The Control of Breathing During Mechanical Ventilation

Magdy Younes, MD, FRCPC, PhD[a,*], Laurent Brochard, MD[b,c]

KEYWORDS

• Patient–ventilator interactions • Inspiratory time • Respiratory time constant

KEY POINTS

- Nonsynchrony between patients and ventilators is very common.
- Nonsynchrony takes different forms that vary with the ventilator mode, the mechanical properties of the respiratory system, the level of consciousness, the level of respiratory muscle effort, and the undistressed respiratory rate of the patient.
- Poor patient–ventilator interaction can result in serious complications that may adversely affect the outcome.

INTRODUCTION

The respiratory system of patients on mechanical ventilation (MV) is uniquely challenged; a single gas exchange system (the lungs) is controlled by 2 different pumps that interact in complex ways, depending on the ventilator mode, the mechanical properties of the respiratory system, and the level of consciousness. At one extreme, these interactions result in an ideal outcome: gas exchange is maintained at acceptable levels without distress and without inducing lung damage or diaphragmatic atrophy or injury. At the other extreme, the interaction may be associated with severe abnormalities in gas exchange, distress, lung injury, and/or diaphragm atrophy or injury. These complications adversely affect clinical outcome. Hence, it is critical that clinicians learn how to identify and respond to these abnormal interactions. Because of space limitation, only a brief overview of the complex mechanisms involved can be given. Interested readers can refer to several reviews for more detail.[1–13]

PHYSIOLOGIC PRINCIPLES UNDERLYING PATIENT–VENTILATOR INTERACTIONS

The Patient's Control System

The respiratory control system consists of respiratory centers in the brain stem; efferent pathways (spinal tracts and respiratory nerves), which transfer instructions from the centers to pump muscles; the thorax, which performs gas exchange and contains the pump muscles; and afferent sensory pathways, which inform the centers about the adequacy of gas exchange (chemoreceptors), the state of lung inflation (mechanoreceptors), and the presence of pathologic conditions in the lungs

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[a] Department of Medicine, University of Manitoba, 1001 Wellington Crescent, Winnipeg, Manitoba R3M0A7, Canada; [b] Medical and Surgical Intensive Care Unit, Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, 209 Victoria Street, 4th Floor, Room 4-079, Toronto, Ontario M5B 1T8, Canada; [c] Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada
* Corresponding author.
E-mail address: mkyounes@shaw.ca

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(nociceptors). In addition, this basic control system is subject to the influence of higher centers that, when the patient is conscious, provide additional inputs to the respiratory centers that can alter breathing in response to anxiety, excessive effort, pain, and other disturbances. The following features are particularly relevant to responses of the control system during MV (further discussion on this topic is provided in Update on Chemoreception: Influence on Cardiorespiratory Regulation and Patho-Physiology).

Mechanical properties of the thorax

The mechanical properties of the thorax underlie almost all abnormal interactions with ventilators. Gas exchange requires cyclic expansion and emptying of the thorax. This is achieved through cyclic activity of pump muscles and, during MV, cyclic changes in airway pressure. Clearly, tidal volume (V_T) and frequency are related to amplitude and frequency of the applied pressure. However, for any given amplitude of applied pressure V_T and flow-rate depend highly on the resistance and compliance of the thorax. Although also relevant during inhalation (see Pressure Support Ventilation section), it is simpler to illustrate their operation during exhalation:

Once inflated, the thorax must exhale what went in during inspiration before the next inspiration. Rate of emptying is primarily related to resistance and compliance of the respiratory system. It is intuitively obvious that for a given end-inspiratory volume (ie, peak alveolar pressure) rate of emptying is slower if airway resistance is higher. Likewise, for a given peak alveolar pressure at end inspiration, lung volume is higher if compliance is higher. Thus, more time is required to exhale this larger volume.

Without expiratory muscle activity to force air out at a faster speed, rate of emptying is a function of the product (resistance * (or x) compliance), generally referred to as the respiratory time constant. Because compliance units are in liters per centimeter of water (cmH_2O) and resistance units are in cmH_2O per liter per second, the product of the 2 has units of time. For a normal compliance of 0.1 L/cmH_2O and normal resistance of 5.0 $cmH_2O/L/s$, the time constant is 0.5 second. This means that volume and flow will reach one-third of their peak values at 0.5 second into exhalation and one-third of the latter values (ie, one-ninth of peak values) at 1.0 seconds, and so forth (**Fig. 1**). The thorax can, therefore, return to functional residual capacity (FRC) well within the normal expiratory time. However, if resistance is 12 $cmH_2O/L/s$, the time constant is 0.1 $\times$ 12, or 1.2 seconds. Three seconds are needed to reach FRC. This expiratory time may not be available. The next inspiration would then begin before FRC is reached, resulting in what is called dynamic hyperinflation (DH). Slow emptying is responsible for many of the poor patient–ventilator interactions. By contrast, when the time constant is short (stiff lungs or relatively normal resistance), the lungs may respond too rapidly to the applied pressure, resulting in different abnormal interactions (see Control of Breathing with Different Ventilator Modes section).

The respiratory control system consists of respiratory centers in the brain stem; efferent pathways (spinal tracts and respiratory nerves), which transfer instructions from the centers to pump muscles; the thorax, which performs gas exchange and contains the pump muscles; and afferent sensory pathways, which inform the centers about the adequacy of gas exchange (chemoreceptors), the state of lung inflation (mechanoreceptors), and the presence of pathologic conditions in the lungs (nociceptors).

Influence of higher centers Control of breathing during MV can differ substantially between wakefulness and sleep or obtundation. In sleeping or obtunded patient, control is dominated by chemoreceptors' feedback. Chemoreceptors' input increases whenever ventilation is inadequate (increasing P_{aCO_2}), resulting in greater inspiratory efforts and V_T. In addition, above a threshold chemical drive, the respiratory rate (RR) also increases. These responses moderate the increase in P_{aCO_2}. With overventilation, chemoreceptors' output decreases. Amplitude of respiratory efforts decrease but, unlike the case with hypercapnia, the RR does not decrease until a certain P_{aCO_2}, which is only slightly below normal P_{aCO_2}, is reached (apneic threshold). At this point, respiratory efforts suddenly cease completely (central apnea). Apnea continues until P_{aCO_2} increases above the apneic threshold again. Thus, unless the ventilator responds to the weaker efforts by lowering applied pressure, overventilation continues until P_{aCO_2} decreases below the apneic threshold and the patient then develops recurrent central apneas (see also Update on Chemoreception: Influence on Cardiorespiratory Regulation and Patho-Physiology and Pathogenesis of Obstructive Sleep Apnea).

During wakefulness, higher centers may alter this homeostatic response in 2 ways:

1. Respiratory efforts no longer cease when P_{aCO_2} decreases below the apneic threshold. Thus, the mechanism by which chemical control

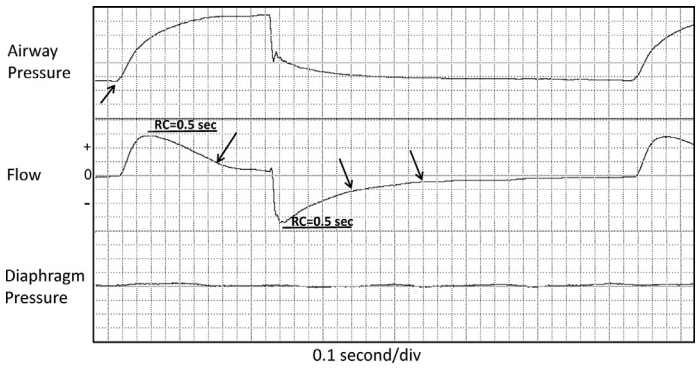

Fig. 1. Time course of flow during inspiration during pressure support ventilation with minimal inspiratory effort. Note the minimal triggering effort in airway pressure (*up arrow*) and minimal inspiratory deflection in diaphragm pressure. The patient's time constant is 0.5 second. Flow decreases to one-third of its peak value with each elapsed time constant (*down arrows*), both in inspiration and expiration. div, division.

Tau=The time in which a physical system's response to a step-wise change in an external variable reaches approximately 63% of its final (asymptotic) value.

prevents severe hypocapnia (apnea) no longer operates and $Paco_2$ can decrease to very low levels.

2. Behavioral responses intrude into the control system. Typically, events are not perceived unless they are different from what is expected or desired. For example, the brain expects lung volume to increase when inspiratory muscle activity is ramping up during inspiration, and vice versa. Any deviation from this expected behavior, such as failure of the ventilator to trigger at the onset of inspiratory effort or to cycle-off when effort ends, is rapidly sensed and triggers defensive responses. These defensive responses are highly unpredictable and range from increasing efforts and use of expiratory muscles to entrain the ventilator to inspiratory efforts, to acquiescing to the ventilator and making only triggering efforts. The impact of these abnormal sensations on mood and sleep should also not be underestimated.

Determinants of desired breathing pattern

Breathing pattern is determined by the RR and the ventilation required to satisfy ventilatory demands. V_T is a dependent variable and is adjusted via chemical feedback to provide the required ventilation at the prevailing RR. There is a tendency in intensive care unit (ICU) medicine to equate a high RR with distress. Although the RR tends to increase when ventilatory demands are high, a high RR does not necessarily denote distress or high demand. The RR varies from 5 to 25 per minute in perfectly normal subjects. Adjustments to this basic (undistressed) RR are made in response to disease, body temperature, and emotional factors. An important difference between a high RR due to distress and one that is not, is whether the RR decreases if the ventilator assist is increased. If it does not, it can be assumed that it is not distress related.

An important feature of the patient's control system is that ventilation and V_T vary considerably as the control system responds to changes in metabolic rate (eg, related to muscle activity), changes in higher centers' activity (eg, sleep, anxiety), fluctuation in blood gas tensions or blood pressure, and so forth. These fluctuations can be large and may occur over short (eg, breath by breath) or long intervals (eg, wake vs sleep). As previously indicated, higher centers expect sensory feedback to reflect these changes in demand. When normal subjects are placed on a ventilator delivering a constant V_T, and V_T is set to equal average V_T off the ventilator, they become uncomfortable, presumably because average V_T fails to meet V_T demand in some breaths. Comfort returns when V_T is set well above their normal average V_T, resulting in hypocapnia.

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CONTROL OF BREATHING WITH DIFFERENT VENTILATOR MODES

The ventilator settings essentially determine whether patient–ventilator interactions will be optimal or not, and what type of poor interactions will result. They are also tools by which clinicians can optimize interactions, with different patients requiring different settings to achieve optimal interaction.

Settings Relevant to Patient–Ventilator Interactions

Settings common to all modes

Settings common to all modes include trigger sensitivity and positive end-expiratory pressure (PEEP) level. PEEP level is important if DH exists.

By definition, with DH, alveolar pressure at end-expiration is above external PEEP (intrinsic or auto-PEEP). All ventilators require the patient to lower airway pressure below external PEEP and then some more by an amount that produces the change in airway pressure or flow required for triggering (trigger sensitivity). In such cases, a higher external PEEP reduces the difference between end-expiratory alveolar pressure and external PEEP and facilitates triggering. Regardless of DH, low trigger sensitivity requires more effort to trigger a breath. Particularly when efforts are weak (muscle weakness or overassist), some efforts fail to trigger the ventilator (expiratory ineffective efforts [IEs]). On the other hand, high trigger sensitivity promotes false triggering by circuit noise or cardiac oscillations, which may result in overventilation. Adjustments to these settings may be quite effective in mitigating poor interactions and the direction of adjustment depends on the nature of poor interaction (eg, increase trigger sensitivity with IEs and decrease it with false triggering).

Mode-specific settings The mode-specific settings most relevant to control of breathing on MV are those that determine V_T and duration of inflation (T_I):

Volume-cycled and pressure-control ventilation In the volume-cycled mode, both V_T and T_I are preset. In the pressure-control mode, T_I is preset, whereas the set pressure determines a minimum V_T that, similar to volume-cycled mode, will not decrease if efforts become weak. Considering that patient's RR does not decrease in response to hypocapnia (see Determinants of desired breathing pattern section), there is no way in either case for hypocapnia to be mitigated unless efforts cease completely (central apnea). At this point, however, the backup ventilator rate is activated. Whether breathing efforts resume depends on the set V_T or pressure (minimum V_T) and the backup rate. If the backup rate is sufficiently high, central apnea continues and the patient is then in totally controlled ventilation with all its complications. If efforts resume, $Paco_2$ decreases again below the apneic threshold and the patient alternates between triggered and automatic breaths with continued overventilation. The tendency for these modes to cause overventilation is compounded because, in alert patients, constant V_T is not tolerated unless ventilation is higher than what is required to maintain normocapnia (see Determinants of desired breathing pattern section). Thus, among the main disadvantages of these modes is the tendency to result in overassistance and respiratory muscle dysfunction.

V_T and T_I determine the mean inspiratory flow. The setting of peak-flow in assist-control ventilation has a specific influence on the respiratory drive and the patient's effort. An insufficient peak-flow compared with the needs of the patient is very uncomfortable and leads to increased effort. When this parameter is not directly set or displayed, a low peak flow will create air hunger or flow starvation. If misdiagnosed by the clinician, it will prompt the administration of sedation, whereas a readjustment of the setting will quickly improve the clinical tolerance. A drawback of high flow in the era of low tidal ventilation is that it may result in a very short insufflation phase. The latter may facilitate the occurrence of double triggering when neural inspiratory time is prolonged beyond the end of the insufflation.

Other types of poor interactions with these modes are related to the set T_I. The ventilator has no way of knowing when the patient's effort ends. Furthermore, the patient's T_I varies over a wide range (0.4–2.0 seconds). Thus, it is difficult to set a T_I that matches the patient's T_I. To compound matters, inspiratory pressure must increase a finite amount before triggering occurs (see Settings common to all modes section). Thus, a substantial portion of the patient's inspiratory phase can elapse before triggering (trigger delay). In most patients, the end of inflation is well beyond the end of patient's effort. Little time is then available for lung volume to return to FRC before the next effort. What happens then depends on the speed of lung emptying (the time constant; see Mechanical properties of the thorax), how strong the inspiratory efforts are, and how much time is available before the next effort. In one extreme (a long time constant and/or weak efforts and/or little available time) the next effort begins at a time when DH is high and fails to trigger (IE; **Fig. 2**). On the other extreme (a short time constant), lung volume can return to close to FRC. A new breath is triggered with every effort. With a high undistressed RR, the ventilator is triggered at a high rate, resulting in overventilation.

Other types of timing abnormalities can occur with these modes. If ventilator T_I is set too short relative to the patient's T_I, the patient's effort continues after airway pressure is reset to PEEP. A second breath can be triggered from the same initial effort, resulting in double triggering and breath-stacking. Finally, a ventilator-triggered breath can trigger a patient's inspiratory effort that would not have occurred otherwise, a phenomenon called entrainment or reverse triggering. Timing of the entrained breath can vary. Regular and repeated activation of respiratory muscles after time-initiated ventilator cycles during controlled MV is

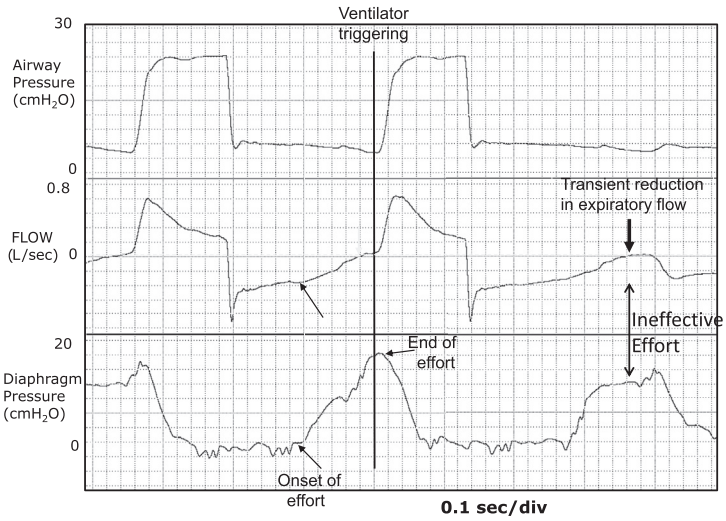

Fig. 2. Impact of long time constant on synchrony. A patient with severe COPD. Note that the onset of effort in diaphragm pressure began when expiratory flow was well above 0, indicating DH. Much of patient's inspiratory time was spent simply reducing the expiratory flow to 0 (note the change in trajectory of expiratory flow at the onset of diaphragm activity). This effort just managed to trigger the ventilator. The ventilator's inhalation phase is completely out of phase with patient's cycle. The next inspiratory effort fails to trigger the ventilator (Ineffective Effort at *arrows*), identified by transient reduction in expiratory flow.

referred to as respiratory entrainment or phase-locking phenomenon. Regular entrainment is not always present, and the pattern can be irregular or modified by the reverse breaths, such as incomplete expiration, air trapping, or double cycling. Reverse triggering has been described in ICUs in sedated mechanically ventilated patients with acute respiratory distress syndrome (ARDS) but also in brain dead patients, suggesting that different mechanisms may explain its occurrence. Should the entrained breath occur during the ventilator's exhalation phase it can result in an IE or trigger an extra breath (resulting in overventilation), depending on how strong the entrained effort is. If it occurs during inhalation, it may result in double triggering and breath-stacking.

Overassistance leading to hyperventilation and respiratory muscle dysfunction, insufficient peak-flow, and entrainment or reverse triggering are some of the drawbacks of volume-cycled and pressure-control ventilation.

Pressure Support Ventilation As with pressure control ventilation, the set pressure in pressure support ventilation (PSV) dictates a minimum V_T that does not decease no matter how weak the efforts are. Unlike pressure control, however, ventilator T_I is not fixed, and there is no backup rate. These differences result in substantial differences from the control of breathing during controlled modes.

In PSV inhalation ends when the inspiratory flow, which peaks early in the inflation phase, decreases to a preset level or percent of the peak flow. Similar to the lung emptying during exhalation, the rate at which the volume increases and the inspiratory flow declines during inspiration is exponential, as determined by the time constant. With a long time constant (eg, chronic obstructive pulmonary disease [COPD]), the inhalation phase may continue for several seconds, pending the decline of flow to the threshold level. During this long inhalation, one or more inspiratory efforts may occur. Because the ventilator is already triggered, they present as transient increases in flow above the background exponential decline (inspiratory IEs; **Figs. 3** and **4**). For the same reason, (a long time constant) flow rate declines slowly during exhalation, which can result in expiratory IEs (see **Figs. 2–4**). Several breathing cycles may occur within one ventilator cycle (**see Fig. 4**).

Clearly, such a state would be poorly tolerated in alert patients. Alert patients are capable of establishing synchrony because of their higher respiratory drive or through operation of high-level reflexes that require wakefulness. However, once the patient falls asleep, respiratory efforts decrease and consciousness-dependent reflexes no longer operate. Slow deep breathing with IEs may suddenly develop on falling asleep or after sedation. Here, the change in breathing pattern with sleep onset is simply unmasking the presence of a long time constant.

The solution to excessive IEs is to reduce the pressure support level so that respiratory efforts become stronger and more able to overcome the DH that results from the long time constant. When the pressure level is reduced in such cases, the breathing pattern may rapidly change from slow deep breathing (with IEs) to rapid shallow breathing (see **Fig. 4**). This is often interpreted as respiratory distress even though it simply reflects the

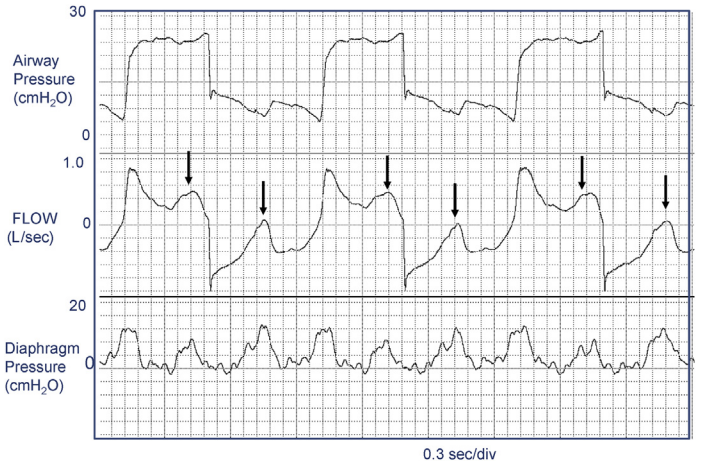

Fig. 3. A more severe case of nonsynchrony with IEs occurring both during the inhalation and exhalation phases of the ventilator (*arrows*), resulting in 3:1 rhythm (the patient's RR is 3 times that of the ventilator).

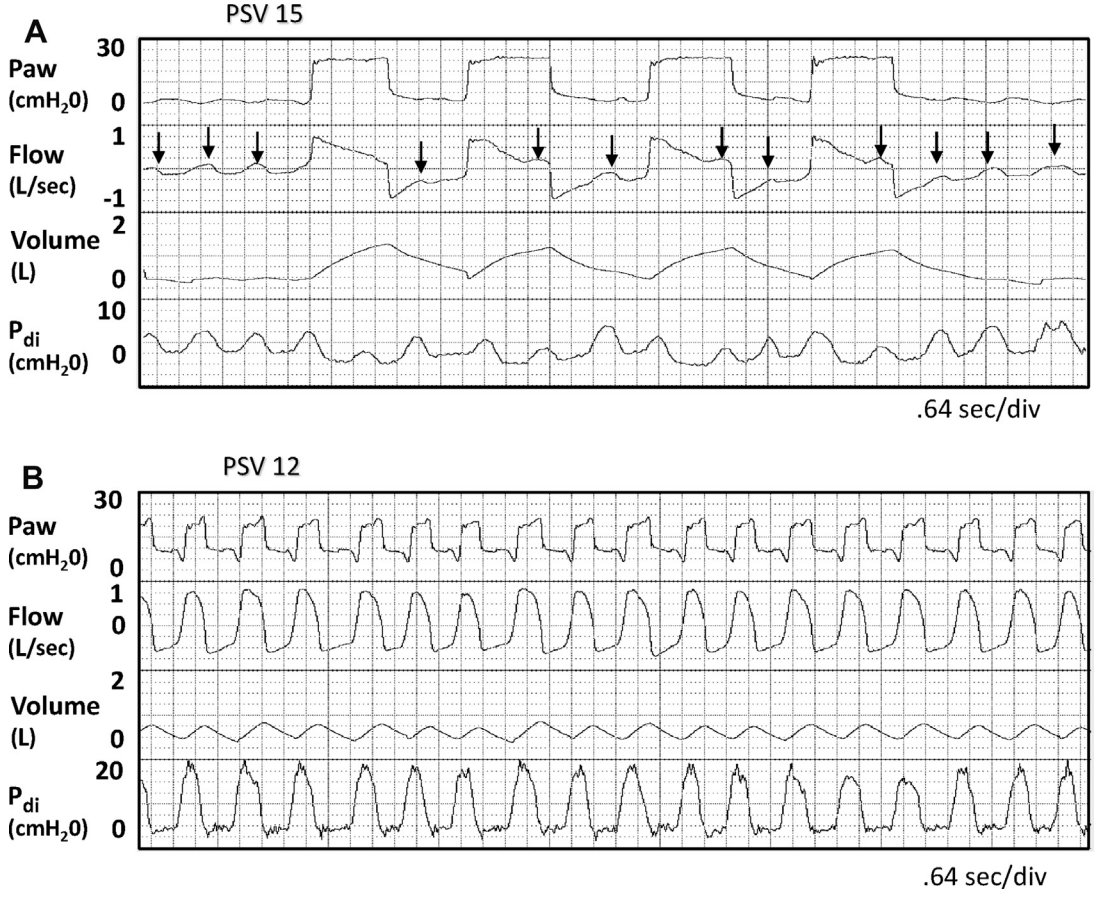

Fig. 4. Thirty-second tracings before (*A*) and after (*B*) reducing pressure support from 15 to 12 cmH_2O. Note the marked change in breathing pattern from slow deep breathing to rapid shallow breathing. However, the patient's RR remained the same (35/min). The amplitude of inspiratory efforts increased following reduction of pressure assist, resulting in the patient being able to trigger the ventilator with every effort. V_T decreased in part because of the lower PSV pressure but mostly because inspiratory duration is now much shorter, which, in the presence of a long time constant, results in incomplete filling of the lungs at the end of the short inhalation phase. Arrows in A indicate IEs. Paw: airway pressure; Pdi, diaphragm pressure. (*Reprinted* by permission from Springer Nature: Springer Control of Breathing During Mechanical Ventilation by M. Younes Copyright 2005.)

unmasking of the patient's true RR. Pressure is increased again, perpetuating the overassist and associated nonsynchrony. Lack of awareness of this phenomenon can result in unnecessary delays in extubation. An increase in the RR on reduction of PSV pressure should not be considered a sign of distress unless accompanied by other indications of distress (eg, accessory muscle use, tachycardia).

By contrast, in patients with a short time constant (eg, stiff respiratory system) lung filling during inhalation is fast so that the patient receives the minimum V_T (which could be large) with every triggered breath. Furthermore, the flow threshold for terminating inhalation is reached quickly. There is, accordingly, no encroachment on exhalation time. This and the fast emptying during exhalation preclude DH and IEs. Thus, the ventilator is triggered with every inspiratory effort. Patients with fast undistressed RR will receive relatively large V_T at a fast rate. $Paco_2$ declines rapidly, resulting in central apnea. Without a backup rate, apnea persists until $Paco_2$ increases to above the apneic threshold. Rapid breathing with large V_T resumes and the cycle repeats. Development of recurrent central apneas on PSV should be attributed to high PSV pressure unless there are other signs of respiratory depression (hypercapnia, acidemia).

An advantage of PSV is that marked overventilation cannot develop. In patients with a long time constant, reduction in inspiratory efforts associated with mild hypocapnia will result in some efforts failing to trigger so that ventilator rate decreases. In patients with a short time constant, delivered ventilation will be reduced by intermittent central apnea. In either case, $Paco_2$ is constrained to be near the apneic threshold but not much below it.

Although PSV has the advantage of not being associated with marked hyperventilation, the inhalation phase may continue for several seconds, depending on the decline of flow to the threshold level in patients with a long time constant (eg, COPD). During this long inhalation, one or more inspiratory efforts may occur. Because the ventilator is already triggered, they present as transient increases in flow above the background exponential decline. Due to a long time constant, the flow rate declines slowly during exhalation, which can result in expiratory IEs. Thus, several breathing cycles may occur within one ventilator cycle.

Proportional assist ventilation and neurally adjusted ventilatory assist Proportional assist ventilation (PAV) and neurally adjusted ventilatory assist (NAVA) are radically different from conventional modes in that there is no set V_T, airway pressure, or inspiratory time. The pressure assist is simply made proportional to the instantaneous inspiratory effort of the patient. What is adjusted is the proportionality between the instantaneous effort and the pressure generated by the ventilator. The ventilator simply amplifies the effort of the patient and the control of breathing is relegated back to the patient's control system.

When working properly, these modes are well synchronized with patient efforts so that comfort is enhanced and there are few, if any, IEs or central apneas. Because there is no minimum V_T, the risk of overventilation is minimal, thereby protecting against respiratory muscle dysfunction.

The 2 modes differ in the way the instantaneous inspiratory effort is detected. In PAV, it is calculated noninvasively from the pressure and flow signals. With NAVA, instantaneous inspiratory activity is measured using a specialized esophageal catheter that measures diaphragm activity. The main disadvantage of PAV is that triggering is still conventional; therefore, the effort must first increase to overcome any DH and the triggering threshold before the ventilator begins responding to the effort. In patients with DH and brief inspiratory effort (fast undistressed rate), this leaves little time for the ventilator to provide assist (note that ventilator cycles off when inspiratory effort ends). Patients may then develop distress despite high levels of assist. This can be obviated by using the initial increase in calculated inspiratory pressure to trigger. However, this is not yet available. NAVA is not subject as much to this problem because triggering occurs when inspiratory activity begins regardless of the presence of DH. Nonetheless, to avoid false triggering, diaphragm activity must still increase above a set threshold before triggering occurs; therefore, the same problem can occur if there is important baseline noise in the diaphragm activity signal. This mode also entails insertion of an esophageal catheter and requires the diaphragm signal to be stable over extended periods (days).

In the event that the patient's undistressed rate is high, and in the presence of many IEs before switching from another mode, switching to either of these modes will be associated with a sudden, often marked, change in the breathing pattern to a rapid shallow breathing. As in the case of reducing PSV pressure in patients with excessive IEs (see Pressure Support Ventilation), such a change simply unmasks the high undistressed RR of the patient and should not be considered as reflecting respiratory distress in the absence of other signs of distress. Particularly if the change occurs suddenly (eg, within 15 seconds after

switching) it is almost certain that it is not distress related. Distress due to underassist takes a minute or more to develop.

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CLINICAL CONSEQUENCES OF POOR PATIENT–VENTILATOR INTERACTIONS

Patient–ventilator dyssynchrony is associated with poor outcomes, including higher mortality and longer durations of ventilation. Although an association is not a synonym of causality, these observations could be explained by several factors. Mechanisms of lung or diaphragm injury may coexist. It is possible that spontaneously breathing patients develop self-inflicted lung injury and dyssynchronies can contribute to this result. Repeated ultrasound examination of diaphragm thickness have shown that almost 60% of patients exhibit changes in thickness over time under MV; mostly decreased thickness but also increased thickness, suggesting muscle injury.

In cases of a high respiratory drive with volume control ventilation, high inspiratory efforts, presenting as flow starvation, can result in both diaphragm (excessive effort) and lung injury, through the generation of high regional forces generating pendelluft. When the respiratory drive is high and/or in the concomitant presence of inspiratory threshold loading by auto-PEEP and high airway resistance, load-induced diaphragm injury may develop. In both volume and pressure control, these efforts can also induce double cycles and breath-stacking. Then, increased V_T can lead to failure of lung protective ventilation, resulting in a worse outcome.

In sedated patients with a low respiratory drive, respiratory entrainment and reverse triggering can also generate double cycling with similar deleterious consequences due to a high delivered ventilation. In addition, because diaphragm contractions start late during the insufflation phase, peak activity occurs during the expiration, at a time when the lung volume is decreasing and the muscle is lengthening. This creates conditions of eccentric or plyometric contraction, which can be injurious for the diaphragm. In patients with ARDS, paralysis in the first 2 days of MV suppresses all these dyssynchronies, which may explain an observed reduction in mortality.

Finally, in patients with ineffective triggering, the same mechanisms may exist. In addition, the reduction in pressure support unmasks these nontriggered respiratory efforts, and this apparent increase in RR is often misinterpreted as a sign of distress. The patient is kept with excessive levels of support that result in delayed weaning from the ventilator. Also, as previously explained, repeated apneas during sleep result in multiple arousals and awakenings and a very poor sleep quality, with the potentially important consequence of sleep deprivation. IEs are most often related to overassistance. As previously explained, overassistance is very frequent with assisted ventilation and it can lead to disuse atrophy of the respiratory muscles, diaphragmatic weakness, and subsequent difficulties in weaning. If overassistance is avoided during MV or the diaphragm is activated by phrenic nerve stimulation, disuse atrophy is attenuated. Therefore, it is important to suspect it and the presence of IEs and low RR (below 20 per minute) is a simple clinical way to detect it.

Different studies have shown that IEs were associated with increased duration of MV and a lower rate of weaning success. Using the ratio of the number of dyssynchronous breaths to the total number of breaths, it was shown that having an asynchrony index higher than 10%, which existed in 26% of the patients, was associated with a longer duration of MV and a higher rate of tracheostomy. These results were confirmed using multivariate analysis to demonstrate that a high level of asynchrony was an independent predictor of a prolonged stay. The development of automatized techniques made the analysis of longer recordings feasible and not limited by the time to visually review recordings. Using such techniques over prolonged duration, it was shown than a high level of mortality was associated with higher ICU and hospital mortality. Finally, it has been observed that patients often present clusters of dyssynchrony; for example, more than 30 dyssynchronies in a 3-minute period. These events were very strongly associated with poor outcomes.

Patient–ventilator dyssynchrony is associated with higher mortality and longer durations of ventilation. Although it remains uncertain whether this reflects a cause-and-effect relationship, lung and/or diaphragm injury may coexist, leading to a poorer outcome.

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Control of breathing and ventilation

(Notes from :

“The Control of Breathing During Mechanical Ventilation “

”The Injurious Effects of Elevated or Nonelevated Respiratory Rate during Mechanical Ventilation”)

Normal control

T**ime constan**t - (best look at expiration - simpler)

T.C of emptying = **R x C**
(if increased compliance, the lung volume at beginning of expiration is larger, therefore longer to empty)

Normal compliance - 0.1 L/cm H20
Normal resistance = 5 cm/H20/L/sec

Normal time constant = 0.5 sec (i.e., volume and flow will be 1.3rd of peak - I.e., **66% empty**)
(at 1 sec = 1/9th)

Therefore it will reach FRC during normal expiration time. If R increases, it will exceed time to reach FRC and will lead to PEEPi - assynchrony.

NB. Driving pressure is tidal volume scaled to compliance

Respiratory Rate (RR)

RR changes minimally in response to : assist level, pCO2

In conscious volunteers -> **RR is an insensitive to assist nor pCO2**.

RR -> response minimal to CO2 between (23-45). **CO2 works mainly through inspiratory effort**.

Sleep- removing wakefulness stimulus to breath -> **RR depends on CO2**. Normal or **decreased CO2 by 3-4 mmHg from normal -> apnoea** = Apnoeic Threshold (AT)

During sleep - as CO2 decreases RR stable until -> AT =0

Between normal CO2 -> AT - ventilatory control only by change in effort (RR insensitive to change in CO2).

Beyond a level of **respiratory drive increase** which is **3-4 X higher than resting** -> **RR increases substantially**.

ARDSNet protocol allows RR during ventilation up to 35/min to keep pH >7.3 but a high RR can cause VILI

Higher centres

1) ***Sleep*** - control is mainly via chemoreceptors.

Increased pCO2 will increase respiratory **drive** not RR. At **3-4 X increase of drive above normal, then RR will increase.**

Hypocapnia - RR does not decrease until **pCO2 slightly below normal (3-4** mmHg) = **apneic threshold (AT) - therefore stops breathing.**

Therefore over ventilation continues until CO2 decreases below AT - recurrent apneas.

2) ***Awake*** - higher centres work here

-Respiratory center does **NOT cease below AT** - causing severe drop in pCO2.

-Behavioral response - breathing events not perceived unless different from what is expected - highly unpredictable response.

Desired breathing patterns -

Breathing pattern determined by RR and ventilation needed to satisfy metabolic demands

Vt is a **dependant** variable - it is **adjusted** to provide **ventilation at the prevailing RR.**

A **high RR does not necessarily denote distress or increased demand**.

RR normally **5-25**

To differentiate a ”normal” increased RR from distressed RR, **in distress, the RR decreases if ventilator assist is increased**, if not - not distressed related.

Normally there are large fluctuations of Vt - put a normal volunteer on a ventilator, give a fixed Vt, which equals the average Vt for that person - it is very uncomfortable! Comfort returns if you increase the Vt well above the average, but this leads to hypocapnia.

Control of breathing with different ventilatory modes

PEEPi - alveolar pressure at end expiration is **ABOVE** external PEEP.
To trigger, you must be below external PEEP.
Sometimes by **increasing external PEEP** - reduces the difference and **aids triggering.**

*1)**Volume cycled***

Vt and Ti are preset

*2) **Pressure cycled***

Ti is preset
Set pressure determines minute ventilation
NB. Patient’s RR does not decrease in response to hypocapnia.

These 2 modes tend to over ventilate. In alert patients, constant Vt is poorly tolerated unless ventilation is high - leading to hypocapnia. Therefore **tends to over assist leading to respiratory muscle dysfunction.**

Vt and Ti determine mean inspiratory flow

Peak flow - influence of respiratory drive and patient effort

If peak flow too low -> v. Uncomfortable (=**air hunger**)

If peak flow **too high** -> v. Short insufflation phase -> **"double triggering"** (neuro inspiratory time is longer than ventilators inspiratory time).

Ti -

Patient's Ti **varies** (**0.4 - 2.0 seconds)**, therefore difficult to match.
If Ti too short -> double trigger

Types of inappropriate triggering:

"Double triggering"
Neuro inspiratory time is longer than ventilators inspiratory time).

"Reverse trigger" -
A ventilator controlled triggered breath - due to increased lung volume (stretch receptors, etc) - can trigger a patient's inspiratory effort that would not have occurred otherwise.Cause eccentric diaphragmatic damage.

"reverse triggering" -> breath stacking -> increased Vt -> VILI

3) Pressure support ventilation

Set pressure determines minimum Vt
Unlike pressure control, **Ti is not fixed** and there is no backup rate. Therefore very different in control of breathing.

Inspiration ends when inspiratory flow - which peaks early - **decreases** to a **preset** level or a %

In **PSV**, minute **ventilation depends** on **assist** level, **mechanics** and **RR** - when ventilation -> a **drop in CO2** below normal -> only **inspiratory effort decreases** - **RR** does **not change**.

Rate of volume increase and inspiratory flow decline are **determined by the time constant**.

Long TC (ex. COPD)
a long TC -> long inhalation - therefore **inspiratory efforts may occur** ->
transient increase in flow above background flow decline.

For same reason, f**low rate declines slowly during expiration** -> **expiratory ineffective efforts (IEs)**. Therefore there are **several breath cycles during a single ventilator cycle.**

Solution to Its is to reduce pressure support so that respiratory **efforts** are **strønger** and **can overcome the PEEPi that results from a long TC**.
Change in pattern from slow, deep -> **rapid, shallow does not mean distress**, but **unmasks** the patient's **true RR** (NB. Not distress **unless** increase **use of accessory muscles** and/ or tachycardia, etc).

Short TC (ex. Stiff lung)

Patient receives Vt very quickly -> exhalation is also so fast, that there is no PEEPi, nor IE but pCO2 declines quickly -> central apnea -> persists until pCO2 rises above AT -> cycle continues.

PSV - marked **overventilation tends not** to develop.

Clinical consequences of asynchrony

60% of patients show **changes** (increases or decreases) of **diaphragmatic thickness** on U/S.

Reverse trigger - double cycling -> high delivered ventilation.
Diaphragmatic **contraction starts late** during insufflation -> **peak activity during exhalation** when **lung volume is decreasing and muscle lengthens = eccentric contraction**

Ineffective effort -> **fail to trigger** -> **most common form of assynchrony**.

The **patients RR is higher then the ventilator RR** -> therefore **most efforts during expiration (harmful** as inspiratory muscles activated while lung volume decreasing).

If PEEPi due to over assist -> ineffective efforts. Therefore **decrease assistance -> increased RR - this is nøt due to distress** but now each trigger is effective.

If **assistance is increased** -> decrease RR due to complex feedback reflexes.
Awake - RR will **not change if decrease in pCO2** but **could decrease respiratory drive** -> **ineffective efforts -> weaning failure**.

Insensitivity of RR to low CO2 resulting from a high assistance -> decrease effort -> **increase Ventilator Induced Diaphragmatic Dysfunction** (which is **2 X** more common the CIPPM).