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INTRODUCTION TO THE BiPAP autoSV CLINICAL APPLICATIONS GUIDE

In the 1980s and most of the 1990s we firmly believed that Obstructive Sleep Apnea (OSA) and Central Sleep Apnea (CSA) were distinct disorders. We treated OSA with CPAP and CSA less effectively with oxygen, acetazolamide, etc. It is now becoming increasingly clear that these disorders overlap in many patients and that individualized approaches may be required to treat patients with what is now often termed “complex apnea.”

To understand how these disorders overlap, a physiology lesson is required. Upper airway patency is largely a product of the individual’s basic anatomy and the activity of the pharyngeal dilator muscles. If an individual has a sufficiently large pharyngeal airway where patency is present in the total absence of muscle activity, that individual will never develop obstructive sleep apnea. He or she may develop Central Sleep Apnea if the ventilatory control system becomes unstable, but OSA will never be a problem. On the other hand, if an individual’s pharyngeal anatomy requires dilator muscle activity to maintain patency, the potential for pharyngeal collapse and obstructive apnea is real and depends on the control/activity of these muscles.

The two principal drivers of pharyngeal dilator muscle activity are the respiratory system (i.e., input increases or decreases with respiratory drive) and negative pressure sensitive mechanoreceptors in the airway (primarily in the larynx). If an individual has particularly bad anatomy (a very small pharyngeal airway), the dilator muscles, driven by the negative pressure reflex, will compensate for the anatomy while awake, but may fail to do so at sleep onset when the airway closure often occurs. Such an individual will virtually always have predominantly obstructive sleep apnea. The complexity arises in the individual with a more borderline airway in whom fluctuations in respiratory drive to the upper airway muscles can importantly influence patency. In such an individual, the upper airway will generally remain patent allowing adequate ventilation as long as respiratory drive is stable. The problems arise when ventilatory control becomes unstable.

Ventilatory control instability can take a variety of forms. In Cheyne-Stokes Respiration (CSR) the combined prolonged circulation time (due to heart failure) and high hypercapnic responsiveness yield a waxing and waning of ventilation. Airway collapse at the nadir of the respiratory cycle can certainly occur, yielding obstructive apneas and hypopneas. At high altitude, due to low barometric pressure and thus hypoxia, ventilatory control instability commonly develops, yielding periodic breathing. Whether this can contribute to the development of obstructive apnea at
INTRODUCTION

high altitude or convert obstructive to Central Sleep Apnea varies and may depend on the severity of hypoxia and the individual’s response to the decreased PO2. It is unclear at this time whether CPAP-Emergent Central Sleep Apnea truly represents ventilatory control instability.5 In some individuals this seems to be the case, and would suggest that these patients have a collapsible airway (yielding primarily OSA on a diagnostic study) and high hypercapnic responsiveness (yielding Central Sleep Apnea when airflow obstruction is eliminated with CPAP). In others, the Central Sleep Apneas may simply be a product of an unstable state (frequent arousal and subsequent return to sleep) which can yield a waxing and waning of ventilation, a CPAP pressure that is too high or yet-to-be defined mechanisms. Finally, narcotic-induced Central Sleep Apnea is somewhat different from the disorders described above in that ventilatory drive is quite low in this disorder.6 Low drive can also yield unstable ventilation in the wake-sleep transition, although the cycles tend to be less regular and a bit more chaotic or ataxic. These individuals also may demonstrate both central and obstructive events, although the pathophysiologic mechanisms leading to obstructive apnea are less well defined.

References:
5) Thomas RJ, Daly RW, and Weiss JW. Low-concentration carbon dioxide is an effective adjunct to positive airway pressure in the treatment of refractory mixed central and obstructive sleep-disordered breathing. SLEEP 2005; 28:68-77.
Acknowledgements

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At Respironics we understand that therapy is only effective if it corrects the patient’s breathing at night. That is why we continue to look for new and better ways to deliver PAP therapy, such as our BiPAP autoSV system. This new device takes the complexity out of treating complicated sleep-disordered breathing. The result: the right therapy for the right patient – which can lead to greater patient satisfaction and improved lives.
BiPAP autoSV TECHNOLOGY

The BiPAP autoSV is a servo-ventilation device that was specifically designed to treat complicated sleep-disordered breathing (SDB) patterns such as Cheyne-Stokes Respiration, Complex or CPAP-emergent central sleep apnea, and a variety of other complicated breathing patterns commonly seen in a sleep center. The BiPAP autoSV utilizes clinically proven ventilation technologies, such as Digital Auto-Trak™ developed by Respironics.

The BiPAP autoSV Algorithm

Obstructive Component

Just like any other PAP (Positive Airway Pressure) therapy, care must be taken to appropriately titrate and treat the Obstructive Sleep Apnea component of these complicated breathing patterns. With this device, the EPAP (Expiratory Positive Airway Pressure) setting is established in the sleep lab utilizing the Respironics recommended titration protocol included in this guide.

Maintenance of Stable Breathing

The BiPAP autoSV attempts to maintain a stable breathing pattern for these patients by adjusting the level of IPAP (Inspiratory Positive Airway Pressure) on each breath, when necessary. A peak flow target is calculated for every breath based on a 4-minute moving window. The level of IPAP is determined on each breath based on the device’s algorithm.

Central Component

The device also has an automatically calculated back-up rate when central sleep apnea occurs. This rate is based on the patient's spontaneous breathing rate, but allows for natural pauses in a patient’s breathing. The purpose of this conservative back-up rate is to ensure that the device does not over-ventilate the patient. Given the different needs of each of these truly complicated patients, the device allows the automatic back-up rate to be turned off and a fixed rate to be initiated between 4-30 bpm.

The treatment of SDB with both central and obstructive components can be challenging. Expiratory positive airway pressure (EPAP) can be set to eliminate obstruction and servo-control algorithms (such as those in the BiPAP autoSV device) can be used to stabilize respiratory pattern. The cases described in this booklet will provide examples of how this can be accomplished.
For the complicated sleep apnea patient, everything in life is more difficult – from getting a good night’s sleep to functioning at work to actively participating in basic daily activities that most of us take for granted. Fortunately for the patients you have successfully diagnosed, our technology provides much-needed therapy that can transform their lives literally overnight.
In the United States, the Centers for Medicare and Medicaid Services (CMS) define Complex Sleep Apnea (CompSA) as: a form of central sleep apnea specifically identified by the persistence or emergence of central sleep apneas or hypopneas upon exposure to CPAP or an E0470 device (bi-level device in the S mode) when obstructive events have disappeared. These patients have predominately obstructive or mixed apneas during the diagnostic sleep study occurring at greater than or equal to 5 times per hour. With use of a CPAP or E0470, they show a pattern of apneas and hypopneas that meets the definition of CSA described below.

Central sleep apnea (CSA) is defined as:

1. an apnea hypopnea index greater than 5; and
2. Central sleep apneas/hypopneas greater than 50% of the total apneas/hypopneas; and
3. Central sleep apneas/hypopneas greater than or equal to 5 times per hour; and
4. symptoms of either excessive sleepiness or disrupted sleep.

The prevalence of complex sleep apnea in patients referred to a sleep center has been described by a group from the Mayo Clinic in the US as well as a group from Australia. In the Mayo Clinic study,\(^1\) the prevalence of complex sleep apnea syndrome (in 223 adults consecutively referred over 1 month) was 15 percent. In the Australian study,\(^2\) the prevalence of CSA-CPAP was found to be 13 percent.

Although it seems that the above studies agree on the prevalence estimates, the literature is currently unclear on the treatment approach for these patients. Many feel that with a few weeks of CPAP treatment the emergent central sleep apneas will clear. Others feel that utilizing a back-up rate with a bi-level S/T type of product is more effective. However, to date there has been very little research on this subject.

The BiPAP autoSV system has effectively treated these types of patients with a manually titrated EPAP, an automatically calculated or fixed back-up rate and the breath-to-breath adjustment of pressure support. The following case is an example of how the BiPAP autoSV effectively treats the Complex Sleep Apnea patient.

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1) Morgenthaler, et al. Sleep 2006; 29 (9):1203-9
Figure 1:1 is a 5-minute tracing showing typical disordered breathing events in a patient during the diagnostic night. All of the events are hypopneas (indicated by the Flow and NAF channels, as shown in pink shading). The hypopneas are brief and punctuated by an arousal (orange shading on O1M2 channel). There is minimal desaturation.

Clinical polysomnography does not allow central hypopneas to be distinguished from obstructive ones. Esophageal pressure monitoring is needed for this. Nevertheless, most of the events in this figure exhibit well-rounded flow patterns (except for the third hypopnea from the right). That is, they lack the characteristic blip-plateau pattern suggestive of upper airway obstruction. This is one clue that the events might be primarily central. Other clues include the lack of snoring and the lack of thoraco-abdominal paradox.
Later in the night, however, many of the hypopneas are associated with snoring, and there is the classic blip-plateau flow pattern in the second and third events from the right. Also, note that in the third hypopnea from the right there is crescendo increase in the abdominal effort without an increase in flow, suggesting that the upper airway is limiting the amount of flow the patient can generate. Thus, upper airway obstruction appears to be contributing to the disordered breathing in this patient, and therefore we anticipate that CPAP therapy would be helpful.

Even if we did not see signs of obstruction, we would still attempt CPAP therapy in this situation, since the distinction between central and obstructive hypopneas is not definitive in clinical studies.
The patient has now been placed on CPAP at a pressure of 6 cm H₂O. This is associated with several central sleep apneas. During the diagnostic night, we did not see any central sleep apneas; we simply saw hypopneas. Thus, we would classify this patient as having "CPAP-emergent centrals" since the central events seemed to emerge once the patient started CPAP therapy. However, the diagnostic study suggests that the patient had some underlying predisposition to central events (because many of the hypopneas appeared central in nature), and therefore it is not a complete surprise that we observed central events once the patient was on CPAP.

It is a surprise, however, that the patient exhibited central sleep apneas (and not central hypopneas) on CPAP. It’s also a surprise that the disordered breathing seems to be getting worse on CPAP. (The RDI was higher on CPAP than during the diagnostic night). We would anticipate that the relief of obstruction would improve the RDI at least partially, but it does not. Thus, this is not a case in which there is simply incomplete resolution of disordered breathing on CPAP. Rather, it is a case in which there is no resolution at all.

The cause of CPAP-emergent centrals is not clear. It may be a maladaptive response to CPAP in which patients take larger than normal breaths because they are not accustomed to breathing on positive airway pressure. The larger-than-normal breaths produce “post-hyperpnea pauses.” If the patient has a predisposition to central events, which we suspect in this patient, then some of these pauses might be prominent enough to meet criteria for a central sleep apnea. There is evidence that CPAP-emergent central sleep apneas improve over time in many patients, presumably because they become more habituated to the pressure.
Since hypopneas are still present (see the first and fourth events from the right of Figure 1:3), it is reasonable to increase the CPAP pressure further to see if there is any improvement.

Further increases in CPAP pressure do not improve the disordered breathing; central sleep apneas persist. Note that the technician indicated that there was a high leak, and that the patient exhibited mouth breathing at the top of the record. This could be another reason that CPAP does not seem to work. Mask leak or mouth breathing, however, would not produce CPAP-emergent central sleep apneas. Rather, they would be associated with obstructive-looking events (abdomen and thoracic movement without airflow). Nevertheless, it is important to check for mask and mouth leaks during the titration procedure.

This was deemed an unsuccessful titration study, and the interpreting physician suggested a repeat titration using bi-level S/T with a back-up rate of 12.
Bi-level S/T is being administered at 9/5 with a back-up rate of 12. The best part about this study is the aggressive back-up rate which prevents apneic “pauses” that would otherwise destabilize the ventilatory control system; an apnea leads to a larger ventilatory overshoot, which then produces another apnea, and so on. Even though the ventilator-administered breaths (indicated by the arrows) do not provide sufficient tidal volume (because the differential is only 4 cm H₂O), there are fewer arousals and more stable breathing than during the diagnostic and CPAP nights.
If we increase the differential (Figure 1.6), then we risk amplifying ventilation more than necessary during spontaneous breaths.

The differential between IPAP and EPAP is now 6 cm H₂O. While breathing is quite stable in this tracing, greater than 70 percent of the breaths are ventilator-triggered. Essentially, the patient is being completely ventilated, like someone in the ICU with respiratory failure. Because there are no large overshoots or undershoots, and because there are few arousals and no desaturations, some might consider this a successful way to manage this patient. However, it does not allow the patient to remain in control of the patient’s own ventilation and is probably excessive.
Why is Bi-level S/T not the most effective treatment?

Almost all of the breaths in Figure 1:7 are ventilator-triggered (i.e., the ventilator has completely “captured” the patient’s respiration). It is more appropriate to use a less aggressive approach to manage this patient (e.g., with a BiPAP autoSV device). BiPAP autoSV provides breaths only when they are needed, and it does not amplify the ventilatory overshoot (which makes the patient “more apneic” and thereby ventilator-dependent). Rather, with BiPAP autoSV, the patient can remain in control of his or her own ventilation for a larger percentage of breaths.

SUMMARY

The Complex Apnea Patient

This patient with an unstable ventilatory control system would be more appropriately managed with a device such as the BiPAP autoSV, which acts to stabilize the ventilatory control system. Bi-level S/T, on the contrary, tends to destabilize an already unstable ventilatory control system primarily by overventilating the hyperpnea breaths and driving the patient further into an apneic state (and thus making him or her even more dependent on back-up, ventilator-triggered breaths for adequate respiration).

BiPAP autoSV provides a form of ventilatory support that tends to stabilize the ventilatory control system, whereas bi-level S/T tends to destabilize it in patients with Complex Sleep Apnea. One can always regulate the breathing pattern with bi-level S/T and an aggressive back-up rate, but BiPAP autoSV provides a more physiologically appropriate form of treatment since it aims to correct the primary underlying abnormality.
The upper airway is held open by the contraction of skeletal muscles and motor neuron input. When a patient experiences a central sleep apnea due to the brainstem shutting down, both the diaphragm and the tongue have reduced neural inputs from the brainstem, which will cause both the diaphragm and the tongue to stop working. As a result, the tongue muscles relax and the tongue falls into the back of the throat and obstructs the airway.

For patients who have central sleep apneas during the night, adjustment of the CPAP level is necessary to prevent the tongue muscles from deactivating and occluding the upper airway. During periods of low ventilatory motor output, demonstrated when the patient encounters a decrease in respiratory drive or when the brainstem controller shuts down, the tongue muscles relax and the airway obstructs, causing a higher upper airway resistance.

When the brainstem controller activates (peak of the motor output tracing), the airway opens ($R_{UA}$ decreases) because the tongue contracts and stiffens the airway. However, if the patient is being supported with servo ventilation, he or she may encounter periods when the brainstem still shuts down and respiratory support is provided completely by the servo ventilator. It is critical to ensure that the upper airway is patent with the delivery of a breath.

Following is an example of this phenomenon seen during the diagnostic night, CPAP night and with support from the BiPAP autoSV system.
Figure 2:1 shows purely obstructive apneas; there is respiratory effort throughout the duration of the apnea.

While these are obstructive apneas, the events in Figure 2:2 are mixed. The abdominal and thoracic movements decrease to near zero in several of the events.
In Figure 2.3 the patient exhibits events later in the night that appear more clearly mixed than in the previous tracings. The second and third events could be labeled as mixed apneas.

Some of the events in Figure 2.4 could be scored as mixed. The presence of mixed apneas indicates that the patient’s ventilatory control system might be unstable. Thus, relief of upper airway obstruction with CPAP alone might not be sufficient to eliminate the disordered breathing since ventilation may continue to fluctuate due to ventilatory control system instability. In these patients, treatment with the BiPAP autoSV device might be necessary to regulate the breathing pattern.
This patient has substantial upper airway obstruction. This is identified by evaluating the impact of the lack of inspiratory flow (indicated by arrows) with a machine-delivered breath along with the minimal movement of the thorax and abdomen. This may appear because the airway is severely narrowed or closed. As a result, the pressure provided to the patient does not move the thorax or abdomen in sync with the breath. Thus, increasing the EPAP might help. If the servo-ventilation is being triggered, then the IPAP is not high enough to administer reasonable flows during the apnea/hypopnea breaths.

Figure 2:6 highlights a sample of closed airway central apnea. This is indicated by the arrows, showing a decrease in flow with a machine-delivered breath.
Figure 2.7 is a two-minute tracing taken from Figure 2.6. First, notice the red CFlow signal from 0 to 20 seconds. There is a central sleep apnea at the beginning followed by five spontaneous breaths. Note that during the five spontaneous breaths only a small amount of inspiratory pressure is applied (see the PatPress channel). This is good because we do not want to amplify these spontaneous breaths (i.e., we don’t want to amplify the ventilatory overshoot). If we do amplify the spontaneous breath, then this will produce a subsequent central sleep apnea.

In the 20 to 50 second area, the patient has a central sleep apnea (arrow on patient CFlow channel) upon falling back to sleep after the five spontaneous breaths. We know it is a central sleep apnea because there is no chest or abdominal excursion. BiPAP autoSV detects the central sleep apnea and applies two ventilator-triggered breaths (indicated by downward signal and arrow on PatPress channel). The downward spike in PatPress indicates that EPAP is switched to IPAP.

The result of the ventilator-triggered breaths is two very small tidal volume breaths. Why is this happening? The tidal volumes should be larger, especially on the second ventilator-triggered breath when there is considerable inspiratory pressure applied (arrowhead). The reason for the small tidal volume breaths is that the airway is closed (or nearly closed). Even though the patient is having a “central” apnea, it is labeled as such only because there is no chest/abdominal effort to reveal the obstructed airway. The patient is having a “closed airway central.” This is not uncommon because the diaphragm turns off during a central sleep apnea, and the upper airway muscles may also turn off. As a result, the airway loses its tone and closes.
Figure 2.8 demonstrates how BiPAP autoSV should respond with an open airway during a central event. EPAP has been increased to 10 cm H₂O, thereby allowing IPAP to deliver adequate flows during the central sleep apnea. When the patient receives a machine-triggered breath, the flow channel demonstrates an increase and that PatPress and CFlow fluctuations are exactly anti-synchronous. Even though the patient has a respiratory event here, the expected result is for breathing to soon be stabilized.
Breathing has stabilized with BiPAP autoSV.

SUMMARY
It is important that the EPAP is titrated effectively. Normally, with a bi-level platform, we titrate EPAP to eliminate obstructive apneas and IPAP to eliminate hypopneas. Thus, if obstructive hypopneas persist on bi-level, we simply increase the IPAP (and not the EPAP). This is not suggested when using the BiPAP autoSV. The BiPAP autoSV needs to know how much flow is likely resulting from a given IPAP (it is a peak flow stabilizer). It is much better to raise the EPAP to keep the airway as patent as possible so that minimal amounts of IPAP are adequate to prevent ventilatory overshoot and further instability with the ventilatory control system.
Cheyne-Stokes Respiration (CSR) is another form of central sleep apnea (CSA). CSR stems from a variety of different issues but is commonly associated with patients who have a cardiac history; more specifically, the congestive heart failure population. One issue leading to this pattern is the increased chemosensitivity (responsiveness) for CO$_2$. Other issues include hypocapnia resulting from lung edema (high filling pressures) and a prolonged circulation time (reduced ejection fraction).

The combination of these factors contributes to destabilizing the ventilation that leads to the typical decrescendo and crescendo pattern of breathing.

The typical cycle time for these patients is 60 to 90 seconds. CSR occurs primarily in non-REM sleep. In severe patients (NYHA III/IV) it can also be detected in wakefulness. However, it is uncommon in REM sleep likely due to decreased hypoxic and hypercapnic responsiveness. High chemosensitivity responsiveness and increased circulation time are required to manifest CSR. This is not seen in all patients with congestive heart failure.

The CSR breathing pattern can be seen as well in patients with brain lesions, strokes, traumatic brain injuries, brain tumors, renal failure and at high altitude.

The therapeutic target of the BiPAP autoSV device is to stabilize ventilation (waning – waxing) during the initial phase of CSR. A quick response by the device to stabilize the hypopneic episodes and stabilize CO$_2$ levels will help to minimize the responding hyperpneic phase. This combination leads to stabilized breathing.

Following is an example of this phenomenon during the diagnostic night and treatment night with the BiPAP autoSV device.
This patient has classic Cheyne-Stokes Respiration (CSR). Figure 3:1 is a five-minute screen; the cycle period is approximately one minute. Here, the events look almost completely central.

Several of the events, however, have a mixed component, indicating that upper airway obstruction is contributing to the process (indicated by the arrows). Note the snoring and the fact that there are thorax and abdominal movements without flow at the end of the events. Also, the first breath after the apnea is large. If there was no obstruction, the first breath would be small, and the patient would crescendo into the hyperpnea phase.
This 2.5-minute tracing (Figure 3:3) clearly shows that there is upper airway closure during the central sleep apnea, as chest-abdominal movements produce no flow toward the end of the event.

As usual, breathing tends to stabilize during REM sleep in patients with CSR. The upper airway is typically at its most susceptible to collapse during REM due to skeletal muscle paralysis. So, why are we not seeing upper airway collapse here? We already saw earlier that the patient had complete upper airway obstruction in NREM sleep. Thus, we should also see it here. However, note in this tracing that there is no waxing and waning of respiratory effort (thorax and abdominal movements are fairly constant). Apparently, central sleep apnea is required to produce upper airway obstruction in this patient. Figure 3:4 indicates that if you control the patient’s CSR, then he or she will be able to maintain upper airway patency even during the most vulnerable stage of sleep.
CSR PATIENT – BiPAP autoSV NIGHT

(Please note: the flow signal is not optimal in Figure 3:5). With the application of BiPAP autoSV at minimal settings, you can already see that there is a more regular breathing pattern compared to the diagnostic night. BiPAP autoSV works by trying to maintain a constant peak inspiratory flow. It does so by administering more inspiratory support during the “apneic” phase than during the “hyperventilation” phase. Thus, in a simplistic way, you can think of BiPAP autoSV as a bi-level device with a rate during a central sleep apnea, pressure support during the hypopneic phases, and CPAP alone when there is normal spontaneous breathing. Note that although the flow pattern has not been completely regularized here, there are no arousals or desaturations and the abdomen and thorax movements are less oscillatory.
In Figure 3:6, BiPAP autoSV does not seem to be working. However, a closer look could reveal that these are obstructive hypopneas and that the EPAP needs to be increased.

BiPAP autoSV is working fairly well here but the EPAP still needs to be increased. The waxing and waning CSR that we saw in the diagnostic night is no longer seen.
In Figure 3:8, BiPAP autoSV is not eliminating the apnea/hypopnea. An increase in both EPAP and IPAP is probably necessary to deliver more reasonable tidal volumes.

In Figure 3:9, breathing has regularized but hypopneas are still present.
BiPAP autoSV is now successful as shown in Figure 3:10. There are no arousals.

The definition of “success” needs to be determined. Some clinicians might not consider this a success because of the waxing and waning effort and the occasional small breaths. However, airflow and sleep state are fairly stable.
SUMMARY

Why Standard Bi-level S/T is Not Effective

If standard bi-level PAP therapy with a back-up rate was administered to this patient, we could successfully treat the apnea phase because the back-up rate would give breaths even when the patient was not spontaneously breathing. However, in order to provide a reasonable tidal volume during triggered breaths (i.e., during the apnea), the patient would need a large differential between IPAP and EPAP, approximately 10 to 15 cm H₂O. During the hyperpnea phase, this large differential would augment the already large tidal volumes, and eventually produce additional central sleep apneas and exacerbate the swings in ventilatory motor output.

With BiPAP autoSV, it is not necessary to choose between the tradeoff of a large tidal volume to be administered during the apnea phase and the risk of excessively large tidal volumes during the hyperpnea phase. The device will regulate the volume as long as the airway is patent and the IPAP pressures are set appropriately.
In the past, drug treatment with opioids for chronic pain was common in cancer patients. Today, we find widespread acceptance of opioids as long-term therapy for chronic pain unrelated to cancer. An increasing number of patients with nonmalignant chronic pain are receiving around-the-clock pain relief through opioid therapy.

Chronic pain and sleep disturbances frequently occur together. It is unclear if they are causally related or represent two different disorders.\(^1\) Approximately 70 percent of patients suffering from chronic pain also report sleep disturbances.\(^2\) Around-the-clock intake of pain killers, opioids, methadone and benzodiazepines is common. Experience shows that treatment of chronic pain with drugs increases the risk of developing SDB while undergoing therapy. Different breathing patterns can be found such as OSA, Prolonged Obstructive Hypopneas (HYP) and CSA.\(^1,3\) Drug treatment suppresses the respiratory drive and contributes to the development of CSA.

Studies show a direct dose-response relationship between central sleep apnea and intake of methadone and benzodiazepines. The results show a higher than expected prevalence of SDB in chronic pain patients treated with opioids. Where OSA is known to be underdiagnosed but has been estimated at approximately two to four percent of the adult population, obstructive and central sleep apnea syndromes occurred in the studied population at a far greater rate (75 percent) than is observed in the general population. CSA is estimated at five percent in people older than 65 years, and from one and a half percent to five percent in men younger than 65 years of age.\(^4\)

To treat the underlying SDB in chronic pain patients with combined SDB patterns (CSA, OSA and flow limitations), intelligent devices are necessary to treat the different SDB patterns.

Following is an example of this phenomenon during a treatment night with the BiPAP autoSV device.

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3) Roehrs et al. Sleep loss and REM sleep loss are hyperalgesic. Sleep 2006  
CENTRAL SLEEP APNEA

The patient is drifting in and out of sleep in Figure 4:1. Look at the flow tracing. Breathing is very irregular, especially if you disregard the ventilator-triggered breaths (noted by downward line on the PatPress channel). Of note, the irregularity is non-periodic, which is quite different from the marked periodicity seen in Cheyne-Stokes Respiration (CSR).

The cause of non-periodic central sleep apnea is not clear and is likely multifactorial. It's safe to say, however, that it is not due to an unstable ventilatory control system as seen in CSR. The cardinal feature of ventilatory control instability is a strong crescendo-decrescendo periodic breathing pattern. Without such a pattern, it is difficult to attribute the central sleep apneas to ventilatory control system instability.

In general, the more periodic the ventilatory fluctuations, the more likely the fluctuations are due to respiratory control instability. The less periodic (or more irregular) the ventilatory pattern, the less likely the ventilatory pattern is due to respiratory control instability.
Figure 4:2 is a figure from early Stage 2 sleep, and it reveals the patient’s physiology: he or she is hypoventilating. Eight of the 14 breaths in this 2-minute tracing are ventilator-triggered. While the ventilator only delivers a breath once every 8 to 9 seconds, it is still greater than the patient’s intrinsic respiratory rate. This figure indicates that the patient’s respiratory drive is too low and is probably the cause of central sleep apneas. This is often seen in patients taking medications that suppress respiration, such as narcotics. A recommendation for this patient could be to increase the back-up rate to at least 9 or 10 breaths per minute.

In the third epoch from the left, at time 70 seconds, the patient “stacks” a spontaneous breath on top of a ventilator-triggered breath. Stacking should not be a problem unless it happens often or causes arousal. While a faster back-up rate could potentially produce more stacking, it is likely necessary, especially in patients who hypoventilate.
Figure 4:3 is taken from Stage 2 sleep later in the night. Breathing is completely stable. Thus, the patient has compensated. **NOTE:** In the previous discussion, it was noted that the patient’s back-up rate could be increased to approximately 8 to 9 bpm. However, if during the diagnostic night the patient demonstrates the ability to stabilize breathing on his or her own, then it is probably not necessary to be overly aggressive with the treatment (i.e., back-up breaths could only be administered as “rescue” breaths [possibly 8 breaths per minute] until the patient can recover on his or her own).

Figure 4:4 is showing stable breathing. It is mainly at the wake to sleep transition (see Figure 4:5) that the patient’s ventilatory control system has trouble maintaining adequate ventilation.
Figure 4:5 is light Stage 1 sleep, and the patient’s breathing is becoming variable again. Deciding what to do in these cases can be difficult. However, one should not be too concerned about the patient’s variable breathing because there is not significant desaturation; the patient is likely to compensate eventually on his or her own with help from the BiPAP autoSV device.

After a period of time, the patient again exhibits stable breathing, as shown in Figure 4:6.

**SUMMARY**

BiPAP autoSV worked fairly well in this patient with central sleep apnea due to hypoventilation (non-periodic central sleep apnea). One recommendation could be that perhaps a slightly faster back-up rate would provide a smoother transition from wake to sleep. This can be accomplished with the BiPAP autoSV by simply turning off the auto back-up rate and substituting a somewhat more aggressive fixed back-up rate.
LONG-TERM FOLLOW-UP WITH ENCORE DATA MANAGEMENT SOFTWARE
At Respironics, we appreciate how much effort you put into fitting each patient with therapy that will not only be effective, but also be something they can be comfortable living with. We make every effort to develop products that are designed around your patients, not around technology. The result is therapy options that are easier to adapt to and live with for long-term compliance.
ENCORE DATA INTERPRETATION

Encore patient management software solutions provide physicians and sleep providers the ability to manage their patients’ sleep data objectively. EncorePro™ client-based and EncoreAnywhere™ web-based platforms monitor and report basic and advanced compliance information using data collected from Respironics’ sleep therapy devices. Encore reports compliance data including hours of use, pressure profile, apneas and hypopneas, periodic breathing, patient triggered breaths, patient and machine rate, peak flow, and large leak. Encore can also help manage patient files, create cross patient reports and track the overall treatment progress of your patient populations. Through graphical and statistical illustrations, a patient’s therapeutic history is displayed allowing you to better manage your patients and their compliance outcomes.

Encore reports are divided into five sections. These sections will be discussed on the following pages using actual data from patients using the BiPAP autoSV device.
BiPAP autoSV - PATIENT 1

The data provided by Encore comprises device usage, long-term trending and daily detailed trending of data that allow the clinician to determine both compliance with therapy and effectiveness of treatment. This is very valuable information, particularly in patients with complicated SDB who are often sick and have various co-morbidities. In these patients, it is important to objectively confirm that the SDB treatment is working. Simply relying on the resolution of subjective symptoms is not adequate.

Compliance Information

The initial portion of the Encore report provides valuable data on the number of hours per day and number of days that the patient is actually using the device. If that number fell below four hours for any particular day the green bar would turn red. This provides a quick and simple visual indication of the usage patterns of the patient. For this case, compliance is not an issue. The patient has used the device more than four hours on each of the 35 days shown in the report.

LONG-TERM TRENDS
Pressure Profile

The maximum and minimum IPAP settings are shown here (16 and 10 cm H2O, respectively). In this case, EPAP is set 1 cm H2O below IPAPmin, likely for a degree of comfort for the patient. Typically, EPAP and IPAPmin are set to the same level to deliver CPAP during stable breathing. The average peak IPAP for each day is shown in gold.
**Periodic Breathing/CSR**

The percentage of the night spent in periodic breathing varies across the 35 days. Comparing the percent of the night in periodic breathing shown in the Encore report to the percent of the night in periodic breathing shown in the diagnostic study can be a valuable tool. In this case, over the course of the 35 days, this patient spent approximately 5.1 percent of the night in periodic breathing.

**Apnea/Hypopnea Index**

The average AHI in this patient was 4.5/hr (lower right-hand corner of graph). The reduction in the AHI to <5.0/hr is a clear indication that the device is effectively treating the patient over the long-term course of treatment. It is always a goal to try to reduce the AHI to approximately 5/hr.

For the patient above, the long-term trending information makes it clear that the patient is being adequately treated by the BiPAP autoSV device. Looking at the daily details could possibly garner further information.
Look carefully at the following daily detail page from the same patient:

- The patient displays large mask leak at the beginning of this particular night. This is called out by the dark black bars at the top of the leak graph (highlighted red circle above).

- Controlling leak is important in order to have the most effective algorithm.
  - The high leak in this case could possibly lead to ineffective treatment (as evidenced by the residual apnea and hypopnea events circled above).
  - High leak could also lead to the IPAP pressure being driven to the maximum level (as evidenced by the pressure profile circled above).

**BiPAP autoSV - PATIENT 2**

To understand other areas to look for when reviewing the daily detail reports, let’s look at another patient. To determine what, if any adjustments are necessary, we need to see single representative nights of what the IPAP, EPAP and the back-up rate are doing. How many breaths were being triggered by the patient and how many by the ventilator? Were the residual events central or obstructive? This data is shown below.

**Current Settings:**

<table>
<thead>
<tr>
<th>EPAP</th>
<th>10 cm H₂O</th>
<th>IPAP&lt;sub&gt;min&lt;/sub&gt;</th>
<th>10 cm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate</td>
<td>Auto</td>
<td>IPAP&lt;sub&gt;max&lt;/sub&gt;</td>
<td>15 cm H₂O</td>
</tr>
</tbody>
</table>
DAILY DETAILS - NIGHT 1

The first two hours look good. Note that during the first two hours, peak IPAP fluctuated between the minimum and maximum values and the patient had relatively few events.

Between hours 2 and 4 (and later), however, the patient spent much of the time in periodic breathing, and the peak IPAP is virtually “maxed out.” It is doubtful that these are obstructive apneas, since the EPAP is relatively high; however, referring to the titration study could confirm this.

Recommendation 1:
Increase the IPAP\textsubscript{max} to 20 cm H\textsubscript{2}O. This will allow BiPAP autoSV to apply a differential pressure (IPAP – EPAP) of up to 10 cm H\textsubscript{2}O during central apneas and periodic breathing events. This should be adequate to deliver enough tidal volume to eliminate the event. Preferably, the peak IPAP should not actually reach the IPAP\textsubscript{max} very often as the IPAP\textsubscript{max} is simply a precautionary measure to prevent excessive PAP.

Also, it is possible the residual hypopneas (brown bars) are actually periods where the patient had central sleep apnea and the ventilator-triggered a breath. However, the ventilator did not deliver enough tidal volume and hence a “hypopnea” occurred.

Recommendation 2:
Check the back-up rate versus the patient rate. If the back-up rate is adequate, there would be a decrease in residual apnea events. If the back-up rate is not adequate, it is recommended to increase the back-up rate to approximately 2-3 bpm below the patient’s resting rate (see titration protocol).

The purple line depicts the percent of patient-triggered breaths during the night. Between hours 2 and 4 (as well as between hours 5 and 6 and 7 and 8), when the patient seems to be having the most trouble, a significant proportion of the breaths are ventilator-triggered, indicating that indeed the residual events are probably central sleep apneas.
Here is another night for the same patient (with the same settings) showing an excellent response to the BiPAP autoSV device. The patient’s data looked like this for approximately half of the nights. We would like to see these types of trends for all of the nights. **The amount of ventilatory control system instability can vary from night to night, in different sleep stages and in different positions.** Thus, bringing the patient back to the sleep lab for a single night will not provide an adequate picture of how the patient responds to BiPAP autoSV. The value of Encore reporting is that one can observe data from many nights.

**Had we just observed this single night in the lab, we would not have known to change some of the ventilator settings, and the patient would receive suboptimal treatment.**
SUMMARY

Although there is nothing wrong with seeing ventilator-triggered breaths, the presence of ventilator-triggered breaths indicates that the patient is continuing to have central sleep apneas (i.e., the ventilatory control system has not been stabilized). The benefit of the BiPAP autoSV is that it has the potential to stabilize the unstable ventilatory control system, which is the primary problem in many patients with complex sleep apnea. The breathing pattern could be normalized using bi-level S/T with an aggressive back-up rate (in which case the majority of breaths would be ventilator-triggered and the bi-level S/T completely ventilates for the patient). But simply normalizing breathing is not the goal. The goal is to correct the underlying problem (the unstable ventilatory control system) so that triggered breaths are no longer needed.
With complicated patient needs come complicated challenges for you and your team. We’ve worked hard to provide you with tools like BiPAP autoSV that can help to simplify treatment, reduce patient complaints and free more of your time to work with other patients. It’s a patient-focused approach to design that’s intended to simplify healthcare management for you.
Whether patients have obstructive sleep apnea, central sleep apnea, neuromuscular disease or restrictive thoracic disorders, bi-level therapy may be appropriate for treating the underlying disorder. Respironics is continually looking for new and better ways to deliver bi-level therapy. Understanding how the devices function and their methods of titration are critical to effectively treating patients. And, matching the right therapy to the right patient can lead to improved outcomes and better patient satisfaction.
BiPAP autoSV is designed for patients who have mixed apneas, complex apnea, periodic breathing or central apnea.

BiPAP autoSV provides three types of support:
- CPAP or BiPAP to prevent airway collapse during OSA events
- Back-up rate for central apneas
- Pressure support ventilation during periods of hypoventilation

Settings for autoSV:
- Rate
- Rise Time
- Inspiratory Time
- EPAP = Expiratory Pressure
- IPAP\text{_{min}} = Minimum Inspiratory Pressure
- IPAP\text{_{max}} = Maximum Inspiratory Pressure

CPAP may be a requirement for patients prior to the initiation of BiPAP autoSV.

Reimbursement criteria for patients with central apnea:
- AHI >5, AND
- Central apnea >5
- Excessive daytime sleepiness
- Excessive daytime sleepiness of the total events
TITRATION PROTOCOL FOR BiPAP autoSV FOR PERIODIC BREATHING

Switch mode to BiPAP autoSV

Patient demonstrates periodic breathing during diagnostic sleep study

EPAP: 4 cm H2O
IPAPmin: same as EPAP
IPAPmax: 10 cm H2O above IPAPmin
Rate: Auto
Rise Time: 2 or 3

ASSESS PATIENT

Observe for obstructive apneas
If yes: Raise EPAP, IPAPmax and IPAPmin by 1 cm H2O
If no: Continue

Observe for partial airway obstruction
If yes: Check for leaks, if leak is not identified and if hypopnea is obstructive in nature, increase EPAP by 1 cm H2O, maintain difference between IPAPmax and IPAPmin
If no: Continue

Central apneas not corrected by Auto Rate
If yes: Set fixed rate to a minimum of 10 BPM or 2 below starting respiratory rate, set I-time for 1.2 sec
If no: Continue

Observe for continued periodic breathing
If yes: Raise IPAPmax by 2 cm H2O
If no: Continue

BIPAP autoSV Prescription:
IPAPmin = _______ cm H2O
IPAPmax = _______ cm H2O
EPAP = _______ cm H2O
Interface: ____________
Rate = _______ BPM
I-time = _______ sec (if non-auto rate)

This protocol is recommended for adult patients only.
BiPAP autoSV is designed for patients who have mixed apneas, complex apnea, periodic breathing or central apnea.

BiPAP autoSV provides three types of support:
- CPAP or BiPAP to prevent airway collapse during OSA events
- Back-up rate for central apneas
- Pressure support ventilation during periods of hypoventilation

Settings for autoSV:
- Rate
- Rise Time
- Inspiratory Time
- EPAP = Expiratory Pressure
- IPAP_{min} = Minimum Inspiratory Pressure
- IPAP_{max} = Maximum Inspiratory Pressure

CPAP may be a requirement for patients prior to the initiation of BiPAP autoSV.

Reimbursement criteria for patients with central apnea:
- AHI >5, AND
- Central apnea >5
- Excessive daytime sleepiness
- Central apneas are greater than 50% of the total events

or

Criteria for complex apnea:
- AHI >5, AND
- Emergence or persistence of central apnea upon exposure to CPAP or BiPAP S therapy
- Patient also meets criteria for central sleep apnea during treatment with CPAP/BiPAP S therapy
BiPAP autoSV PROTOCOL FOR COMPLEX BREATHING

Switch mode to BiPAP autoSV

Patient cannot tolerate CPAP titration due to central apnea emerging during OA titration

EPAP: last pressure that relieved obstructive apnea
IPAP_{min}: same as EPAP
IPAP_{max}: 25 - 30 cm H₂O
Rate: 8 - 10 BPM or 2 below spontaneous rate
I-Time: 2 - 3
I-Time: 1.2 sec

Observe for obstructive apneas
If no
Observe for partial airway obstruction
If no
Observe for central apneas
If no

If yes
Raise EPAP, IPAP_{min} and IPAP_{max} by 1 cm H₂O

If yes
Check for leak; if leak is not identified, and if obstructive in nature, increase EPAP by 1 cm H₂O
If caused by periodic breathing, increase IPAP_{max} by 2 cm H₂O

If yes
Increase rate by 1 BPM

Return to ★
Return to ★
Return to ★

BiPAP autoSV Protocol:
EPAP_{min} = _____ cm H₂O
IPAP_{max} = _____ cm H₂O
EPAP = _____ cm H₂O
Interface: __________

Recommendation:
This protocol is recommended for adult patients only.
In the end, everything you do is about improving lives. And what we do at Respironics is build solutions to help you achieve that mission in simpler, more sensible ways. We thank you for trusting Respironics in your efforts to provide better care and improved patient outcomes.
OVERVIEW

(HCPCS E0470 and E0471)

The following information describes the DME Regional Carriers’ (DMERCs)/DME Program Safeguard Contractors’ (DME PSCs) medical policies for Respiratory Assist Devices related to central and complex apnea and periodic breathing. Information was obtained from the DMEPOS Supplier Manuals and Local Coverage Decisions from each region. This is to be used as a guide. For specific instructions, please reference your Supplier Manual, or contact your DMERC/DME PSC medical director or DME Medicare Administrative Contractor (MAC) provider helpline.

General Coverage Guidelines

The treating physician must be one who is qualified, by virtue of experience and training in noninvasive respiratory assistance, to order and monitor the use of respiratory assist devices.

For the purpose of the policy, polysomnographic studies must be performed in a sleep study laboratory, and not in a home or in a mobile facility. The laboratory must also comply with all applicable state regulatory requirements. For the purpose of the policy, arterial blood gas, overnight oximetry and polysomnographic studies may not be performed by a DME supplier. This prohibition does not extend to results of studies conducted by hospitals certified to do such tests.

If at any time the patient discontinues use of E0470 or E0471, the supplier is expected to ascertain this and discontinue billing for the equipment and related accessories and supplies.

The treating physician must fully document in the patient’s medical record, the symptoms characteristic of sleep-associated hypoventilation, such as daytime hypersomnolence, excessive fatigue, morning headache, cognitive dysfunction, dyspnea, etc.

Central Sleep Apnea or Complex Sleep Apnea

Note: All coverage criteria below, including those outlined in the CSA and CompSA definitions, must be met for coverage.

CRITERION A

The diagnosis of central sleep apnea (CSA) or complex sleep apnea (CompSA).

and

CRITERION B

The ruling out of CPAP as effective therapy if either CSA or OSA is a component of the sleep-associated hypoventilation.

and

CRITERION C

Significant improvement of the sleep-associated hypoventilation with the use of an E0470 or E0471 device on the settings that will be prescribed for initial use at home, while breathing the patient’s usual FIO₂.

If all above criteria are met, either an E0470 or E0471 device will be covered for the first three months of NPPRA therapy.
Central sleep apnea (CSA) is defined as:

1. An apnea hypopnea index (AHI) greater than 5; and

2. Central apneas/hypopneas greater than 50% of the total apneas/hypopneas; and

3. Central apneas or hypopneas greater than or equal to 5 times per hour; and

4. Symptoms of either excessive sleepiness or disrupted sleep.

Complex sleep apnea (CompSA) is a form of central apnea specifically identified by the persistence or emergence of central apneas or hypopneas upon exposure to CPAP or an E0470 device when obstructive events have disappeared. These patients have predominately obstructive or mixed apneas during the diagnostic sleep study occurring at greater than or equal to 5 times per hour. With use of a CPAP or E0470, they show a pattern of apneas and hypopneas that meets the definition of CSA described above.

### Possible ICD-9 Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-9 Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>327.21</td>
<td>Primary central sleep apnea</td>
</tr>
<tr>
<td>327.22</td>
<td>Central sleep apnea due to high-altitude periodic breathing</td>
</tr>
<tr>
<td>327.27</td>
<td>Central sleep apnea in conditions specified elsewhere</td>
</tr>
<tr>
<td>327.29</td>
<td>Other organic sleep apnea</td>
</tr>
<tr>
<td>786.04</td>
<td>Cheyne-Stokes respiration (Central sleep apnea due to Cheyne-Stokes Breathing Pattern)*</td>
</tr>
</tbody>
</table>

*BiPAP autoSV is cleared for the treatment of periodic breathing, such as Cheyne-Stokes respiration.*