• Important interactions between the infant and the ventilator occur routinely during invasive and noninvasive mechanical ventilation. Some of these interactions can have significant effects on ventilation and gas exchange and may prolong the need for respiratory support.
• Asynchrony between the ventilator and the infant’s breathing effort, excessive peak inflation pressure, or inspiratory time that is too long can affect the infant’s respiratory rhythm and lead to agitation.
• Ventilator waveforms and monitored parameters should be used to determine the adequacy of ventilator settings and detect any adverse condition such as autotriggering.
• The interaction between the infant and new modes of ventilation that become available should be carefully examined before they are widely used.

Mechanical ventilation is an important tool in the management of premature infants with respiratory failure but is associated with an increased risk of acute and chronic lung injury and other associated morbidities. Despite continued efforts to reduce its use, a large proportion of preterm infants eventually require intubation and mechanical ventilation.

The earlier association between mechanical ventilation and the risk for lung injury was primarily believed to be due to aggressive use of the ventilator, which produced injurious lung expansion and chronic lung damage. In part because of the limitations in the older ventilators, clinicians for years elected to impose a respiratory pattern on their patients to take over their ventilation completely. To achieve this, neonates with respiratory failure were sedated, paralyzed, or underwent hyperventilation to suppress their spontaneous respiratory drive. These approaches were associated with many problems that led to prolonged ventilator dependence and higher rates of complications. The likelihood of hyperventilation or hypoventilation is higher during controlled ventilation because the settings are not always adjusted to match the infant’s metabolic demands and changing respiratory mechanics. Moreover, neonates who do not exercise the respiratory muscles for long periods are less likely to be weaned successfully from mechanical ventilation.

Neonatal ventilatory support has evolved from controlled ventilation to assisted ventilation with the evolution of various modes of synchronized ventilation. These gentler strategies have been developed to take maximal advantage of the patient’s own respiratory effort and ameliorate ventilator-associated lung injury. These strategies involve careful management to minimize ventilator support to avoid volume injury and shorten the duration of mechanical ventilation. As a result, the ventilatory support provided to premature infants has changed from a strategy to fully control ventilation, targeting normal blood gas values, to a less aggressive approach in which the ventilator is used to supplement the infant’s spontaneous respiratory effort. During the course of
the mechanical ventilatory support, there is continuous interaction between infant and the ventilator. Some of these interactions can have negative effects on the infant’s spontaneous breathing effort and affect adversely ventilation and gas exchange, whereas other interactions can be beneficial. This chapter describes these interactions, their effects, and discusses alternatives to enhance positive interactions.

**Patient-Ventilator Interaction During Conventional Mechanical Ventilation**

The interaction between the patient and the ventilator can be extremely complex because it is influenced by many factors, including the patient’s respiratory drive, various respiratory reflexes, the mechanical characteristics of the respiratory system, and the timing, flow, and pressure characteristics of the ventilator inflations. Respiratory reflexes influence the infant’s spontaneous respiratory rhythm. Activation of the Hering-Breuer vagal inhibitory reflex by lung inflation can shorten neural inspiration, whereas its activation by lung inflation during neural expiration will delay the onset of the next spontaneous inspiration. Also active in the newborn, Head’s paradoxical reflex can be activated by a rapid lung inflation and elicit a greater inspiratory effort. This could result in a greater transpulmonary pressure, larger tidal volume ($V_T$), and risk of alveolar overdistention. These interactions are illustrated in Fig. 16.1.

**Infant-Ventilator Asynchrony**

Asynchrony between the infant and the ventilator occurs frequently during intermittent mandatory ventilation (IMV) because mechanical inflations are delivered at fixed intervals and duration, which do not coincide with the infant’s spontaneous inspiration. The ventilator positive pressure cycles can interact with the infant’s spontaneous breathing and reflex activity. The effects vary depending on the timing and volume of the spontaneous inspiration or positive-pressure inflation.2–4

Inspiratory asynchrony occurs when the ventilator inflation is delivered toward the end of the spontaneous inspiration and extends beyond the end of inspiration. Fig. 16.2 shows an example of asynchrony during the spontaneous inspiratory phase. The resulting inspiratory hold can affect the spontaneous respiratory rate, and the

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**Fig. 16.1** Activation of Hering-Breuer and Head’s paradoxical reflexes. Recordings of flow, esophageal pressure ($P_{ES}$), airway pressure ($P_{AW}$), and tidal volume ($V_T$) show the activation of the Hering-Breuer inhibitory reflex by a ventilator cycle that delays the initiation of the next spontaneous inspiration. The following ventilator cycle elicits an increase in inspiratory effort (greater negative deflection in $P_{ES}$) within the same spontaneous inspiration that results in a greater $V_T$ in a pattern characteristic of the Head’s paradoxical reflex.
additional lung inflation on top of the spontaneous breath may cause volutrauma. Expiratory asynchrony occurs when the ventilator inflation is delivered during exhalation and prolongs the spontaneous expiratory phase, in turn affecting the spontaneous breathing frequency, as shown in Fig. 16.3. This type of asynchrony can also elicit active exhalation against an elevated pressure at the airway, producing a rise in intrathoracic and probably also intracranial pressure.

Asynchrony between the infant’s spontaneous breathing and the ventilator inflations can have multiple effects, including poor gas exchange, air leaks, and increased risk of intraventricular hemorrhage (IVH).\textsuperscript{5–8}

Asynchrony was common in earlier generations of neonatal ventilators. Monitoring was limited to visual assessment of chest expansion and breathing rate, with limited ability to determine asynchrony or the adequacy of $V_T$. Manipulation of the
ventilator inspiratory and expiratory time has been suggested as a strategy to decrease asynchrony by adapting to the infant’s breathing pattern.\textsuperscript{9,10} This, however, requires frequent adjustment of these settings because of the variability of the infant’s breathing. Use of high ventilator rates has also been suggested as a way to prevent asynchrony.\textsuperscript{11} However, this may not be the most adequate approach for premature infants because of the risk of hypocapnia and its association with IVH and periventricular leukomalacia.

**Patient-Ventilator Interaction During Synchronized Mechanical Ventilation**

Because of the serious drawbacks of controlled ventilation, there has been an almost complete shift toward the use of assisted (i.e., synchronized) ventilation modes. The patient’s spontaneous respiratory drive is not inhibited, so infants are more likely to be weaned sooner from mechanical ventilation because their respiratory muscles remain fit and can cope with the increased work of breathing during the weaning process. Because the ventilator is used only to supplement the infant’s respiratory effort, lower peak inflation pressure (PIP) is needed to maintain adequate minute ventilation. The likelihood of hyperventilation is also reduced by allowing the infant to determine the total minute ventilation.

Ventilators used to provide assisted ventilation must respond on a timely basis to the demands of even the smallest infants. Incorporation of sensors and microprocessors for monitoring and control of different functions has made possible the development of ventilators capable of synchronizing the ventilator positive pressure cycle with the infant’s spontaneous inspiration (i.e., patient-triggered ventilation).

The use of synchronized ventilation to assist the infant’s spontaneous breathing while avoiding the effects of asynchrony can lead to a gentler ventilatory strategy and preservation of the infant’s breathing rhythm. During synchronized ventilation, cycling of the ventilator shortly after the onset of the spontaneous inspiration achieves a larger transpulmonary pressure because of the sum of the positive-pressure cycle to the negative pressure generated by the diaphragm. This produces a larger $V_T$ than that generated by the infant or the ventilator alone, as illustrated in Fig. 16.4. The positive interaction between the infant and the ventilator during inflation explains the better gas exchange and ventilation with more consistent $V_T$ and lower breathing effort during synchronized than during conventional ventilation.\textsuperscript{12–22} One of the most

![Fig. 16.4](image_url)  
**Fig. 16.4** Spontaneous inspiratory effort and synchronization of ventilator cycle. Tracings of flow, tidal volume ($V_T$), airway pressure ($P_{AW}$), esophageal pressure ($P_{ES}$), and electrical activity of the diaphragm obtained from a preterm infant show how the contraction of the diaphragm (measured by electromyography [EMG]) generates the negative pressure responsible for the inspiratory flow. Timely triggering of the ventilator cycle shortly after the onset of the inspiratory flow increases the transpulmonary pressure, and a larger $V_T$ is achieved than in the preceding, nonassisted spontaneous inspiration.
consistent and important advantages of patient-triggered ventilation is that the preservation of spontaneous respiration facilitates weaning from the ventilator and shortens the duration of mechanical ventilation. This explains the improved respiratory outcome with synchronized ventilation, which was more striking among the smaller infants at higher risk for bronchopulmonary dysplasia. Synchronous ventilation has also been shown to reduce the stress response and fluctuations in blood pressure and oxygenation in preterm infants.

**Methods of Synchronization**

Synchronization of the ventilator cycle with spontaneous inspiration is achieved by using different methods to detect inspiratory activity. Their efficacy and reliability vary, and these performance characteristics significantly influence the interaction between the ventilator and the infant’s spontaneous inspiratory effort.

Mainstream (proximal) or internal flow sensors are used in neonatal ventilators to detect the inspiratory flow generated by the infant’s spontaneous inspiratory effort. The ventilator cycle starts when the inspiratory flow exceeds a set threshold (see Fig. 16.4). Flow triggering has been shown to be more sensitive and specific than other methods; the ability to use low flow thresholds for triggering make this method appealing for use in sicker and more immature infants. Flow triggering is limited by the presence of gas leaks around the endotracheal tube. Leaking gas travels through the flow sensor in the same direction as the inspiratory flow and may produce autocyling if this exceeds the trigger threshold. This is less of a problem with some modern ventilators designed specifically for neonatal use, which have effective compensation for even moderately large endotracheal tube leaks.

Although mainstream flow sensors are usually small, they increase the instrumental dead space and may affect carbon dioxide (CO₂) elimination, particularly in smaller infants. This effect, however, is relatively small and is outweighed by the advantages of flow triggering.

Outward motion of the abdomen during inspiration can be detected by a pressure capsule applied on the abdominal surface. The use of this capsule for ventilator triggering is relatively simple but requires individualized sensitivity adjustment to avoid autocyling during patient activity. This capsule has been used effectively to synchronize the ventilator during invasive and noninvasive respiratory support in the past but is no longer available in the United States.

The transmission of the negative pressure changes produced by spontaneous inspiration to the airway can also be used for triggering. However, because of their respiratory disease and relatively weak respiratory pump, preterm infants do not consistently produce the pressure changes at the airway required for triggering, which can lead to lack of or delayed triggering with these systems.

Using the electrical activity of the diaphragm (EA_{DIA}) is an attractive way of triggering ventilator inflations because it eliminates the trigger delay occasioned by pneumatic coupling. Onset of inflation is triggered by an increase in the electrical potential generated by diaphragmatic muscle contraction, as sensed by a special feeding catheter with an array of miniature electrodes. Inflation is terminated when EA_{DIA} declines below a fixed threshold, resulting in optimal synchrony for both initiation and termination of ventilator inflation. EA_{DIA} is unaffected by leakage, making it uniquely suited for synchronization during noninvasive positive-pressure ventilation. Cost and availability (it is currently only available from one manufacturer) are limiting factors for more widespread use of this promising triggering modality.

**Modalities of Synchronized Ventilation**

**Synchronized IMV**

Synchronized IMV (SIMV) is similar to conventional IMV but with synchronous delivery of ventilator cycles. In both IMV and SIMV, the number of ventilator cycles delivered every minute is set by the clinician but the interval between cycles
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( expiratory duration, $T_e$), which is constant in IMV, is variable in SIMV. Fig. 16.4 illustrates how synchrony is achieved during SIMV, and Fig. 16.5 shows a more regular ventilatory pattern during SIM compared with IMV. The disadvantage of SIMV in small preterm infants with narrow endotracheal tubes and insufficient muscle strength is that these immature infants often do not achieve adequate $V_T$ with spontaneous breaths that are in excess of the supported rate. These small breaths largely rebreathe dead-space gas and contribute little to alveolar minute ventilation, which often necessitates a larger $V_T$ for the low rate of SIMV inflations.

Assist/Control Ventilation

In assist/control (A/C) ventilation, every spontaneous inspiratory effort is assisted with a mechanical inflation. These synchronous inflations reduce the work of breathing and improve $V_T$, as illustrated in Fig. 16.6. Because all breaths are supported and easily clear dead space, the $V_T$ needed with A/C is substantially lower than with SIMV. Most preterm infants have an inconsistent respiratory drive. Hence, in A/C ventilation, a backup IMV rate is necessary to prevent hypoventilation during episodes of apnea. Backup ventilator cycles delivered during apnea may not always prevent hyperventilation if the rate is insufficient; optimally the backup rate is set only 10 cycles below the infant’s spontaneous effort to avoid large fluctuations in minute ventilation. On the other hand, a backup rate too near the infant’s breathing frequency or above it may lead to ventilator takeover if it provides all the required minute ventilation. In some neonatal ventilators, the duration of inspiration (Ti) in A/C ventilation is set by the operator, and in others, the ventilator cycle can be automatically terminated in synchrony with the declining inspiratory flow at the end of inspiration. This latter arrangement is also known as flow cycling. This allows the preterm infant to increase breathing frequency without shortening $T_e$ and affecting $V_T$, unlike A/C ventilation with a set Ti. In most ventilators, the mode of A/C with flow cycling is referred to as pressure support ventilation (see the next section).

Pressure-Support Ventilation

Pressure-support ventilation (PSV) is a flow-cycled modality in which, as in A/C ventilation, every breath is assisted and the positive pressure is automatically terminated when the patient ends inspiration. This modality gives the infant complete
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Control of the frequency and Ti. The synchronous support pressure is aimed at compensating for the loads induced by reduced lung compliance and increased airway and endotracheal tube resistance.17,44

A consistent respiratory drive is needed to ensure maintenance of ventilation in PSV, but if apnea occurs, a backup IMV rate prevents hypoventilation. In many ventilators PSV can be combined with SIMV and thus the spontaneous breaths are pressure-supported, eliminating some of the problems of SIMV. Because the aim of PSV is mainly to boost the $V_T$ of spontaneous breaths, the pressure-supported breaths are usually assisted with lower pressures and result in smaller $V_T$ than breaths assisted with SIMV. However, the level of pressure support should be sufficient to achieve a physiologic $V_T$, of at least 3.5 to 4 mL/kg or it will not be effective due to a continued high dead space-to-$V_T$ ratio of the spontaneous breaths.

The addition of PSV to SIMV in preterm infants is aimed at boosting the spontaneous breaths and thus reducing the reliance on the larger SIMV inflations. PSV used with SIMV has been shown to reduce breathing effort and increase $V_T$ in proportion to the support pressure used.45-47 The combined use of SIMV and PSV was found to accelerate weaning in preterm infants compared with SIMV alone, preferentially in infants weighing more than 700 g at birth.48 This advantage is likely due to these infants’ more consistent respiratory drive, which ensures effective triggering of the ventilator.

Infant-Ventilator Maladaptation

Although synchronized ventilation can unload the respiratory pump by sharing the respiratory workload, the opposite occurs when there is maladaptation between the patient and the ventilator and the infant “fights” the ventilator. This lack of adaptation can be due to inadequate function of the synchronization mechanism, which leads to delayed triggering or trigger failure, autocycling, end-inspiratory asynchrony, or flow starvation. These problems may vary among ventilators according to their triggering methods and other characteristics, but there is also great variability during routine clinical practice, depending on the infant population, the underlying lung disease, and the ventilator settings.

Long Inspiratory Time and End-Inspiratory Asynchrony

End-inspiratory asynchrony occurs when the Ti of the ventilator cycle exceeds the patient’s neural inspiration or when there is delayed triggering and the mechanical

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**Fig. 16.6** Transition to synchronized assist/control ventilation. Tracings of flow, tidal volume ($V_T$), airway pressure ($P_{AW}$), and esophageal pressure ($P_{ES}$) during transition from intermittent mandatory ventilation (IMV) to assist/control ventilation show how the delivery of synchronous positive-pressure cycles reduces the inspiratory effort and avoids the disturbances to the infant’s breathing rate observed when IMV cycles are delivered during exhalation.
cycle starts late during spontaneous inspiration. Continuation of the mechanical inflation into neural expiration results in a prolonged inspiratory plateau similar to an inspiratory hold and decreases the time for unopposed exhalation. In some cases, this can elicit active exhalation efforts against the positive pressure. The long Ti can produce a prolonged volume plateau that keeps the lung distended, delays the initiation of the next spontaneous inspiration, and affects the infant’s breathing rhythm (illustrated in Fig. 16.7). This effect is mediated by the Hering-Breuer inhibitory reflex.

In A/C ventilation, an excessive Ti may also result in an inverse inspiration-to-expiration ratio, insufficient expiratory time, and gas trapping, if the spontaneous breathing frequency increases (Fig. 16.8). This can limit breathing frequency and disrupt the neural breathing pattern. To prevent this situation, in addition to

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**Fig. 16.7** Effect of excessive inspiratory time. Tracings of flow, tidal volume ($V_T$), airway pressure ($P_{AW}$), and electromyographic activity of the diaphragm (EA_DIA) show the effects of a ventilator cycle with a prolonged inspiratory time (Ti) on the neural respiratory activity in a preterm infant. The prolonged volume plateau extends beyond the inspiratory activity and prolongs the neural expiratory phase, delaying the start of the following spontaneous inspiration.

**Fig. 16.8** Gas trapping at fast breathing rate with long inspiratory time. Tracings of flow, tidal volume ($V_T$), and airway pressure ($P_{AW}$) during assist/control ventilation with a constant inspiratory time (Ti) that exceeds the duration required to complete inspiration. Note the prolonged periods near zero flow and volume plateau. An increase in the spontaneous frequency produces an inverse inspiration-to-expiration ratio that results in gas trapping because of insufficient time to complete exhalation.
avoiding a Ti that is too long, mechanical inflations can be terminated automatically based on the decline of the inspiratory flow below a set threshold, known as termination criteria. Fig. 16.9 shows an example of automatic termination of Ti (flow cycling as used in PSV). In ventilators not specifically designed for newborn infants, this automatic termination of ventilator inflations may not work properly when a large gas leak around the endotracheal tube is present, because the leak can maintain the measured inspiratory flow above the breath termination criteria. Manual adjustment of the termination criteria is possible to deal with this issue, but because the leak is often variable, this is difficult. Setting the termination criteria too high (e.g., 30% or 40% of peak flow) would lead to premature breath termination when the leak decreases. Specialized neonatal ventilators have effective leak compensation that eliminates this problem. On the other hand, a set Ti that is shorter that the infant’s spontaneous inspiration can result in inadequate transpulmonary pressure and insufficient VT. Flow cycling largely eliminates this problem by automatically adjusting the Ti in response to changing lung mechanics and spontaneous inspiratory time of the infant.

**Trigger Delay**

Delayed triggering of the inflation relative to the onset of the spontaneous inspiration can lead to increased work of breathing. The delay can result in prolonged inspiratory hold similar to the IMV cycles that occur late in inspiration. In A/C ventilation the effects may be similar to those of long Ti described previously. Delayed triggering is usually due to a relatively insufficient trigger sensitivity setting with flow triggering. In modern neonatal ventilators with effective leak compensation that minimizes the risk of autotriggering, sensitivity should be always be set at the most sensitive level to minimize trigger delay. Long trigger delay was a common problem when pressure triggers were used in the past, but virtually all modern ventilators now use flow or diaphragmatic trigger. However, not all ventilators used in the neonatal intensive care unit (NICU) are designed for newborns. Universal ventilators are primarily designed for adults with cuffed endotracheal tubes and may not have effective leak compensation, thus requiring trigger sensitivity adjustment that may lead to inspiratory asynchrony.
**Trigger Failure**

Trigger failure occurs because of trigger sensitivity that is too low—for instance, an excessive flow trigger threshold that exceeds the inspiratory flow produced by the infant’s spontaneous inspiratory effort. As a result, the infant will be supported only by the IMV or AC ventilation backup rate in a nonsynchronized mode. Trigger failure should be rare with appropriate settings on neonatal ventilators but remains a problem when leak compensation is lacking, a situation similar to long trigger delay.

**Autotriggering**

Autotriggering is one of the most common problems with patient-triggered ventilation. It occurs when the ventilator inflations are triggered by artifact, rather than in response to the patient’s inspiratory effort. The most common causes of autotriggering are gas leaks around the endotracheal tube and water condensation in the ventilator circuit, both of which produce changes in gas flow or oscillations in pressure that are detected by the flow sensor as the onset of the infant’s spontaneous inspiration. Leaks around the endotracheal tube are common among infants who remain ventilated for long periods because the immature tissues of the larynx and trachea stretch over time with positive-pressure ventilation (acquired tracheomegaly). Less frequently, infants may actually outgrow the tube size. Small leaks can be compensated for by an increase in the flow trigger threshold. Newer specialty neonatal ventilators have automatic leak compensation systems capable of compensating for leaks of up to 60%. However, when the leaks are too large or variable, leak compensation becomes less effective and sometimes the endotracheal tube needs to be replaced with a larger one to reduce the leak and avoid autotriggering. A former 600-g infant who is 3 weeks old but still only weighs 750 g may need a 3.0-mm endotracheal tube to eliminate a large leak; the guidelines for endotracheal tube size based on birth weight apply only for the initial intubation and should not prevent the use of appropriate size tube when a large leak is present.

Autotrigger may also occur due to water condensation in the unheated expiratory limb of the circuit and generate oscillations that trigger the ventilator at a very rapid rate. This problem is not solved by leak compensation. Water traps located at the lowest point in the circuit can be helpful, but even more effective is the use of modern semipermeable expiratory circuits that allow the water to move out of the circuit, virtually eliminating autotriggering caused by condensation.

The consequences of autotriggering are more serious in A/C ventilation or PSV because none of the currently available neonatal ventilators offers the option to limit the frequency. In these modalities, autotriggering at a high ventilator rate can induce hyperventilation, hypocapnia, and gas trapping. If the autotriggering persists, it is likely to blunt the spontaneous respiratory drive through hyperventilation. In contrast, the effects of autotriggering in SIMV are limited because the ventilator rate is set by the clinician, and therefore the ventilator behaves as if it were in the IMV mode instead of SIMV. A high rate alarm should always be set at an appropriate value when using A/C or PSV to alert the caregivers to the possibility of autotriggering.

**Excessive or Insufficient Circuit Flow**

*Flow starvation* occurs when the flow through the ventilator circuit is lower than the peak inspiratory flow generated by the patient’s own inspiratory effort. In older patients, flow starvation produces a sensation of air hunger and anxiety. In infants it can be a cause of agitation and maladaptation to the ventilator, because there is not enough fresh gas for the infant’s spontaneous inspiration between or during ventilator cycles. Some ventilator modes have the capacity to automatically increase the flow to match the patient demand (demand flow), but if this feature is not available, it is critical that the ventilator flow be adjusted to meet the demands of the patient. Flow starvation can be recognized when the patient struggles during inspiration and by a characteristic appearance of the pressure waveform. When the circulating flow in the ventilator circuit is insufficient, the ventilator does not consistently reach the peak pressures set by the operator. Although uncommon in small infants, because their flow requirements are relatively low and seldom exceed the available flow, it is
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important to recognize this condition because the infant may be receiving less ventilatory support than intended, which is commonly associated with agitation.

At the other extreme, excessive circuit flows can modify the pressure profile of the ventilator cycle, resulting in a rapid increase to the PIP. Ventilators differ in how inspiratory flow is regulated. In older devices there is a fixed inspiratory flow rate adjustable by the user. More recently the rate of inspiration is controlled by adjusting the “rise time” or slope of the rate of pressure increase. Rapid inspiratory flow results in fast lung inflation rates that are not observed during normal spontaneous breathing and may be injurious to the airways. Damage from excessively high inspiratory flow, referred to as rheotrauma, is not well documented but may be a legitimate concern. Optimal inspiratory flow rate/risetime are currently unknown.

Excessive Peak Inflation Pressure

Ventilator cycles triggered by the onset of the infant’s inspiration generally deliver a greater \( V_T \) than that produced by the spontaneous effort alone. Although it does not occur in a consistent manner, the larger lung inflation produced by triggered ventilator cycles with high PIP can inhibit the infant’s neural inspiration through activation of the stretch inhibitory reflex, as illustrated in Fig. 16.10. The conditions that can lead to inhibition of the neural inspiratory activity by lung inflation in preterm infants have not been clearly defined. In addition to the magnitude of the inflation, the sensitivity of the infant’s respiratory center to stretch receptor activity is likely modulated by the chemical respiratory drive and possibly by the rate of lung inflation.

Although the possible impact of inhibition of the infant’s inspiratory effort on his ability to maintain a consistent breathing rhythm is unknown, the occurrence of such inhibition in a persistent manner over time may have unwanted consequences. On the other hand, it is possible that inhibition of spontaneous inspiration when \( V_T \) is excessive is a protective mechanism. Hence, an inconsistent or decreased sensitivity to stretch receptor activity may increase the infant’s risk for lung injury when PIP is excessive during synchronized ventilation.

All modern ventilators now incorporate some means of monitoring \( V_T \); therefore excessively high PIP and \( V_T \) are largely preventable with close monitoring even when using pressure-controlled modes of ventilation. The problem can also be avoided by the use of volume-targeted ventilation.

Excessive Positive End-Expiratory Pressure

The beneficial effect of positive end-expiratory pressure (PEEP) on oxygenation was demonstrated long ago and is due to resolution of areas of atelectasis and decreased pulmonary shunting. The use of adequate PEEP to maintain alveolar recruitment

![Fig. 16.10](image)

**Fig. 16.10** Inhibition of spontaneous inspiration by large tidal volume. Recordings of flow, tidal volume (\( V_T \)), airway pressure (\( P_{AW} \)), and electromyographic activity (EMG) of the diaphragm during spontaneous intermittent mandatory ventilation show inhibition of the infant’s inspiration by a synchronous ventilator cycle that produces a \( V_T \) that is considerably greater than the \( V_T \) produced by the preceding spontaneous inspiration.
and functional residual capacity at end-exhalation is a crucial component of lung-protective ventilation strategies because it ensures even distribution of $V_T$ into an open lung. However, excessive levels of PEEP can produce a rise in CO$_2$ owing to greater anatomic dead space resulting from distention of airways, increased alveolar dead space owing to incomplete exhalation (gas trapping), and decreased ventilation owing to overdistention of the lung, thus leading to reduced lung compliance.$^{54-57}$ The reduction in compliance is caused by a rise in lung volume to the flatter portion of the pressure-volume relationship. It is important to note that, because of alveolar recruitment, an increase in PEEP achieves a greater gain in lung volume than the gain in $V_T$ achieved by an increase in PIP of the same magnitude.$^{58}$

In small preterm infants, increasing PEEP does not produce a compensatory increase in diaphragmatic activity to keep ventilation unchanged.$^{57}$ The reason may be activation of inhibitory stretch receptors at higher lung volumes.$^{59}$ The inability to maintain ventilation at rising PEEP levels may also be affected by decreased contractility and tension generation when the diaphragm is displaced downward at higher lung volumes.$^{60}$ On the other hand, PEEP levels that produce excessive lung volumes can elicit activation of expiratory muscles to actively exhale against the pressure generated by the ventilator,$^{61}$ as illustrated in Fig. 16.11.

Although the optimal PEEP level in preterm infants is difficult to determine, it is clear that both insufficient and excessive PEEP can lead to negative infant-ventilator interactions.

**Patient-Ventilator Interaction During Volume Targeted Ventilation**

Automatic adjustment of inflation pressure in response to changing lung mechanics and alterations in patient respiratory effort is an example of a closed-loop system that maintains a relatively stable $V_T$ during pressure-controlled ventilation. Volume guarantee (VG) has for the most part become the industry standard for volume-targeted ventilation (VTV) and some version of the algorithm is now available in most ventilators used in the NICU. The benefits and operating characteristics are described in Chapter 19; here we focus on the patient-ventilator interactions during VTV. The key concept to understanding this interaction is the recognition of...
the fact that the \( V_T \) reaching the patient’s lungs results from the combination of the positive pressure generated by the ventilator and the negative inspiratory pressure generated by the infant. With pressure-controlled ventilation, the ventilator component of the transpulmonary pressure is fixed, while the immature infant’s inspiratory effort is sporadic and highly variable from breath to breath. This results in large fluctuations in transpulmonary pressure and consequently the delivered \( V_T \). With VTV, the ventilator compares the exhaled \( V_T \) with the target \( V_T \) and adjusts the inflation pressure to attempt to maintain the target \( V_T \). Thus the ventilator component of the transpulmonary pressure is also variable—in general in inverse proportion to the infant’s effort—attempting to maintain a stable transpulmonary pressure and thus \( V_T \). Because the breath-to-breath change in the ventilator pressure is limited to avoid overshoot, the \( V_T \) fluctuates to some extent, but less so than without this adaptive mechanism.\(^{62}\) Appropriate choice of \( V_T \) is critical to the success of VTV. In general, a higher target \( V_T \) will result in a decrease in inspiratory effort—attempting to maintain a stable transpulmonary pressure and thus \( V_T \). Because the breath-to-breath change in the ventilator pressure is limited to avoid overshoot, the \( V_T \) fluctuates to some extent, but less so than without this adaptive mechanism.\(^{62}\) Appropriate choice of \( V_T \) is critical to the success of VTV. In general, a higher target \( V_T \) will result in a decrease in inspiratory effort—attempting to maintain a stable transpulmonary pressure and thus \( V_T \). Because the breath-to-breath change in the ventilator pressure is limited to avoid overshoot, the \( V_T \) fluctuates to some extent, but less so than without this adaptive mechanism.\(^{62}\) Appropriate choice of \( V_T \) is critical to the success of VTV.

**Patient-Ventilator Interaction During Neurally Adjusted Ventilatory Assist**

The most recent innovation in patient-ventilator interaction is the advent of neurally adjusted ventilatory assist (NAVA). NAVA uses the EADi not only to trigger onset of inflation but also to modulate inflation pressure in proportion to the infant’s diaphragmatic activity and to cycle into expiration when diaphragmatic activity wanes. The patient effectively determines the rate, volume, and inspiratory time of each inflation. This is an example of very sophisticated patient-ventilator interaction that has gained increased acceptance in the NICU, despite a lack of long-term studies that demonstrate the safety and efficacy of this approach. In
short-term studies NAVA has been shown to provide ventilation comparable to SIMV with lower $E_{A_{DIA}}$. A higher NAVA gain setting can lead to a reduction in $E_{A_{DIA}}$, reflecting a decreased inspiratory effort. Data on the most appropriate NAVA gain or the rationale and approach to set this parameter in premature infants have not been clearly described.

Although it is theoretically very attractive, use of NAVA assumes a mature respiratory control center, which is clearly not a valid assumption in very premature infants. The concern here is that the positive feedback principle of NAVA could accentuate the periodic breathing seen in preterm infants and lead to fluctuations in the arterial partial pressure of $CO_2$ ($Pa_{CO_2}$) and intermittently to excessively large inflations leading to volutrauma. Although the proponents of NAVA argue that excessively large inflations should not occur because of the stretch inhibitory Hering-Breuer reflex, it is equally likely that large inflations could trigger the Head paradoxical reflex, leading to an even larger inflation. There are no data on the stability of $V_T$ during NAVA or the number of excessively large inflations, nor are there long-term studies evaluating the effect of NAVA on lung injury and risk of chronic lung disease.

NAVA assumes the respiratory control center is functioning normally and it provides proportional assist to enable the patient to do what he or she is attempting to do: a strong inspiratory effort, such as may occur when the infant is disturbed, generates higher inflation pressure, while during hypoventilation little support is provided. A backup ventilator rate needs to be set appropriately to deal with periods of apnea, but the backup will not kick in when the infant merely hypoventilates because of shallow breathing. Fig. 16.13 illustrates the need for a backup ventilator rate to avoid hypoventilation during apnea. To reduce the risk of excessive or prolonged lung inflation during NAVA it is necessary to ensure limits to peak pressure and inspiratory duration are set adequately. Fig. 16.14 provides an example of a large and prolonged increase in ventilator pressure during NAVA.

Fig. 16.13  Neurally adjusted ventilatory assist (NAVA) during variable spontaneous respiratory drive. Recordings of ventilator pressure ($P_{Vent}$), flow, tidal volume ($V_T$), and diaphragmatic electrical activity ($E_{A_{DIA}}$) from a premature infant on NAVA show $P_{Vent}$ is proportional to $E_{A_{DIA}}$, while during periods of apnea the infant receives backup pressure-controlled breaths (red arrows) to prevent hypoventilation.
NAVA and VG take a diametrically opposite approach. VG was specifically developed for preterm infants with immature respiratory control. With VG, when there is a decline in inspiratory effort, more pressure is generated by the ventilator to maintain a stable \( V_T \). This is in contrast to NAVA with which a decline in breathing effort will result in lower ventilator pressure. This explains the findings of studies in which \( EADIA \) was shown to be higher during NAVA compared with VG.\(^{55}\)

**Patient-Ventilator Interaction During Noninvasive Ventilation**

Noninvasive ventilation (NIV) was one of the earliest forms of support used in neonates, and it is again used increasingly to reduce the need for intubation or facilitate weaning from invasive ventilatory support in preterm neonates. NIV is commonly provided with the same ventilators used for conventional mechanical ventilation. In contrast to invasive ventilation, in which the endotracheal tube bypasses the infant’s upper airway and ensures the transmission of the positive pressure to the infant’s airways, pressure transmission during NIV depends on the patency and resistance of the upper airway and on the large leaks present in an open system. The complexity of the mechanisms that determine upper airway patency and modulate its resistance makes it difficult to predict the degree of transmission of the positive pressure applied on the nose to the infant’s distal airways.\(^{66-71}\)

Sufficient transmission of the positive pressure during apnea is particularly important, because nasal ventilation is often used in infants with immature respiratory control. The efficacy of nasal ventilation during apnea is not consistent, and it is inadequate if the infant’s upper airway is not patent. In contrast, when the airway is patent the positive-pressure cycles produce lung inflation, as shown Fig. 16.15, but this is actually uncommon, because during apnea the upper airway is usually closed, which reduces the effectiveness of noninvasive IMV. A study demonstrated

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**Fig. 16.14** Neurally adjusted ventilatory assist (NAVA) and increased diaphragmatic activity. Recordings of ventilator pressure \( (P_{vent}) \), flow, tidal volume \( (V_T) \), and diaphragmatic electrical activity \( (EADIA) \) from a premature infant receiving NAVA show increased \( P_{vent} \) during a large and prolonged contraction of the diaphragm, resulting in a considerably larger \( V_T \) (red arrow).
that only 3% of ventilator inflations were accompanied by a measureable \( V_T \) with nonsynchronized NIV.\(^72\) Thus synchronization during NIV appears to be important. Unfortunately, the Graseby capsule used for synchronization of NIV in many countries is no longer available in the United States.

Adequate transmission of the positive pressure during nasal synchronized ventilation can increase \( V_T \),\(^73\) but this process appears to be more effective in infants with greater ventilatory demands who cannot achieve sufficient ventilation.\(^79\) Another important benefit of synchronized delivery of the positive-pressure cycle is that of unloading the respiratory pump, which is primarily reflected in a lesser inspiratory effort than with continuous positive airway pressure alone.\(^34,73,74\) In stable preterm infants, the reduction in breathing effort appears to be mediated by inhibitory reflexes rather than by decreased central drive, as illustrated by a significant attenuation in inspiratory effort during synchronous nasal IMV cycles (Fig. 16.16). In contrast, nonsynchronized ventilator cycles during nasal IMV do not increase ventilation or reduce breathing effort; instead, they appear to negatively affect the infant’s respiratory rhythm, as is observed with invasive IMV (Fig. 16.17).\(^34\)

Noninvasive NAVA can overcome the problems of nonsynchronized nasal IMV and appears to be quite effective.\(^75\) Its true potential needs to be evaluated in well-controlled clinical trials, which have not been conducted as of this writing.
Important interactions between the infant and the ventilator occur routinely during invasive and noninvasive ventilatory support. Some of these interactions can have significant effects on ventilation and gas exchange, but the extent to which the interactions affect long-term respiratory or neurologic outcome is unknown. Nonetheless,

**Summary**

Important interactions between the infant and the ventilator occur routinely during invasive and noninvasive ventilatory support. Some of these interactions can have significant effects on ventilation and gas exchange, but the extent to which the interactions affect long-term respiratory or neurologic outcome is unknown. Nonetheless,
they may play an important indirect role by prolonging respiratory support and disturbing the development of a stable and consistent respiratory rhythm in the preterm infant. Sophisticated microprocessor-controlled ventilators specifically designed for newborn infants can eliminate most instances of asynchrony when used optimally. When other devices are used, careful attention to optimizing ventilator settings using ventilator-generated waveforms to identify and correct instances of asynchrony can minimize the adverse effects of poor synchronization. The interaction between the infant and new modes of ventilation that become available should be examined before they are widely used.

Equally important is understanding that patient agitation is an important clinical sign of suboptimal ventilator support. It is often believed that gas exchange is poor because the patient is fighting the ventilator. More often, the patient is fighting the ventilator because the settings are suboptimal, leading to poor gas exchange. Therefore, rather than prescribing sedation or paralysis, the clinician must go to the bedside and carefully evaluate patient-ventilator interactions to identify the cause of agitation.

REFERENCES


