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A COMPARISON OF FOUR METHODS OF WEANING PATIENTS FROM MECHANICAL VENTILATION

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Abstract *Background.* Weaning patients from mechanical ventilation is an important problem in intensive care units. Weaning is usually conducted in an empirical manner, and a standardized approach has not been developed.

Methods. We carried out a prospective, randomized, multicenter study involving 546 patients who had received mechanical ventilation for a mean (±SD) of 7.5±6.1 days and who were considered by their physicians to be ready for weaning. One hundred thirty patients had respiratory distress during a two-hour trial of spontaneous breathing. These patients were randomly assigned to undergo one of four weaning techniques: intermittent mandatory ventilation, in which the ventilator rate was initially set at a mean (±SD) of 10.0±2.2 breaths per minute and then decreased, if possible, at least twice a day, usually by 2 to 4 breaths per minute (29 patients); pressure-support ventilation, in which pressure support was initially set at 18.0±6.1 cm of water and then reduced, if possible, by 2 to 4 cm of water at least twice a day (37 patients); intermittent trials of spontaneous breathing, conducted two or more times a day if possible (33 patients); or a once-daily trial of spontaneous breathing (31 patients). Standardized protocols were followed for each technique.

Results. The median duration of weaning was 5 days for intermittent mandatory ventilation (first quartile, 3 days; third quartile, 11 days), 4 days for pressure-support ventilation (2 and 12 days, respectively), 3 days for intermittent (multiple) trials of spontaneous breathing (2 and 6 days, respectively), and 3 days for a once-daily trial of spontaneous breathing (1 and 6 days, respectively). After adjustment for other covariates, the rate of successful weaning was higher with a once-daily trial of spontaneous breathing than with intermittent mandatory ventilation (rate ratio, 2.83; 95 percent confidence interval, 1.36 to 5.89; $P<0.006$) or pressure-support ventilation (rate ratio, 2.05; 95 percent confidence interval, 1.04 to 4.04; $P<0.04$). There was no significant difference in the rate of success between once-daily trials and multiple trials of spontaneous breathing.

Conclusions. A once-daily trial of spontaneous breathing led to extubation about three times more quickly than intermittent mandatory ventilation and about twice as quickly as pressure-support ventilation. Multiple daily trials of spontaneous breathing were equally successful. (N Engl J Med 1995;332:345-50.)

ALTHOUGH often lifesaving, mechanical ventilation causes numerous life-threatening complications,[1] making it important to discontinue ventilator support at the earliest possible time. More than 40 percent of the time that a patient receives mechanical ventilation is spent trying to wean the patient from the ventilator.[2] Considering the proportion of staff time devoted to weaning, it is surprising that the process continues to be managed empirically and that a standardized approach has not been developed.

Weaning techniques differ considerably from one another.[3] Traditionally, intermittent trials of spontaneous breathing, conducted one or more times a day, have been used. Intermittent mandatory ventilation was introduced amid claims that it was superior to the traditional weaning approach. It allows the patient to breathe spontaneously between ventilator-delivered breaths[4]; thus, weaning can be considered to begin with the institution of mechanical ventilation. In the 1980s, pressure-support ventilation became available[5]; it provides a titratable pressure boost to every inspiratory effort, and weaning is accomplished by gradually decreasing the level of the pressure boost.

Efficacy studies of weaning techniques can be faulted for having a retrospective design, inappropriate study

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populations, and poorly standardized protocols; in addition, most were conducted before the use of pressure-support ventilation became widespread.[6-8] Accordingly, we performed a prospective, randomized study involving patients who were deemed ready to discontinue mechanical ventilation. In a subgroup of patients who were difficult to wean we compared the length of time required for weaning with the use of four techniques: intermittent mandatory ventilation, pressure-support ventilation, intermittent trials of spontaneous breathing conducted several times a day, and a once-daily trial of spontaneous breathing.

METHODS

Patients

The study was conducted between October 1992 and October 1993 in the medical–surgical intensive care units of 14 teaching hospitals in Spain. The study population consisted of 546 patients (378 men and 168 women), with a mean (±SD) age of 58.2±18.4 years. All received mechanical ventilation for more than 24 hours because of acute respiratory failure. The following underlying conditions were present: chronic obstructive pulmonary disease with acute respiratory failure in 128 patients, acute lung injury in 319, neurologic or neuromuscular disorders in 85, and miscellaneous causes in 14. The acute lung injury was a result of surgery in 74 patients, infection in 73, heart failure in 69, multiple trauma in 51, adult respiratory distress syndrome in 23, and other pulmonary causes in 29. On admission to the intensive care unit, the patients had a mean score of 18.7±7.0 on the Acute Physiology and Chronic Health Evaluation (APACHE II) scale.[9] Until the first attempt was made to discontinue ventilator support, all patients received assist–control ventilation. The patients received mechanical ventilation for a mean of 7.5±6.1 days before weaning was started. No hospital contributed more than 10 percent of the study population.

To be enrolled in the study the patients had to have an improvement in or resolution of the underlying cause of acute respiratory failure; adequate gas exchange, as indicated by a ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) above 200 with a positive end-expiratory pressure of ≤5 cm of water; a core temperature below 38°C; a hemoglobin level above 10 g per deciliter; and no further need for vasoactive and sedative agents. In addition, the attending physician had to agree that the patient was in stable condition and ready to be weaned from the ventilator. Patients with a tracheostomy were excluded. The study was approved by the ethics committees of the hospitals, and the patients provided informed consent.

Protocol

After patients were enrolled in the study, assist–control ventilation was stopped and the patients breathed spontaneously for three minutes through a T-tube circuit, with the FiO_2 set at the same level (0.38±0.05) as that used during mechanical ventilation. Tidal volume and respiratory frequency were measured with a spirometer during this period. Maximal inspiratory pressure was measured three times in succession, and the most negative value was selected. Patients who met at least two of the following criteria underwent a trial of spontaneous breathing lasting up to two hours: maximal inspiratory pressure below −20 cm of water, tidal volume above 5 ml per kilogram of body weight, and a respiratory frequency of less than 35 breaths per minute. Weaning was considered to have begun with the onset of this trial. During this trial, patients received humidified oxygen-enriched gas through a T-tube circuit. The primary physician terminated the trial if a patient had any of the following signs of distress: a respiratory frequency of more than 35 breaths per minute, arterial oxygen saturation below 90 percent, heart rate above 140 beats per minute or a sustained increase or decrease in the heart rate of more than 20 percent, systolic blood pressure above 180 mm Hg or below 90 mm Hg, agitation, diaphoresis, or anxiety. Patients who had none of these features at the end of the trial were extubated. After extubation, the patients received supplemental oxygen by face mask. If a patient had signs of poor tolerance at any time during the trial, assist–control ventilation was reinstituted. For the purpose of the study, these patients were designated as being difficult to wean from mechanical ventilation.

Even if there were no signs of distress by the end of this trial, extubation could be postponed for a maximum of 24 hours if the primary physician thought that a patient might not be able to clear secretions or protect the airway against aspiration. Patients continued to breathe spontaneously through the T-tube circuit. If they met criteria for poor tolerance, mechanical ventilation was reinstituted. These patients were not included in the weaning-protocol group.

Patients who were designated as being difficult to wean from mechanical ventilation were stratified according to center and randomly assigned with the use of a random-number table[10] to be weaned in one of four ways: intermittent mandatory ventilation, pressure-support ventilation, intermittent trials of spontaneous breathing, and a once-daily trial of spontaneous breathing. The patients were assigned to the groups in a blinded fashion with the use of opaque, sealed, numbered envelopes, which were opened only when a patient did not successfully complete the two-hour trial of spontaneous breathing. All adjustments for each weaning technique were made by the primary physician.

Intermittent Mandatory Ventilation

In the group that received intermittent mandatory ventilation, the ventilator rate was initially set at half the frequency used during assist–control ventilation; this initial rate was 10.0±2.2 breaths per minute, and mechanical breaths were synchronized with inspiratory effort. We attempted to decrease the ventilator rate, usually by two to four breaths per minute, at least twice a day. The ventilator rate was decreased more rapidly if tolerated by the patient, as reflected by clinical assessment and blood gas monitoring. Patients who tolerated a ventilator rate of five breaths per minute for two hours without signs of distress were extubated. A continuous positive airway pressure of ≤5 cm of water was permitted.

Pressure-Support Ventilation

In the group that received pressure-support ventilation, pressure was titrated to achieve a frequency of ≤25 breaths per minute. Pressure support was initially set at 18.0±6.1 cm of water, and we attempted to reduce this level of support by 2 to 4 cm of water at least twice a day. The pace was increased if the patient did not have signs of distress (the same criteria were applied as in the initial trial of spontaneous breathing, except that a respiratory frequency of ≤25 breaths per minute was required). Patients who tolerated pressure support at a setting of 5 cm of water for two hours with no apparent ill effects were extubated. A continuous positive airway pressure of ≤5 cm of water was permitted.

Intermittent Trials of Spontaneous Breathing

Patients assigned to intermittent trials of spontaneous breathing were disconnected from the ventilator and allowed to breathe spontaneously through either a T-tube circuit or a continuous-flow circuit designed to provide a continuous positive airway pressure of ≤5 cm of water. The duration of the trials was gradually increased, and they were attempted at least twice a day. Between the trials, assist–control ventilation was provided for at least one hour. Patients able to breathe on their own for at least two hours without signs of distress were extubated.

Once-Daily Trial of Spontaneous Breathing

Patients assigned to a once-daily trial of spontaneous breathing were disconnected from the ventilator and allowed to breathe spontaneously through a T-tube circuit for up to two hours each day. If signs of intolerance developed, assist–control ventilation was reinstituted for 24 hours, at which time another trial was attempted. Patients who tolerated a two-hour trial without signs of distress were extubated.

For all four methods, weaning was considered to have failed if reintubation was necessary within 48 hours after extubation or if

extubation was not possible after 14 days of weaning. Weaning was considered successful if extubation was achieved within the 14-day period and reintubation was not required within 48 hours of extubation.

Statistical Analysis

The chi-square test was used to compare categorical data, and the Kruskal–Wallis test was used to compare continuous variables among the groups. The Kaplan–Meier method was used to determine the probability of the success of a particular method of weaning over time.[11] The relative probability of success over time was examined by a Cox proportional-hazards model.[12] Base-line covariates included in the model were the weaning technique, age, APACHE II score, ratio of PaO_2 to FiO_2, maximal inspiratory pressure, spontaneous respiratory frequency, spontaneous tidal volume per kilogram, duration of previous ventilator support, and the length of time to the failure of the initial trial of spontaneous breathing. Backward elimination was used to reduce the model to the subgroup of factors that made statistically significant contributions to variation in the time required for successful weaning. Data were censored on 2 patients who died during the study, 2 patients in whom weaning was interrupted because of intercurrent illness, 23 patients who required reintubation within 48 hours of extubation, and 11 patients who were still receiving ventilator support on day 14. We calculated that 31 patients were needed in each group to detect at a power of 80 percent a difference in weaning time between groups of two days, with a two-tailed alpha error of 0.05. Data are presented as means ±SD, medians, or proportions, as appropriate.

Table 1. Characteristics of the Study Population at Base Line.*

Characteristic	Intermittent Mandatory Ventilation (N = 29)	Pressure-Support Ventilation (N = 37)	Intermittent Spontaneous-Breathing Trials (N = 33)	Once-Daily Spontaneous-Breathing Trial (N = 31)
Age — yr	64.2±13.3	59.9±16.4	59.1±16.4	65.0±14.3
APACHE II score	20.8±7.0	18.9±7.6	20.1±6.8	18.3±6.6
Chronic obstructive pulmonary disease —no. (%)	8 (27.6)	18 (48.6)	12 (36.4)	14 (45.2)
Acute lung injury — no. (%)	19 (65.5)	17 (45.9)	18 (54.5)	14 (45.2)
Neurologic disorder — no. (%)	2 (6.9)	2 (5.4)	3 (9.1)	3 (9.7)
Ratio of PaO_2 to FiO_2	243.5±57.9	242.3±60.3	223.6±61.8	229.2±65.6
Maximal inspiratory pressure — cm of water	−25.9±11.9	−30.7±16.7	−31.4±18.7	−30.8±13.4
Tidal volume — ml/kg	5.3±0.9	6.6±1.7	5.2±1.8	7.4±2.1
Respiratory frequency — breaths/min	28.4±5.4	26.8±6.4	28.9±5.4	29.9±8.4
Duration of ventilator support before weaning begun — days	6.5±4.5†	10.8±8.6	11.5±7.4	8.4±5.3
Time to failure of 1st spontaneous-breathing trial — min	48.5±33.2	52.3±34.6	46.5±23.6	52.5±32.7

*Plus–minus values are means ±SD.

†P = 0.037 for the comparison with the other three groups.

Results

Of the 546 study patients, 416 (76.2 percent) successfully underwent a two-hour trial of spontaneous breathing, and 372 (89.4 percent) of them were immediately extubated. Of these 372 patients, 58 (15.6 percent) required reintubation within 48 hours. Extubation was postponed for 24 hours in 44 patients, primarily because of concern about their ability to maintain clear airways. These patients breathed through a T-tube circuit for up to 24 hours, but 16 (36.4 percent) required reinstitution of mechanical ventilation during this period. The remaining 28 (63.6 percent) were extubated within this 24-hour period, and only 2 required reintubation within the subsequent 48 hours.

One hundred thirty patients (23.8 percent) had signs of poor tolerance during the initial trial of spontaneous breathing, which lasted a mean (±SD) of 50.1±31.2 minutes (range, 5 to 110). These patients were randomly assigned to intermittent mandatory ventilation (29 patients), pressure-support ventilation (37), intermittent trials of spontaneous breathing (33) involving the use of a T-tube (27) or continuous positive airway pressure (6) interspersed with assist–control ventilation, or a once-daily trial of spontaneous breathing alternating with assist–control ventilation (31). The groups were similar with respect to the patients' characteristics, the indications for mechanical ventilation, and respiratory function; the only significant difference was in the duration of ventilatory support before weaning was begun, which was shorter in the patients who received intermittent mandatory ventilation than in the other groups (Table 1).

Kaplan–Meier plots of the probability of successful weaning with the use of each technique are shown in Figure 1, and the associated median times to successful extubation are listed (with first and third quartiles) in Table 2. Cox proportional-hazards regression analysis revealed four factors that predicted the time

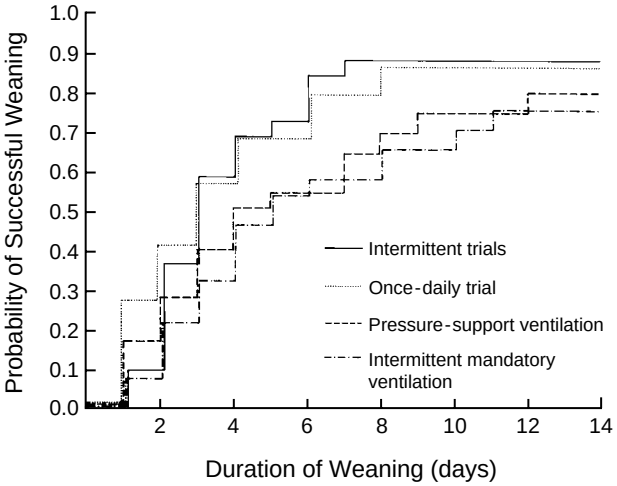

Figure 1. Kaplan–Meier Curves of the Probability of Successful Weaning with Intermittent Mandatory Ventilation, Pressure-Support Ventilation, Intermittent Trials of Spontaneous Breathing, and a Once-Daily Trial of Spontaneous Breathing.

After adjustment for base-line characteristics in a Cox proportional-hazards model, the rate of successful weaning with a once-daily trial of spontaneous breathing was 2.83 times higher than that with intermittent mandatory ventilation ($P<0.006$) and 2.05 times higher than that with pressure-support ventilation ($P<0.04$).

Table 2. The Length of Time from the Initiation of Weaning to Successful Extubation in the Four Groups.

Weaning Technique	Median	First Quartile	Third Quartile
		days	
Intermittent mandatory ventilation	5	3	11
Pressure-support ventilation	4	2	12
Intermittent trials of spontaneous breathing	3	2	6
Once-daily trial of spontaneous breathing	3	1	6

required for successful weaning: age ($P<0.02$), the duration of ventilatory support before weaning was begun ($P<0.005$), the time to the failure of the first trial of spontaneous breathing ($P<0.001$), and weaning technique (Table 3). The adjusted rate of successful weaning was higher with a once-daily trial of spontaneous breathing than with intermittent mandatory ventilation (rate ratio, 2.83; 95 percent confidence interval, 1.36 to 5.89; $P<0.006$) or pressure-support ventilation (rate ratio, 2.05; 95 percent confidence interval, 1.04 to 4.04; $P<0.04$) but not significantly different from that with intermittent trials of spontaneous breathing (rate ratio, 1.24; 95 percent confidence interval, 0.64 to 2.41; $P=0.54$). The adjusted rate of successful weaning with intermittent trials of spontaneous breathing was higher than that with intermittent mandatory ventilation (rate ratio, 2.28; 95 percent confidence interval, 1.11 to 4.68; $P=0.024$), but it was not significantly different from that with pressure-support ventilation (rate ratio, 1.66; 95 percent confidence interval, 0.87 to 3.16; $P=0.126$). The adjusted rate of successful weaning with pressure-support ventilation was not significantly different from that with intermittent mandatory ventilation (rate ratio, 1.38; 95 percent confidence interval, 0.68 to 2.79; $P=0.32$).

Table 3. Rate of Successful Weaning with the Various Techniques and According to Base-Line Characteristics.*

Variable	Relative Rate of Successful Weaning (95% Confidence Interval)	P Value
Weaning technique		
Once-daily trial of spontaneous breathing vs. intermittent mandatory ventilation	2.83 (1.36–5.89)	<0.006
Once-daily trial of spontaneous breathing vs. pressure-support ventilation	2.05 (1.04–4.04)	<0.04
Once-daily trial of spontaneous breathing vs. intermittent trials of spontaneous breathing	1.24 (0.64–2.41)	0.54
Duration of ventilator support before weaning begun (1-day increments)	0.94 (0.90–0.98)	<0.005
Time to failure of first trial of spontaneous breathing (10-min increments)	1.15 (1.07–1.24)	<0.001
Age (10-yr increments)	0.83 (0.71–0.96)	<0.02

*Proportional-hazards regression analysis was used to estimate the 95 percent confidence interval of the relative rate of successful weaning.

Table 4 lists outcomes for the various techniques. More patients in the group that received intermittent mandatory ventilation required continued ventilatory support on the 14th day than in the groups that received once-daily trials ($P=0.07$) or intermittent trials ($P=0.06$) of spontaneous breathing. The rates of extubation and reintubation did not significantly differ between the four groups.

Discussion

This study has two major findings. First, in a selected group of patients who were difficult to wean from mechanical ventilation, the rate of successful weaning depended on the technique employed: a once-daily trial of spontaneous breathing led to extubation about three times more quickly than intermittent mandatory ventilation and about twice as quickly as pressure-support ventilation. There was no significant difference in the rate of success between a once-daily trial and multiple daily trials of spontaneous breathing or between intermittent mandatory ventilation and pressure-support ventilation. Second, ventilator support was discontinued without any special weaning technique in two thirds of an unselected group of patients, and only a small proportion required reintubation within 48 hours.

Intermittent Mandatory Ventilation

Several advantages have been claimed for intermittent mandatory ventilation as a weaning technique: it is supposed to prevent a patient from "fighting" the ventilator, reduce respiratory-muscle fatigue, and expedite weaning.[4,13] However, there are few data to support these claims.[14] Intermittent mandatory ventilation is usually delivered in a synchronized manner with demand-valve circuitry, which increases the work of breathing.[14,15] The intermittent nature of assistance also poses a problem. It was previously assumed that the degree of respiratory-muscle rest was proportional to the level of machine assistance. However, recent evidence indicates that respiratory-sensor output does not adjust to breath-to-breath changes in respiratory load,[16,17] and intermittent mandatory ventilation may therefore contribute to the development of respiratory-muscle fatigue or prevent recovery from it.

Studies of the efficacy of intermittent mandatory ventilation in weaning have serious limitations. Schachter et al.[6] compared it with conventional ventilation and noted no difference between the two techniques in the duration of ventilator support. Their study suffers from a retrospective design, nonuniform study groups, and inadequate description of the protocol. Hastings et al.[7] compared trials of spontaneous breathing with intermittent mandatory ventilation at a fixed rate (4 breaths per minute) in patients in stable condition after cardiac surgery. The length of time to extubation was similar in

Table 4. Outcomes in Patients Who Were Difficult to Wean from Mechanical Ventilation.*

Weaning Technique	Successful Weaning and Extubation	Reintubation	Continued Mechanical Ventilation after 14 Days
		no. of patients (%)	
Intermittent mandatory ventilation	20 (69.0)	4 (13.8)	5 (17.2)
Pressure-support ventilation	23 (62.2)	7 (18.9)	4 (10.8)
Intermittent trials of spontaneous breathing	27 (81.8)	5 (15.2)	1 (3.0)
Once-daily trial of spontaneous breathing	22 (71.0)	7 (22.6)	1 (3.2)

*The percentages do not total 100 percent in the groups that received pressure-support ventilation and a once-daily trial of spontaneous breathing because one patient died in each group and weaning was interrupted because of an intercurrent illness in two patients in the pressure-support group.

the two groups — approximately 2.6 hours. Their study provides little insight, however, because 24 hours had already elapsed since the operation and the patients had good pulmonary function; thus, little difficulty in weaning was anticipated. In patients in stable condition who received ventilator support for 3.6 days, Tomlinson et al.[8] found that the duration of weaning was similar with spontaneous-breathing trials and intermittent mandatory ventilation — approximately 5.6 hours. This study was weighted toward patients who received short-term ventilatory support, and two thirds of those weaned within 2 hours were patients who received ventilatory support for less than 72 hours postoperatively.

In contrast, we studied difficult-to-wean patients who had received mechanical ventilation for 6.5±4.5 days. Although most patients could theoretically have met the extubation criteria within 24 hours of study entry, 17 percent were receiving ventilatory support after 14 days. Weaning took longer than in either of the trials of spontaneous breathing.[7,8] Despite the use of randomization, the patients in the group assigned to intermittent mandatory ventilation had received ventilation for a shorter time than the patients in the other groups. This actually resulted in a bias in their favor, since weaning was accomplished more rapidly in patients receiving short-term support.

Pressure-Support Ventilation

Pressure-support ventilation is commonly used to counteract the work of breathing imposed by endotracheal tubes and ventilator circuits. Theoretically, this should help with weaning, because a patient who is comfortable at the compensatory level of pressure support should be able to sustain ventilation after extubation. However, the level of pressure support necessary to eliminate the work imposed by endotracheal tubes and ventilator circuits varies considerably (from 3 to 14 cm of water)[18,19]; thus, any prediction of a patient's ability to sustain ventilation after extubation is likely to be misleading.

Brochard et al.[20] recently reported that the duration of weaning was significantly shorter with pressure support (5.7±3.7 days) than with intermittent mandatory ventilation (9.9±8.2 days) or trials of spontaneous breathing (8.5±8.3 days). In contrast, we found that weaning with pressure-support ventilation took longer than weaning with a once-daily trial of spontaneous breathing and was not superior to weaning with intermittent mandatory ventilation. We suspect that the apparent superiority of pressure support in the study by Brochard et al. was due to the constrained manner in which they used other techniques. Patients had to tolerate an intermittent mandatory ventilation rate of ≤4 breaths per minute for at least 24 hours before being extubated. This poses a considerable ventilatory challenge and is not the usual approach to this technique.[3,4,14,21] In contrast, we extubated patients when they tolerated a ventilator rate of five breaths per minute for two hours. In the study by Brochard et al., physicians could request up to three trials of spontaneous breathing over a 24-hour period, each lasting 2 hours, before deciding to extubate a patient. Again, this is a considerable ventilatory challenge — especially in patients who have already had difficulty in weaning. We consider the findings of their study and ours to be complementary. Both show that the pace of weaning depends on the manner in which a technique is employed. When intermittent mandatory ventilation and spontaneous-breathing trials are used in a constrained manner, weaning is slower than with pressure-support ventilation.[20] Weaning is expedited when a trial of spontaneous breathing is attempted once a day. In both studies, the results pertain to specific regimens for each weaning technique and cannot be extrapolated to other regimens using these techniques.

Trials of Spontaneous Breathing

Some physicians gradually increase the duration of spontaneous-breathing trials while reinstituting mechanical ventilation between trials. Other physicians go directly from offering a high level of ventilatory assistance to a trial of spontaneous breathing, and if the trial is successful, extubate the patient without any further weaning. In the present study, two thirds of the patients initially enrolled were extubated after their first trial of spontaneous breathing. A once-daily trial of spontaneous breathing also allowed speedier weaning than approaches offering partial ventilatory support. This approach simplifies management, since a patient's ability to breathe spontaneously without ventilatory support needs to be assessed only once a day. In contrast, with intermittent mandatory ventilation and pressure-support ventilation, ventilator settings must be adjusted repeatedly and each adjustment is usually followed by an arterial-blood gas measurement.

An implied goal of the various weaning techniques is to recondition respiratory muscles that may have been weakened during the period of mechanical ventilation. Theoretically, a once-daily trial of spontaneous breathing and a prolonged period of rest may be the most effective method of eliciting adaptive changes.[22,23] This

approach meets the three principal requirements of a conditioning program: overload, specificity, and reversibility.[22] During the trial, patients breathe against an elevated intrinsic load, thus satisfying the overload requirement. Specificity is also satisfied, in that the trial is an endurance stimulus and the desired objective is enhanced endurance. Finally, the use of a daily trial prevents regression of the adaptive changes. It must be emphasized that this reasoning is based on indirect evidence and that the effect of different weaning techniques on respiratory-muscle reconditioning has not been investigated.

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APPENDIX

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REFERENCES

1. Tobin MJ. Mechanical ventilation. N Engl J Med 1994;330:1056-61.
2. Esteban A, Alía I, Ibañez J, Benito S, Tobin MJ, Spanish Lung Failure Collaborative Group. Modes of mechanical ventilation and weaning: a national survey of Spanish hospitals. Chest 1994;106:1188-93.
3. Tobin MJ, Alex CG. Discontinuation of mechanical ventilation. In: Tobin MJ, ed. Principles and practice of mechanical ventilation. New York: McGraw-Hill, 1994:1177-206.
4. Downs JB, Klein EF Jr, Desautels D, Modell JH, Kirby RR. Intermittent mandatory ventilation: a new approach to weaning patients from mechanical ventilators. Chest 1973;64:331-5.
5. Brochard L. Pressure support ventilation. In: Tobin MJ, ed. Principles and practice of mechanical ventilation. New York: McGraw-Hill, 1994:239-57.
6. Schachter EN, Tucker D, Beck GJ. Does intermittent mandatory ventilation accelerate weaning? JAMA 1981;246:1210-4.
7. Hastings PR, Bushnell LS, Skillman JJ, Weintraub RM, Hedley-Whyte J. Cardiorespiratory dynamics during weaning with IMV versus spontaneous ventilation in good-risk cardiac-surgery patients. Anesthesiology 1980;53: 429-31.
8. Tomlinson JR, Miller KS, Lorch DG, Smith L, Reines HD, Sahn SA. A prospective comparison of IMV and T-piece weaning from mechanical ventilation. Chest 1989;96:348-52.
9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818-29.
10. Altman DG, Doré CJ. Randomisation and baseline comparisons in clinical trials. Lancet 1990;335:149-53.
11. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457-81.
12. Cox DR. Regression models and life-tables. J R Stat Soc [B] 1972;34:187-220.
13. Venus B, Smith RA, Mathru M. National survey of methods and criteria used for weaning from mechanical ventilation. Crit Care Med 1987;15:530-3.
14. Sassoon CSH. Intermittent mandatory ventilation. In: Tobin MJ, ed. Principles and practice of mechanical ventilation. New York: McGraw-Hill, 1994: 221-37.
15. Gibney RTN, Wilson RS, Pontoppidan H. Comparison of work of breathing on high gas flow and demand valve continuous positive airway pressure systems. Chest 1982;82:692-5.
16. Marini JJ, Smith TC, Lamb VJ. External work output and force generation during synchronized intermittent mandatory ventilation: effect of machine assistance on breathing effort. Am Rev Respir Dis 1988;138:1169-79.
17. Imsand C, Feihl F, Perret C, Fitting JW. Regulation of inspiratory neuromuscular output during synchronized intermittent mechanical ventilation. Anesthesiology 1994;80:13-22.
18. Brochard L, Rua F, Lorino H, Lemaire F, Harf A. Inspiratory pressure support compensates for the additional work of breathing caused by the endotracheal tube. Anesthesiology 1991;75:739-45.
19. Nathan SD, Ishaaya AM, Koerner SK, Belman MJ. Prediction of minimal pressure support during weaning from mechanical ventilation. Chest 1993; 103:1215-9.
20. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawing from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994;150:896-903.
21. Luce JM, Pierson DJ, Hudson LD. Intermittent mandatory ventilation. Chest 1981;79:678-85.
22. Faulkner JA. Structural and functional adaptations of skeletal muscle. In: Roussos C, Macklem PT, eds. The thorax. Part B. Vol. 29 of Lung biology in health and disease. New York: Marcel Dekker, 1985:1329-51.
23. Rochester DF. Does respiratory muscle rest relieve fatigue or incipient fatigue? Am Rev Respir Dis 1988;138:516-7.