<u>*CHAPTER 5*</u>

Noninvasive ventilation: modes of ventilation

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Principles

In theory, noninvasive ventilation (NIV) can be delivered using similar modalities to those used with an endotracheal tube or a tracheotomy cannula [1]. In reality, because the circumstances of ventilation are different, the population of patients more circumscribed, and the equipment available is often more limited with NIV, this is not the case. In addition, leaks are virtually a constant feature of NIV [2]. NIV is usually delivered in the form of assisted ventilation where every breath is supported by the ventilator. Rarely, controlled mechanical ventilation is used. Two types of breaths can be used, either volume targeted or pressure-targeted.

With volume targeted breaths, a predetermined tidal volume is delivered, usually with a set peak-flow rate and a controlled flow wave shape, over a fixed inspiratory time. Unfortunately, some of the "old" generation ventilators (especially those designed for home ventilation or for anaesthesia), did not have sufficient internal power to cope with external impedance, and had to lengthen their inspiratory time to deliver the set volume, if they could not maintain flow. With modern ventilators, peak-flow setting is an important feature that is maintained in all circumstances. This is true both of "intensive care" ventilators and for many "turbine" ventilators offering a volume controlled mode. In the case of leaks, the delivered volume is reduced, with no adaptation by the ventilator.

For pressure-targeted breaths, the ventilator maintains a constant preset pressure after the breath has been triggered by the patient, and stops when the flow decreases to a given threshold (pressure support ventilation (PSV)) which is supposed to indicate the end of the patient's effort, or after a fixed, preset inspiratory time (assist pressure control). In all cases, a sudden increase in pressure can stop the ventilator assist. There are several potential advantages in using a pressure targeted mode of ventilation during NIV: 1) in the case of leaks, the preset pressure is maintained, which facilitates achieving an appropriate delivered volume; 2) because the pressure is limited to the mask, the likelihood of leaks and of side effects is reduced; 3) synchrony between the patient and the ventilator is usually good, since these modes have been primarily designed to facilitate the patient's effort to breathe; 4) the combination of PSV and positive end-expiratory pressure (PEEP) has been shown to be very efficient in reducing the work and effort of breathing [3].

Triggering

Because "assisted" ventilation is the primary mode of ventilation used during NIV, the ventilator has to recognize the beginning of an inspiratory effort. This is the role of the

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"triggering function" of the ventilator. Classically, two types of trigger were proposed [4]. The first type is based on a drop in the proximal airway pressure signal and requires a closed circuit, against which the patient tries to inspire. This negative deflection indicates that the inspiratory effort has started, and therefore, opens a "demand-valve" when a preset threshold has been reached. The amplitude of the drop in airway pressure is a function of the preset "sensitivity" but also of the patient's respiratory drive. The higher the drive (and the occlusion pressure or $P_{0.1}$ for instance) the more negative the drop is [5]. The time after which this valve opens is a function of the valve itself (and more generally of the whole electronic/pneumatic circuit), and of the sensitivity setting, it is inversely proportional to the patient's respiratory drive. The higher the drive, the shorter the time delay. Therefore, for a given setting, the effort necessary to trigger the ventilator does not really vary with the patient's drive, since pressure and time go in opposite directions [6].

The other systems are based on the detection of an inspiratory flow from the patient, usually in the presence of a constant and continuous flow washing the expiratory circuit. Because leaks may mimic this "inspiratory flow", some ventilators try to compensate for the estimated leaks. The sensitivity may be an important setting to avoid autocycling.

In mechanically ventilated patients in the intensive care unit (ICU), several studies have shown that the effort required from the patient to trigger the ventilator is less with flow-triggering systems than with pressure-triggering systems [7, 8, 9]. This has also been shown specifically with NIV [10]. The differences observed in work of breathing result from the reduction of the part of effort due to the triggering phase and also to a small reduction in intrinsic PEEP (PEEPi) sometimes observed with flow-triggering systems. The overall difference in effort is of small magnitude, however, and can be totally offset by inadequate settings of the assistance itself, for instance [9].

In addition, leaks may create specific problems, which differ with each system (fig. 1). In case of external PEEP and leaks, the pressure falls in a pressure-triggering system, and this drop triggers a new breath. In the case of a flow-triggering system, the PEEP level is maintained but autocycling may still be present. Decreasing the flow sensitivity setting, *i.e.* increasing the flow threshold, may then allow the maintenance of PEEP and avoid autocycling. Although this phenomenon may be difficult to detect clinically, it may have important consequences. This is a potential advantage of flow-triggering systems.

Positive end-expiratory pressure

PEEP, traditionally used to improve oxygenation and increase lung volume in case of hypoxaemic respiratory failure, is now widely used in patients with chronic lung disease or with sleep apnoea syndrome, to counteract PEEPi in the first case, and to maintain airway patency in the latter. Another indirect reason for the use of PEEP is the need for small turbine ventilators, especially designed for NIV, to maintain a sufficient flow rate during expiration to wash the circuit of expired gas. At a low PEEP level, carbon dioxide (CO_2) rebreathing has been shown to occur in ventilators with no expiratory valve [11, 12, 13].

The main indication for using PEEP is to minimize the effort required to counterbalance PEEPi. In other words, this allows the ventilator to detect the beginning of inspiration much nearer the beginning of the inspiratory effort. Indeed, the time delay induced by the presence of PEEPi to reverse expiratory flow may be as long as 300–400 ms [5], and may thus represent up to 40–60% of the total effort [14]. The use of small levels of PEEP is usually beneficial in reducing this part of the effort [15, 16].

Ideally, this setting should be titrated, based on the real PEEPi of the patient. This

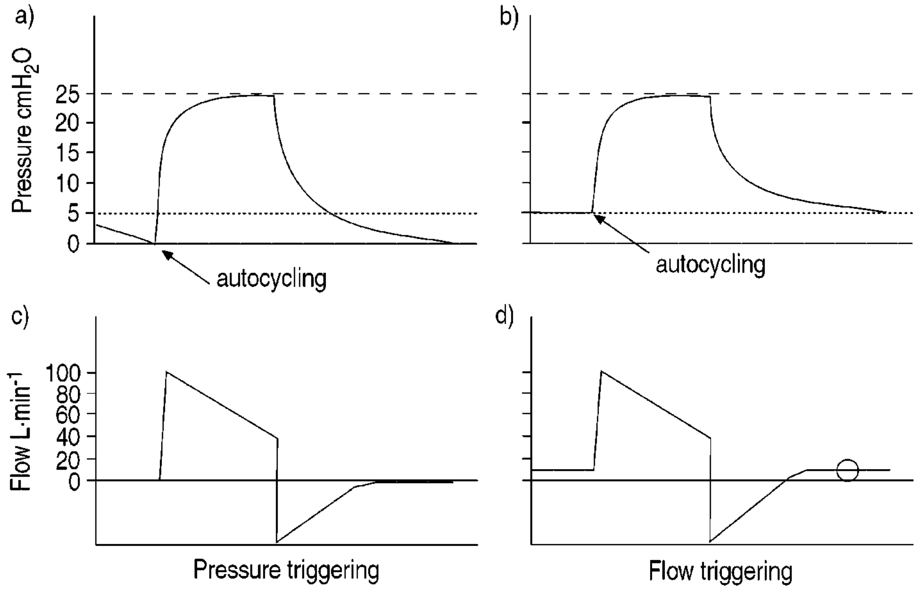

Fig. 1. – Tracings of pressure and flow showing autocycling during pressure triggering (a and c) and during flow triggering (b and d), during pressure support ventilation (PSV) and peak end-expiratory pressure (PEEP). PEEP is only maintained in the latter case. The circle indicates the flow coming from the ventilator, which compensates the expiratory leakage flow and allows for PEEP maintenance. Decreasing the sensitivity solves the problem only in case of flow triggering. In both cases, note that the pressure drop due to the patient's effort does not precede the assisted breath at the beginning of the cycle. Also, in both cases, the presence of leaks can be detected visually by the large difference between the inspiratory and the expiratory flow and volume. – – – –: set PSV; ··········: set PEEP; ————: zero-flow.

value, however, cannot be obtained easily and reliably during NIV, and an empirical setting of a low PEEP ($\leqslant 5$ cmH_2O) can be recommended; this should be kept low, firstly, because dynamic PEEPi in chronic obstructive pulmonary disease (COPD) patients rarely exceeds this range of values (0–5) and, secondly, because the higher the PEEP level, the greater the likelihood of leaks, autocycling and dysynchrony. Excellent clinical results have also been obtained without the use of PEEP [17].

Volume controlled ventilation

Volume controlled ventilation can be used successfully both in acute respiratory failure and in home ventilation. It is frequently recommended to set tidal volume higher than usual, to compensate for possible leaks (12–14 $mL \cdot kg^{-1}$). In "invasively" ventilated patients, much attention has been paid to the importance of the peak-flow setting in relieving the patient's dyspnoea and reducing effort [18–20]. It is surprising to see that volume controlled ventilation has been used frequently for NIV with little attention paid to the importance of this setting, often with ventilators unable to provide an adjustable peak-flow setting. A sufficient peak-flow rate is essential to decrease patient's inspiratory effort, and peak-flows >45–60 $L \cdot min^{-1}$ are recommended in intubated patients. Excessive peak-flow rates, however, also have adverse effects as they can increase the sense of dyspnoea (the patient receives "too much air") [21]. By reducing inspiratory time, *e.g.* <1 s, the patient's spontaneous frequency may increase which tends to favour respiratory alkalosis [22]. During NIV, this setting may cause more difficulties, as peak mask pressure will vary significantly. A high peak flow required for the patient's comfort may result in a high peak mask pressure and leaks.

Excellent clinical results have been obtained using volume controlled ventilation in several series [23], although it may have been one factor producing poor tolerance in other series.

Pressure targeted modes

PSV associated with PEEP is certainly the most widely used mode of support during NIV. Many small turbine ventilators are specifically designed for NIV and deliver bilevel pressure support assistance. Their performances are generally good and sometimes better than ICU ventilators [12, 24, 25]. Pressure support is usually delivered with swings of pressure above baseline ranging 8–20 or 25 cmH_2O. The setting depends on patient's tolerance and on its efficiency in terms of delivered volume and respiratory frequency. In acute respiratory failure, pressures of 8–12 cmH_2O are often insufficient to substantially improve alveolar ventilation [26].

PSV can be delivered with a different ramp of pressures or rate of rise. A "slow" rate is usually inadequate and results in an increased work of breathing because of the delayed delivery of the support [27]. A setting close to maximum may often be useful. The more rapid rise, however, may result in short breaths and low tidal volumes because of premature termination of the breaths.

One specific problem with PSV concerns the termination of the breath in the presence of leaks. Leaks may induce major dysynchrony, but several features are available to solve the problem [28]. To recognize the end of the inspiratory effort and stop the inspiratory assist, the ventilator usually waits until the decelerating flow has fallen to a preset value.

Frequently the amount of leak during inspiration (and high pressures) is such that the leak flow exceeds this threshold, thus impeding the recognition of the end of inspiration. This results in prolonged inspiration, only terminated by the maximum inspiratory time limit or the volume limit when available. This phenomenon probably occurs very frequently during NIV and can be poorly tolerated by the patient. Once the problem is recognized (and still observed after adjustment of the mask), several strategies can be used to solve the problem (fig. 2). One is the adjustment of the expiratory sensitivity setting. The flow threshold can be set above the leak flow rate (fig. 2). This may require the use of expiratory flow sensitivity settings >30–40% of the peak-flow rate. Another approach is to use a time criterion to terminate the breath [28]. This can be done by limiting the inspiratory time during pressure-support ventilation to a value close to 1 s, or by switching to assist pressure controlled ventilation where every breath will have the same duration.

Before employing these strategies, a small reduction in peak pressure (by reducing pressure support or PEEP) may also eliminate dysynchrony by reducing leaks.

Negative pressure ventilation

Negative pressure ventilators act by exposing the surface of the chest wall to subatmospheric pressure during inspiration. During negative pressure ventilation, tidal volume is related to peak inspiratory negative pressure and the pressure waveform generated by the ventilator pump; for the same peak of negative pressure a square wave produces a greater tidal volume than a half sine wave. Although this form of ventilation may have a potential therapeutic role in the treatment of acute on chronic respiratory

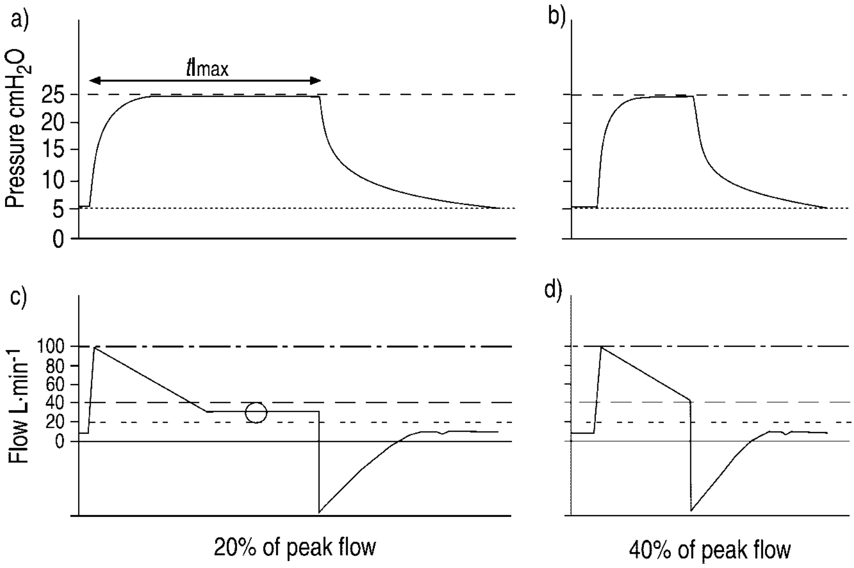

Fig. 2. – Tracings of pressure of flow during pressure support ventilation (PSV) and peak end-expiratory pressure (PEEP), with leaks at the end of inspiration inducing an abnormally long inspiration terminated only when the maximum inspiratory time (*t*Imax) is reached (a and c). Increasing the expiratory flow sensitivity threshold allows the ventilator to terminate the breath despite the leaks (b and d). The circle indicates the inspiratory leakage flow. – – – –: set PSV; ···········: set PEEP; ————: zero-flow; – - – - –: peak inspiratory flow; — — — —: expiratory flow, sensitivity set at 40% of peak flow; - - - - - - : expiratory flow, sensitivity set at 20% of peak flow.

failure in patients with COPD by reducing the need for endotracheal intubation, its use is limited by the cumbersome nature of the apparatus, and the fact that very few centres are equipped with the apparatus. This form of support has been used with good outcomes as a first-line treatment in COPD patients with severe acute respiratory failure and hypoxic hypercapnic coma [29]. A case control study has shown similar results to patients treated with invasive mechanical ventilation [30].

Proportional assist ventilation

Proportional assist ventilation is the only mode of ventilation which has been designed using physiology principles, where the technical solutions offered by ventilators did not come first [31]. There is no setting of volume, pressure or frequency available on the ventilator, since the patient keeps full control of the breathing pattern. The ventilator assists the patient's respiration by providing a specific assist to the resistive and the elastic components of the effort. Based on an analysis of patient's flow and volume, the ventilator provides immediate amplification of this effort by increasing flow by a given amount (flow or resistive assist) and volume by a second gain (volume or elastic assist). A maximum support is provided when these gains equal the resistance and the elastance of the patient, obviating the effort contributed by the patient.

One obvious problem is to set the gains properly and not to "overassist" the patient, which induces high volumes, high pressures and discomfort for the patient.

The great potential advantage of this mode is its adaptation to patient's breathing pattern both in terms of immediate variability and in terms of ventilatory demand over time [32–34].

In the case of NIV, two drawbacks may limit its use. First, measurements of respiratory mechanics, are theoretically needed to adjust the ventilator, and are difficult to obtain in the context of NIV. The solutions adopted for each type of assist are usually different [34, 35]. The elastic assist is usually determined by gradually increasing the gain, until overassistance occurs with excessive volumes and pressures. The gain is then set lower, such as 60% or 80% of the maximum. The resistive assist is determined by empirical values of the patient's resistance, or by looking for optimal comfort with different peak flows. It is surprising to see that, using this latter approach, the authors found values of resistive assist much lower than predicted. This may be related to the second specific problem of this mode during NIV leaks. Leaks from the mask will be measured as patient effort by the ventilator, and assisted accordingly. This may necessitate a marked lowering of the assistance. Clinical experience so far seems to indicate that excellent results can be obtained with this mode, however, provided that close monitoring is performed and that specific training has been provided [36].

Comparison of modes

A few comparative studies have been performed regarding the specific efficacy of different modes of ventilation during NIV.

MEECHAM JONES *et al.* [37] compared pressure and volume controlled modes in COPD patients and found that arterial blood gases were similar with the different modes of ventilation, but with little effect on carbon dioxide tension in arterial blood ($P\mathrm{a,CO_2}$).

VITACCA *et al.* [38] performed the only clinical randomized trial comparing pressure support and assist control ventilation in a group of 30 patients. No real difference in efficacy could be observed between the two techniques and both modes provided a significant reduction in the rate of endotracheal intubation compared to an historical control group. They found, however, that clinical tolerance was better with PSV, with fewer side effects. This is probably explained by the limitation in the peak mask pressure.

GIRAULT *et al.* [39] have performed an interesting physiological study showing that work of breathing is reduced to a greater extent with assist control compared to pressure support [39]. This is probably explained, however, by the higher amount of pressure provided with assist control. Interestingly the comfort of the patient was significantly better with pressure support than with assist control. This probably indicates that the patients tolerate a pressure targeted mode better, but also that it is prudent not to hyperventilate the patients.

In a study focusing particularly on types of mask, NAVALESI *et al.* [40] did not find any effects related to the mode of ventilation on comfort and arterial blood gases.

Proportional assist ventilation and pressure support have been compared in a few physiological and clinical studies. Proportional-assist ventilation may offer short-term physiological advantages in terms of adaptation to mechanical loads, although this result has not been consistently found in all studies. A first clinical trial found no difference in term of efficacy between the two modes.

Monitoring

Whatever the mode used, it is important to stress that the efficacy of noninvasive ventilation will depend essentially on the ability of the ventilatory assist to increase alveolar ventilation [41]. This depends on the adaptation of the patient to the assistance and on the amount of leaks. The most important parameter to be monitored is the expired tidal volume. Although an adequate ventilation is often achieved with a combination of positive end-expiratory pressure and pressure support, different settings may be used to obtain a better exhaled tidal volume, and other modes might be tried when these objectives are not met.

Summary

In theory, noninvasive ventilation (NIV) could be delivered with similar modalities than through an endotracheal tube or a tracheostomy cannula. In practice, controlled mechanical ventilation is rarely used, and two types of breaths are used during assisted forms of ventilation, either volume targeted or pressure targeted. The combination of pressure support ventilation and a positive end-expiratory pressure is by far the most commonly used mode of ventilation. Its efficacy is supported by physiological and clinical studies. Pressure support is usually delivered with swings of pressure above baseline ranging from 8–20 or 25 cmH_2O. The setting depends on patient's tolerance and on its efficiency in terms of delivered volume and respiratory frequency. There are a number of problems and limitations which can be encountered with this modality, however, and other modalities can also work efficiently such as pressure support with no expiratory pressure, assist pressure controlled ventilation and assist volume controlled ventilation. Comparisons between modes are scarce. Leaks around the mask can markedly decrease the efficacy of all modes but to various extents. With pressure support ventilation, leaks can mislead the expiratory trigger mechanism and cause major asynchrony at the end of inspiration. New modalities like proportional assist ventilation have been recently proposed, and interesting physiological results have been reported suggesting a similar efficacy than pressure support ventilation, but with a possible improvement in comfort. In all cases, a sensitive trigger system is essential, but users must be aware of the risks of autocycling with leaks. Monitoring of leaks and expired tidal volume may be important.

Keywords: Assist control ventilation, positive end-expiratory pressure, pressure controlled ventilation, pressure support ventilation, trigger.

References

1. Hill NS. Non invasive ventilation. Does it work, for whom and how? *Am Rev Respir Dis* 1993; 147: 1050–1055.
2. Carrey Z, Gottfried SB, Levy RD. Ventilatory muscle support in respiratory failure with nasal positive pressure ventilation. *Chest* 1990; 97: 150–158.
3. Appendini LA, Patessio S, Zanaboni M, *et al.* Physiologic effects of positive end-expiratory pressure and mask pressure support during exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1994; 149: 1069–1076.
4. Aslanian P, Brochard I. Work of breathing during assisted modes of ventilation. *Curr Opin in Crit Care* 1997; 3: 38–42.
5. Conti G, Cinnella G, Barboni E, Lemaire F, Harf A, Brochard L. Estimation of occlusion pressure during assisted ventilation in patients with intrinsic PEEP. *Am J Respir Crit Care Med* 1996; 154: 907–912.

6. Leung PA, Jubran A, Tobin M. Comparison of assisted ventilator modes on triggering, patient effort and dyspnea. *Am J Respir Crit Care Med* 1997; 155: 1940–1948.
7. Sassoon CSH, Light RW, Lodia R, Sieck GC, Mahutte CK. Pressure-time product during continuous positive airway pressure, pressure support ventilation and T-piece during weaning from mechanical ventilation. *Am Rev Respir Dis* 1991; 143: 459–475.
8. Giuliani R, Mascia L, Recchia F, Caracciolo A, Fiore T, Ranieri VM. Patient-ventilator interaction during synchronized intermittent mandatory ventilation. *Am J Respir Crit Care Med* 1995; 151: 1–9.
9. Aslanian P, El Atrous S, Isabey D, *et al.* Effects of flow triggering on breathing effort during partial ventilatory support. *Am J Respir Crit Care Med* 1998; 157: 135–143.
10. Nava S, Ambrosino N, Bruschi C, Confalonieri M, Rampulla C. Physiological effects of flow and pressure triggering during non-invasive mechanical ventilation in patients with chronic obstructive pulmonary disease. *Thorax* 1997; 52: 249–254.
11. Ferguson GT, Gilmartin M. CO_2 rebreathing during BiPAP ventilatory assistance. *Am J Respir Crit Care Med* 1995; 151: 1126–1135.
12. Lofaso F, Brochard L, Hang T, Touchard D, Harf A, Isabey D. Evaluation of carbon dioxide rebreathing during pressure support with BiPAP devices. *Chest* 1995; 108: 772–778.
13. Lofaso F, Brochard L, Hang T, Lorino H, Harf A, Isabey D. Home *vs* intensive-care pressure support devices: experimental and clinical comparison. *Am J Respir Crit Care Med* 1996; 153: 1591–1599.
14. Coussa ML, Guérin C, Eissa NT, *et al.* Partitioning of work of breathing in mechanically ventilated COPD patients. *J Appl Physiol* 1993; 75: 1711–1719.
15. Petrof BJ, Legaré M, Goldberg P, Milic-Emili J, Gottfried SB. Continuous positive airway pressure reduces work of breathing and dyspnea during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease (COPD). *Am Rev Respir Dis* 1990; 141 281–289.
16. Smith TC, Marini JJ. Impact of PEEP on lung mechanics and work of breathing in severe airflow obstruction. *J Appl Physiol* 1988; 65: 1488–1499.
17. Brochard L, Mancebo J, Wysocki M, *et al.* Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995; 333: 817–822.
18. Marini JJ, Rodriguez RM, Lamb V. The inspiratory workload of patient-initiated mechanical ventilation. *Am Rev Respir Dis* 1986; 134: 902–909.
19. Ward ME, Corbeil C, Gibbons W, Newman S, Macklem PT. Optimization of respiratory muscle relaxation during mechanical ventilation. *Anesthesiology* 1988; 69: 29–35.
20. Cinnella G, Conti G, Lofaso F, *et al.* Effects of assisted ventilation on the work of breathing: volume-controlled *versus* pressure-controlled ventilation. *Am J Respir Crit Care Med* 1996; 153: 1025–1033.
21. Manning HL, Molinary EJ, Leiter JC. Effect of inspiratory flow rate on respiratory sensation and pattern of breathing. *Am J Respir Crit Care Med* 1995; 151: 751–757.
22. Parthasarathy S, Jubran A, Tobin MJ. Assessment of neural inspiratory time in ventilator-supported patients. *Am J Respir Crit Care Med* 2000; 162: 546–552.
23. Bott J, Carroll MP, Conway JH, *et al.* Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet* 1993; 341: 1555–1557.
24. Bunburaphong T, Imanaka H, Nishimura M, Hess D, Kacmarek RM. Performance characteristic of bilevel pressure ventilators: a lung model study. *Chest* 1997; 111: 1050–1060.
25. Lofaso F, Aslanian P, Richard JC, *et al.* Expiratory valves used for home devices: experimental and clinical comparison. *Eur Respir J* 1998; 11: 1382–1388.
26. Brochard L, Isabey D, Piquet J, *et al.* Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med* 1990; 323: 1523–1530.
27. Bonmarchand G, Chevron V, Chopin C, *et al.* Increased initial flow rate reduces inspiratory work of breathing during pressure support ventilation in patients with exacerbation of chronic obstructive pulmonary disease. *Intensive Care Med* 1996; 22: 1147–1154.

28. Calderini E, Confalonieri M, Puccio G, Francavilla N, Stella L, Gregoretti C. Patient-ventilator asynchrony during noninvasive ventilation: the role of expiratory trigger. *Intensive Care Med* 1999; 25: 662–667.
29. Corrado A, Gorini M, Villella G, De Paola E. Negative pressure ventilation in the treatment of acute respiratory failure: an old noninvasive technique reconsidered. *Eur Respir J* 1996; 9: 1531–1544.
30. Corrado A, Gorini M, Ginanni R, *et al.* Negative pressure ventilation *versus* conventional mechanical ventilation in the treatment of acute respiratory failure in COPD patients. *Eur Respir J* 1998; 12: 519–525.
31. Younes M. Proportional assist ventilation, a new approach to ventilatory support. I Theory. *Am Rev Respir Dis* 1992; 145: 114–120.
32. Ranieri V, Giuliani R, Mascia L, *et al.* Patient-ventilator interaction during acute hypercapnia: pressure support *vs.* proportional assist ventilation. *J Appl Physiol* 1996; 81: 426–436.
33. Grasso S, Puntillo F, Mascia L, *et al.* Compensation for increase in respiratory workload during mechanical ventilation. Pressure-support *versus* proportional-assist ventilation. *Am J Respir Crit Care Med* 2000; 161: 819–826.
34. Vitacca M, Clini E, Pagani M, Bianchi L, Rossi A, Ambrosino N. Physiologic effects of early administered mask proportional assist ventilation in patients with chronic obstructive pulmonary disease and acute respiratory failure. *Crit Care Med* 2000; 28: 1791–1797.
35. Ambrosino N, Vitacca M, Polese G, Pagani M, Foglio K, Rossi A. Short-term effects of nasal proportional assist ventilation in patients with chronic hypercapnic respiratory insufficiency. *Eur Respir J* 1997; 10: 2829–2834.
36. Patrick W, Webster K, Ludwig L, Roberts D, Wiebe P, Younes M. Noninvasive positive-pressure ventilation in acute respiratory distress without prior chronic respiratory failure. *Am J Respir Crit Care Med* 1996; 153: 1005–1011.
37. Meecham Jones DJ, Paul EA, Grahame-Clarke C, Wedzicha JA. Nasal ventilation in acute exacerbations of chronic obstructive pulmonary disease: effect of ventilator mode on arterial blood gas tensions. *Thorax* 1994; 49: 1222–1224.
38. Vitacca M, Rubini F, Foglio K, Scalvani S, Nava S, Ambrosino N. Noninvasive modalities of positive pressure ventilation improve the outcome of acute exacerbations in COLD patients. *Intens Care Med* 1993; 19: 450–455.
39. Girault C, Richard JC, Chevron V, *et al.* Comparative physiologic effects of noninvasive assist-control and pressure support ventilation in acute hypercapnic respiratory failure. *Chest* 1997; 111: 1639–1648.
40. Navalesi P, Fanfulla F, Frigerio P, Gregoretti C, Nava S. Physiologic evaluation of noninvasive mechanical ventilation delivered with three types of mask in patients with chronic hypercapnic respiratory failure. *Crit Care Med* 2000; 28: 1785–1790.
41. Brochard L. What is really important to make noninvasive ventilator work. *Crit Care Med* 2000; 28: 2139–2140.