocalcaemia<sup>27</sup> may reduce muscle contractility acutely. The effect of hypoxaemia on muscle function is difficult to assess. Blood flow to muscle increases during hypoxaemia and may offset the decreased carriage of oxygen by blood, thereby maintaining oxygen delivery. In

Table 2 Factors that may impair respiratory muscle contractility in patients in the intensive care unit

Hypophosphataemia <sup>25</sup>
Hypomagnesaemia <sup>26</sup>
Hypocalcaemia <sup>27</sup>
Hypoxia
Hypercarbia <sup>30</sup>
Acidosis
Infection <sup>31 32</sup>
Disuse atrophy <sup>34</sup>
Malnutrition <sup>35</sup>

a carefully designed study, Ameredes *et al*<sup>28</sup> showed no change in muscle function during hypoxaemic conditions. Hypercapnia, however, decreases contractility,<sup>29</sup> especially if combined with acidosis. Hypoxia and hypercapnia may cause a synergistic decrease in force, as has been found in an animal model.<sup>30</sup>

Muscle performance may be diminished by infections. Ventilatory failure occurs as a result of respiratory muscle dysfunction in dogs given septicaemic shock.<sup>31</sup> During an upper respiratory tract infection muscle performance measured in terms of maximum inspiratory and expiratory mouth pressures is reduced by 30%.<sup>32</sup> Muscle atrophy occurs with disuse,<sup>33</sup> and this may be accelerated by sepsis. Anzueto *et al*<sup>34</sup> ventilated primates artificially and found after 11 days that diaphragm strength, measured during phrenic nerve stimulation, was reduced by 46%. Malnutrition occurs in many patients before admission to the intensive care unit, and may continue during the intercurrent illness. Respiratory muscle strength is reduced in undernourished patients<sup>35</sup> and the mass of the diaphragm is decreased in patients who are wasted.<sup>36</sup>

#### LOAD

During mechanical ventilation the work of breathing is performed by the ventilator, and is dissipated during gas compression, overcoming airflow resistance and inflating the chest against elastic components of the lung and chest wall. During spontaneous breathing work external to the lung is performed in moving gas in and out of the chest, which means overcoming the elastic forces of the lung and chest wall during inflation, the resistance to airflow, and minor forces of inertia and gravity. Not all work external to the lung can be measured, as some energy is expended during the breathing cycle that does not contribute to gas flow but deforms the chest wall. Although this may be substantial, the load applied to the respiratory muscles is largely related to the elastic and resistive elements during gas flow.

Table 3 Factors increasing the load on the respiratory muscles in patients in the intensive care unit

Bronchoconstriction <sup>40</sup>
Left ventricular failure <sup>41</sup>
Hyperinflation <sup>52</sup>
Intrinsic positive end expiratory pressure <sup>52</sup>
Artificial airways <sup>47</sup>
Ventilator circuits <sup>51</sup>

In the intensive care unit the ventilatory load is often much higher than normal (table 3).

Load can be increased substantially by airways obstruction. During asthma induced by histamine challenge a fall in FEV<sub>1</sub> of 40% was associated with a threefold increase in load that required an eightfold increase in pressure generation per tidal breath.<sup>37</sup> In patients ventilated for left ventricular failure Rossi *et al*<sup>38</sup> measured compliance and airway resistance, and showed a substantial increase in the load applied to the respiratory muscles. Resting oxygen consumption is increased in chronic airflow limitation, reflecting the increased work of breathing,<sup>39</sup> and in patients being weaned from ventilators the oxygen cost of breathing was four times greater than normal in patients with left ventricular failure.<sup>40</sup> Left ventricular function is impaired in many patients admitted to the intensive care unit, and pulmonary oedema increases the load substantially. This may occur during the transition to negative pressure breathing, as positive pressure ventilation may act to assist the left ventricle via transmitted pressure from the ventilator to the chambers of the heart.<sup>41 42</sup>

During weaning patients breathe through airways, apparatus, and ventilators, and this increases the load substantially.<sup>43</sup> The work required to breathe through an artificial airway is large,<sup>44</sup> greater than the work of breathing through the upper airway alone,<sup>45</sup> and it may double the load applied to the system.<sup>46</sup> The work needed to breathe through a tracheostomy may equal the work of breathing through the longer oral endotracheal tubes,<sup>47</sup> and may itself prevent spontaneous respiration.<sup>48</sup> Increased work is performed when patients are breathing through many circuits, especially when they are required to open valves to achieve inspiration.<sup>49</sup>

In many ventilated patients, especially those with airflow limitation, the time for expiration may not allow complete exhalation to functional residual capacity. Subsequent tidal breaths increase end expiratory volume and pressure; this is termed intrinsic or auto PEEP (positive end expiratory pressure). During a

spontaneous breath the increased elastic recoil pressure of the lungs and chest wall must be overcome, and in patients who are weak this may be as great as half of their maximum inspiratory pressure generating capacity, which imposes a large additional load on the respiratory muscles.<sup>50</sup> Fiastro *et al*<sup>51</sup> measured the work of breathing during weaning from mechanical ventilation and found that patients able to breathe spontaneously had less work than those who failed. In the "failed" group spontaneous respiration was achieved only when the respiratory work was reduced to that observed in the successful group.

#### CENTRAL DRIVE

Force generation of the respiratory muscles is related to output from the central nervous system in terms both of the number of contractile units activated and of stimulation frequency. As motor neurone firing frequency is increased force increases rapidly, but it plateaus at frequencies greater than 50 Hz, with little increase at 100 Hz and beyond. In health and at rest low levels of central drive and concomitant low motor neurone firing frequencies are sufficient to effect an adequate tidal volume; patients with chronic respiratory failure have a higher respiratory drive,<sup>52 53</sup> placing them higher and less favourably on the frequency-force curve.

During weaning patients failing to achieve adequate ventilation have high central drive,<sup>54</sup> and indeed failure to breathe spontaneously has been correlated with an increased central drive that cannot be sustained.<sup>55</sup> Although occasional studies have shown that drive is reduced and may respond to central stimulants,<sup>56</sup> this has not been the case in most investigations. Central stimulants in patients breathing high on the frequency:force curve would not be expected to produce substantially greater ventilation. But any reduction in drive—due to sedation, for example—would lead to a large reduction in the force generated, and to ventilatory failure.

#### THE BALANCE: RESPIRATORY MUSCLE FATIGUE

When the load applied to the respiratory muscles exceeds their capacity to generate pressure the likely outcome is the development of hypercapnic ventilatory failure, leading to acidosis, coma, and death. The hypothesis is that in these circumstances the respiratory muscles cannot sustain the required pressures without fatigue (figure).

Evidence supporting this hypothesis has largely come from studies in normal subjects breathing through inspiratory resistances. It has been shown that ventilation cannot be sustained when the pressure generated per breath exceeds 40% of maximum pressure.<sup>57</sup> The ability to maintain ventilation is also related to the duration of contraction of the inspiratory muscles during each breath. Bellemare and Grassino<sup>58</sup> performed repeated trials of inspiratory resistive loading measuring the time of inspiration (Ti) as a fraction of the respiratory cycle (Ttot). They defined a numerical relation between the strength of the diaphragm (Pdimax) and the duration and

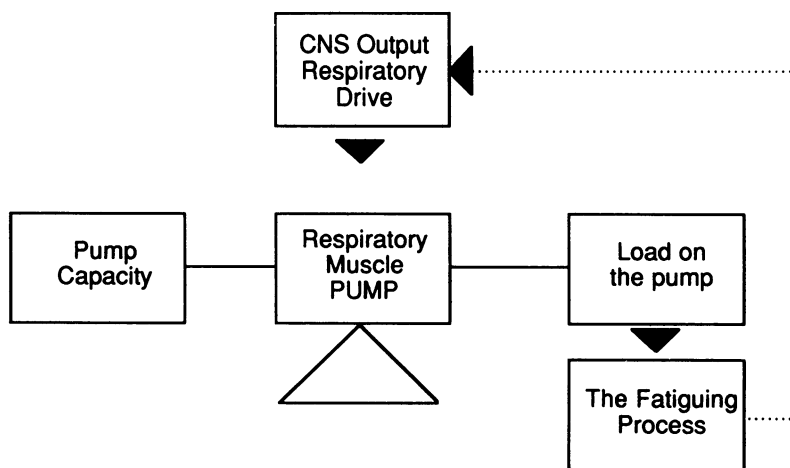


Diagram illustrating the central importance of the respiratory muscle pump and the crucial balance between load and capacity. When the ratio of load to capacity is high, the fatiguing process may be initiated, with (possible) adaptive changes in central nervous system respiratory drive.

fraction of maximum pressure generated during each breath:

$$\text{Tension-time index} = \frac{P_{di}}{P_{di \max}} \times \frac{T_i}{T_{tot}}$$

This tension-time index is equal to 0.05 during resting ventilation. When it exceeds 0.15, through an increase either in the duration of inspiration or in inspiratory pressure (induced experimentally by breathing through a resistance), ventilation cannot be sustained. Few studies have measured the tension-time index in the intensive care unit during weaning. Pourriat and coworkers,<sup>59</sup> however, showed that patients who could not be weaned required a greater fraction of their maximum inspiratory pressure during each breath.

The relation between load, capacity, and fatigue in patients in the intensive care unit has been studied in terms of a modified tension-time index, the inspiratory effort quotient.<sup>60</sup> The mean pressure developed during inspiration is determined by tidal volume and dynamic compliance, and depends also on the shape of the inspiratory pressure curve:

$$\text{Inspiratory effort quotient} = \frac{(k \cdot V_T / C_{dyn}) \times (T_i / T_{tot})}{P_{imax}}$$

We have measured the inspiratory effort quotient in patients during trials of weaning and have found it to be low (0.05) in patients who were weaned satisfactorily and raised in those who could not be weaned and required ventilation.<sup>61</sup> This suggests that success with weaning is related to the balance between the strength of the respiratory muscles and the load applied to them rather than the absolute value of either measure. This may explain the variable predictive power in studies where aspects of strength or load are measured alone. Although the explanation of a high value for the inspiratory effort quotient is more complex in patients who cannot be weaned, high values for the inspiratory effort quotient are likely to result in rapid weaning failure.

Given that excessive load in relation to capacity may lead to fatigue a measurement of fatigue perhaps could be used to monitor patients being weaned from mechanical ventilation. This would enable patients to be reventilated at an appropriate moment, before the development of hypercapnia. With established fatigue maximum inspiratory pressures are reduced but measuring  $P_{imax}$  in patients in the intensive care unit has hitherto been difficult and the results are variable. A recent approach in semiconscious patients is to measure the pressure generated by inspiratory gasps, when the patient is connected to a one way valve that is closed to inspiration. Pressure is measured at the peak of the inspiratory effort, after 8–10 occluded breaths or 20 seconds of occlusion.<sup>62</sup> This is a relatively simple technique, which can be used in patients not capable of making a maximum voluntary inspiratory effort and is surprisingly well tolerated in awake patients. Although this technique may allow a good measurement of

$P_{imax}$  in stable patients it is unlikely to be easily applicable during the dynamic events of weaning.

Complex neuromuscular events occur during the fatiguing process initiated by the excessive loading of the respiratory muscles. In particular, the frequency distribution of the electromyogram changes during a fatiguing load.<sup>63</sup> The electromyogram of the diaphragm and other inspiratory muscles was shown to alter during weaning from mechanical ventilation in those patients who failed to breathe spontaneously,<sup>16</sup> but this technique is not in common use. Recording of electromyographic signals is difficult in patients in the intensive care unit and surface electrodes also record signals from non-respiratory muscles. During fatigue electromyographic changes occur early during loaded breathing, with little subsequent change when failure of force generation occurs, and they do not therefore indicate when reventilation should occur. Thus, although respiratory muscle fatigue probably occurs during weaning failure this phenomenon cannot be detected with currently available techniques.

During muscular activity intense enough to lead to fatigue the speed of contraction and relaxation of muscle slows, and this can best be measured during the relaxation period after contraction has ceased.<sup>64</sup> During a brief inspiratory sniff the rate of relaxation of the respiratory muscles can be measured in terms of the maximum relaxation rate of oesophageal pressure.<sup>65</sup> In normal subjects during fatigue induced by loaded ventilation, the maximum relaxation rate slows and recovers rapidly with rest. Patients in the intensive care unit are usually intubated, with their upper airway bypassed, and unable to perform a sniff. A device that enables intubated patients to perform a sniff like manoeuvre has been used recently to study patients in the intensive care unit.<sup>66</sup> In those who could not be weaned the maximum relaxation rate slowed progressively and recovered after reventilation, suggesting that fatigue of the respiratory muscles was occurring during the attempt at weaning. Patients weaned successfully showed no slowing of the maximum relaxation rate of the respiratory muscles. In the future, maximum relaxation rate could perhaps be used as a reflection of the relation between the capacity of the respiratory muscles and the load that is applied to them when patients being weaned from mechanical ventilation are being assessed and monitored. Slowing of the maximum relaxation rate could provide an early indication that weaning will fail.

### A strategy for weaning

The approach towards the patient who is likely, or has already proved, to be difficult to wean should begin by establishing a diagnosis or a list of clinical problems. When the causative factors that precipitated the need for ventilation are reversed, the patient may be a candidate for weaning. Much attention has been focused on the method of weaning patients from the ventilator, and opinion is divided. One method is

to allow the patient to breathe spontaneously via a T piece circuit for gradually lengthening periods with full ventilation between these, and the other is to provide partial respiratory support by the ventilator and to allow the patient to breathe spontaneously between mechanical breaths (synchronous intermittent mandatory ventilation, SIMV—see article 2 of this series (November 1990;45:885–90) for the different techniques of ventilation and support).<sup>19</sup> Currently there is no evidence to suggest that one method is superior to the other. Weaning is more likely to succeed in an alert, rested, cooperative patient. Sedation, confusion, and tiredness will make weaning less likely. In alert patients central respiratory drive is likely to be optimal; respiratory stimulants are of limited value and potentially harmful. At the centre of any weaning strategy is a detailed assessment of respiratory muscle capacity and load.

#### RESPIRATORY MUSCLE CAPACITY

In general, patients in the intensive care unit are weak, and small changes made to improve their strength or to reduce the load applied to the weakened respiratory muscles will be beneficial.

Correction of hypophosphataemia has been shown to increase strength and to facilitate weaning.<sup>67</sup> Electrolyte abnormalities should also be corrected. Although there is no direct evidence on the effect of hypercapnia and hypoxaemia during weaning, respiratory muscle function is likely to be reduced if the patient is acidotic, and tissue acidosis may be intensified by hypoxaemia. Nutritional support should be provided in the intensive care unit. Patients are often undernourished before admission to hospital, and the deficit may be large. Uptake of nutritional substrates may be impaired during episodes of critical illness, and intravenous feeding may be difficult in patients with complex problems of fluid balance. Patients can seldom be weaned during septic episodes, and weaning failure has been shown to be more likely in patients with a positive blood culture.<sup>5</sup> Respiratory muscle function may be diminished substantially by endotoxaemia. Although drugs, particularly aminophylline, has been reported to enhance respiratory muscle performance,<sup>68</sup> the balance of evidence suggests this is not the case.<sup>69</sup>

#### LOAD

During weaning the load applied to the muscles may alter acutely, precipitating respiratory failure and the need for reventilation.<sup>51</sup> Patients may have fluid overload or hypoalbuminaemia, leading to the development of pulmonary oedema at relatively low filling pressures. The mechanical enhancement of left ventricular performance by ventilation and the changes during weaning require consideration.

Airways obstruction increases the respiratory load and decreases respiratory muscle performance, and should be treated aggressively. Patients may be stable when assessed

during mechanical ventilation yet may develop wheeze during spontaneous breathing, and should therefore be assessed during the weaning trial. Hyperinflation is likely in patients with airways obstruction, and this may be exacerbated by mechanical ventilation, which may increase intrinsic positive end expiratory pressure. Overdistension during mechanical ventilation can be monitored simply by displaying airway pressure during intermittent positive pressure ventilation on the bedside monitor, and watching for the characteristic waveform seen in such patients.<sup>70</sup> Intrinsic positive end expiratory pressure can be measured by occluding the expiratory limb of the ventilator during a prolonged expiratory pause, and measuring the airway pressure transmitted to the pressure gauge of the ventilator.<sup>71</sup> Patients susceptible to hyperinflation may breathe more effectively when removed from the ventilator altogether rather than having intermittent mandatory ventilation.<sup>72</sup>

Breathing apparatus may impose a substantial respiratory load on patients. Flow through endotracheal apparatus is affected by many factors, and is unlikely to be laminar in most cases. Resistance to flow increases with decreased tube diameter, and with a high minute ventilation may impose an unsustainable tension-time index of more than 0.15.<sup>44</sup> This load can be overcome by using inspiratory pressure support.

The benefit of positive end expiratory pressure is difficult to assess in the hyperinflated patient,<sup>73</sup> but it is of value in patients who have muscle weakness or obesity, or postoperative basal collapse. In such patients it increases functional residual capacity, prevents airways closure and atelectasis, increases compliance, and reduces ventilatory work. In these circumstances weaning is usually facilitated by adding continuous positive airway pressure.

#### GENERAL MEASURES

Weaning, especially in patients who have been ventilated for many days or weeks, may be a great burden both physically and mentally. Sleep may be lost and disrupted and morale low, especially if the patient feels “stuck” on the ventilator. Although daytime respiratory drive should not be depressed, the establishment of regular sleeping patterns may require short acting sedative drugs.

The endpoint of a weaning trial is difficult to assess in some patients, as there are no current guidelines about the point where reventilation is mandatory—though the development of hypercapnia and acidosis indicates that reventilation is necessary. In studies of high intensity workloads in skeletal muscle, biopsy material has shown necrosis<sup>74</sup> and such changes probably occur in respiratory muscles if these are sufficiently stressed. Damage to the respiratory muscles, especially in patients who have severe weakness, only impedes successful weaning. In addition, the psychological effect of allowing a patient to breathe to the point of exhaustion demoralises the patient and erodes previous progress, and is therefore counterproductive.

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