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CHAPTER 20

Positive Airway Pressure Treatment for Sleep Apnea

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HISTORY OF POSITIVE AIRWAY PRESSURE

Sullivan and coworkers [1] published the original description of nasal continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnea (OSA) in adults in 1981. Prior to that report, the only effective treatment for moderate to severe OSA was a tracheostomy. Today, positive airway pressure (PAP) is the mainstay of treatment for moderate to severe OSA in adults [2,3,4,5 and 6]. Patients with mild OSA [7,8,9,10,11 and 12], the upper-airway resistance syndrome [13], or even heavy snoring [14,15] have also been treated successfully with positive pressure. Since the original description of CPAP, other methods for delivering PAP have been developed, including bilevel PAP [16], autoadjusting positive airway pressure (APAP) [17,18 and 19], and expiratory pressure relief (Cflex). Many types of interfaces for the delivery of positive pressure, including nasal masks [14,20,21], nasal prong interfaces [22], masks covering both nose and mouth [23,24 and 25], and oral interfaces [26], have been developed. However, even after many technological improvements, the overall therapeutic efficacy of PAP is still critically dependent on a knowledgeable physician directing care and an organized and responsive structure of support personnel [27].

MECHANISMS OF ACTION

It is currently believed that PAP maintains upper airway patency primarily by the "pneumatic splint mechanism." This refers to a simple dilation of the airway by intraluminal pressure that is positive compared with atmospheric pressure. Both computed axial tomography and magnetic resonance imaging have clearly shown that positive pressure increases upper-airway cross-sectional area and volume [28,29 and 30]. The major configurational change appears to be an expansion of the airway in the lateral directions. Upper airway muscle activity tends to actually decrease once the upper airway is splinted open [28,31,32], suggesting that the effect of CPAP on upper-airway patency, in general, does not depend on upper-airway muscle activity. A second possible mechanism is an indirect action on the upper airway mediated by an increase in lung volume induced by PAP. Upper-airway size increases as lung volume increases [33]. One explanation for this effect is that as lung volume increases, there is a downward traction on the trachea (tracheal tug) and other upper-airway structures [34]. By an undefined mechanism, possibly related to stretching or stiffening of upper airway walls, this pull tends to open the airway. A study of one patient with OSA found a decrease in the apnea-hypopnea index (AHI) with negative pressure around the chest and the abdomen [35]. However, another study found that an increase in functional residual capacity (FRC) by subatmospheric pressure via a negative pressure body suit did not decrease the frequency of obstructive events [36]. A third study found little decrease in upper-airway resistance with the application of negative extrathoracic pressure [37]. It appears that most of the effect of CPAP on the upper airway is a direct consequence of the "pneumatic splint." Of note, one study did find a decrease in obstructive events when only expiratory positive airway pressure (EPAP) was applied [38]. Thus, pneumatic splinting, even when confined to expiration, has some benefit.

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Positive Pressure Modes—An Overview

CPAP stabilizes the upper airway by maintaining a nearly constant positive pressure in both inspiration and exhalation (Fig. 20-1). In bilevel pressure, there are two independently adjusted pressures [16]. A higher pressure is provided during inspiration (inspiratory positive airway pressure [IPAP]) and a lower pressure during exhalation (EPAP). The IPAP-EPAP pressure difference is the amount of pressure support provided to assist inspiration. For example, a bilevel PAP of 15/5 cm H_2O provides an IPAP of 15 cm H_2O, an EPAP of 5 cm H_2O, and a pressure support of 10 cm H_2O. Bilevel pressure has two potential advantages over CPAP. First, airway patency can be maintained with a lower pressure during exhalation. A notable number of patients find CPAP uncomfortable, particularly during exhalation, and may find the lower expiratory pressure more tolerable. Second, the IPAP-EPAP difference provides pressure support for inspiration and can augment ventilation. This feature is potentially very useful in patients who hypoventilate during sleep or benefit from pressure support because of lung disease, muscle weakness, or chest wall deformity such as kyphoscoliosis. Although one study failed to find that bilevel PAP increased compliance compared with CPAP [39], individual patients may accept bilevel PAP treatment but not CPAP. There may also be subsets of patients with OSA who tend to prefer bilevel PAP. A study by Resta and coworkers [40] suggested that bilevel PAP may be a better treatment than CPAP in the subsets of

patients with OSA who have chronic obstructive pulmonary disease (COPD) or the obesity hypoventilation syndrome (OHS) [38]. Of note, although uncommonly used in patients with OSA, bilevel devices can also be used with a backup rate (spontaneous timed [ST] mode). If the patient's respiratory rate exceeds the backup rate, the bilevel devices function as usual in spontaneous (S) mode. If the patient's respiratory rate drops below the backup rate, the machine will cycle to IPAP. The duration of IPAP and EPAP are determined as in the S mode. The machines will also cycle from IPAP to EPAP if no exhalation is sensed once the IPAP max time is reached. The bilevel PAP timed (T) mode is very rarely used in sleep apnea but can be used to treat hypoventilation. In this mode, the device delivers IPAP-EPAP cycles only at the set rate. The relative proportion of IPAP-EPAP for the machine breath is set by the clinician. One study suggested that patients with OSA who continue to hypoventilate may benefit from bilevel PAP in the T mode [41]. However, this study did not compare the efficacy of the ST and T modes.

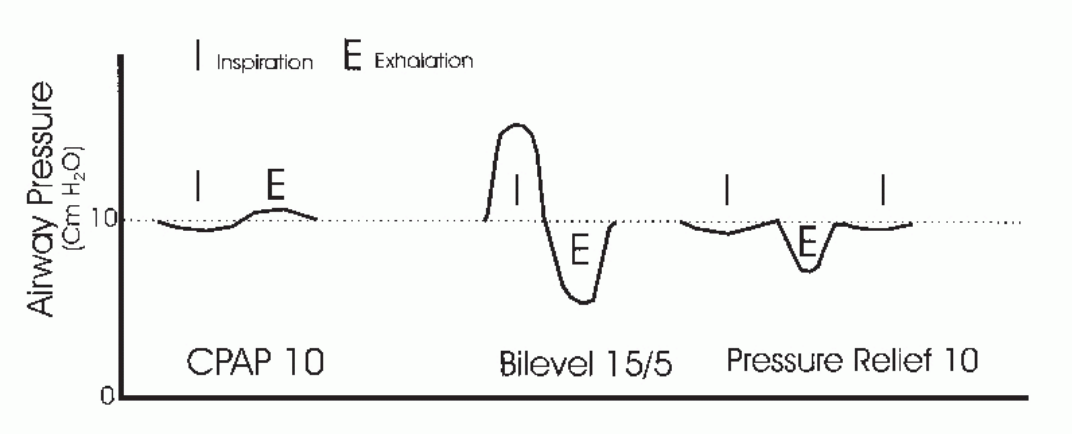

FIGURE 20-1 Positive pressure modes. CPAP, bilevel PAP, and CPAP with pressure relief (Cflex) are illustrated.

A common feature of both CPAP and bilevel PAP treatment is that a fixed level of pressure(s) is delivered during the entire night. This requires that an "optimal" level of fixed pressure(s) must be sufficient in all body positions and sleep stages. However, it has been recognized since the early days of positive pressure treatment that higher pressure is typically needed in the supine position [42,43 and 44]. This has been well documented in systematic comparisons. In addition, higher pressure may be needed during REM sleep in many patients [42]. Alternatively, some patients might require substantially less pressure in the lateral sleeping position or with the head elevated [44]. Thus, a fixed pressure(s) may deliver higher than needed pressure to some patients during variable portions of the night. In theory, the average nightly pressure would be lower if only the minimum pressure required to maintain upper-airway patency was administered at any given time during sleep. It has been postulated that a lower average overnight pressure would increase adherence in some patients. Attended PAP titration to determine the optimal pressure is also a labor-intense procedure that may not be available in all circumstances. These difficulties associated with fixed PAP treatment and attended PAP titration resulted in the development of autotitrating APAP devices [17,18 and 19,45,46,47,48 and 49]. One or more of the following respiratory variables are typically monitored by a given APAP device: airflow magnitude [46], inspiratory airflow flattening (airflow limitation) [48], airway vibration/snoring [47], and airway impedance [49]. The algorithms for pressure change vary between different devices. Pressure changes are made gradually to avoid inducing arousal. For example, the presence of snoring could prompt a pressure increase of 0.5 cm H_2O over 1 minute. If none of the monitored variables is detected, the devices also begin to slowly lower pressure. Thus, APAP devices deliver the lowest effective pressure required in a given circumstance. The clinician sets the lower and upper pressure limits, and the device will deliver pressure as needed between these two *(Print pagebreak 291)* limits (Fig. 20-2). High mask or mouth leak can simulate physiologic events and result in errors in APAP titration. One report of a large experience with the APAP devices estimated that leak exceeded 0.4 L/s (24 L/min) in about 10% of supervised nights and 15% of unsupervised nights [17]. The devices also cannot differentiate between central and obstructive apnea. In many published studies of APAP, patients with central apnea or congestive heart failure (CHF) (increased incidence of Cheyne-Stokes breathing [CSB]—central apnea) were excluded [18]. The use of APAP devices as an alternative to traditional PAP titration will be discussed in the titration section. The evidence that APAP can increase adherence to PAP will be reviewed in the section on PAP adherence.

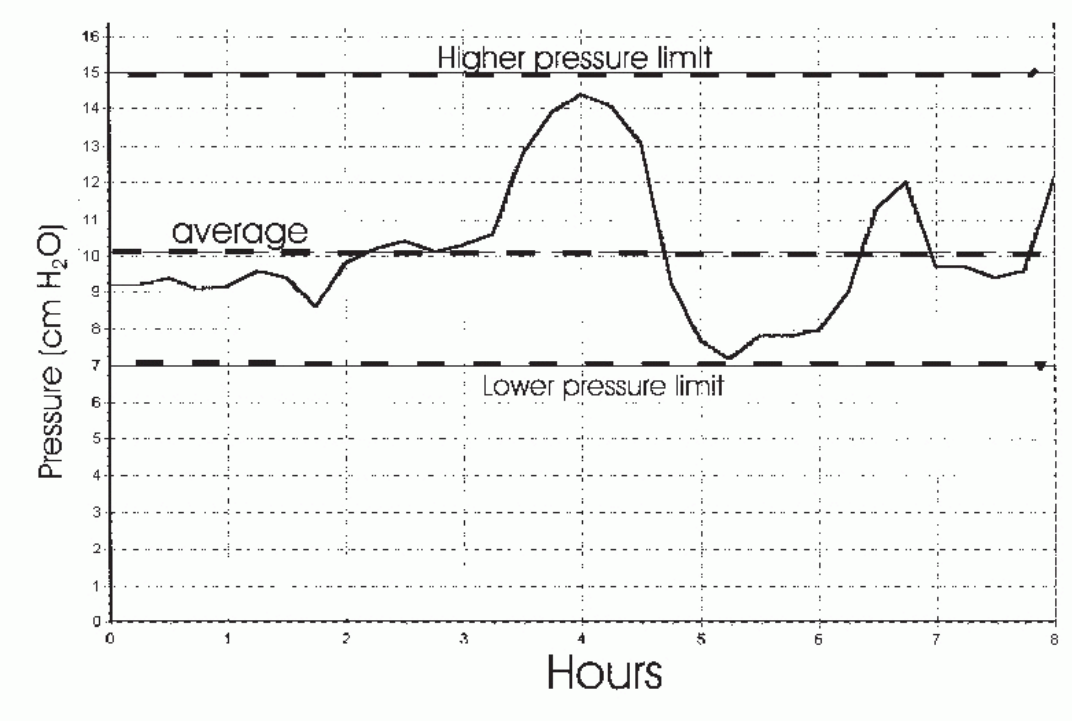

FIGURE 20-2 An example of pressure versus time for APAP treatment over a night. The device titrated between upper and lower pressure limits set by the clinician. The average pressure is lower than an optimal fixed pressure. In this case, treatment with a fixed pressure would require a CPAP of 14 to 15 cm H_2O. (From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia: Hanley and Belfus, 2003:153, with permission.)

The newest method of PAP delivery is a variant of CPAP, expiratory pressure relief (Cflex), which allows the airway pressure to fall during expiration in proportion to expiratory airflow. The airway pressure returns to the prescribed CPAP level at end exhalation. Patients may select one of three levels of pressure relief (e.g., different relationships between expiratory flow and the amount of pressure decrease). This treatment may be useful in pressure-intolerant patients. To date, no information has been published regarding the impact on adherence to treatment. As will be discussed in later sections, pressure intolerance is not the most common PAP side effect.

INTERFACES FOR POSITIVE AIRWAY PRESSURE

Developing an optimal interface between the airflow generator or blower and patient has been the source of tremendous challenge. The PAP industry has recognized this problem, and currently, a large variety of alternatives are available (Figs. 18-3 and 18-4). However, finding an adequate interface remains a significant problem. Mask discomfort (pain from pressure on the nose, cheeks, or upper lip), air leak (noise, eye irritation), and shift in mask position with body position changes may all impair sleep quality. In the original description of CPAP, small cannulalike tubes were placed in the nostrils and held in place with polymer [1]. Later, the idea of a nasal mask was introduced [14,20,21]. In many patients, mouth leaks are not problematic when using a nasal interface because the positive pressure in the nasopharynx moves the soft palate forward against the tongue, sealing off the oral cavity. Otherwise, the patient must maintain or be assisted to maintain a closed mouth (chinstrap) or utilize an oronasal mask, which simultaneously applies pressure to the nasal and oral airways.

Typically, a given type of mask is produced in a series of sizes (small, medium, large), but these rarely provide good fits for all facial structures. Material used for the mask are either compliant and bulge out from pressure against the face (Fig. 20-3A,B,D, and F) or are composed of a soft gel material (Fig. 20-3C). A particular challenge is obtaining a good seal over the bridge of the nose. Leaks of air in this area typically irritate the eyes [50]. Patients without upper teeth may have limited structural support for the upper lip area. In some of these patients, wearing dentures at night may help. To resolve these mask problems, several versions of interfaces have been developed to provide a seal in the nares, such as nasal pillows (Fig. 20-4A) or nasal prongs (Fig. 20-4B) [22]. Two other advantages for this type of device are that patients can read with the interface in place and typically feel less claustrophobic. Another method of handling similar problems is the design of “mini masks” that fit only over the tip/lower portion of the nose (Fig. 20-3E).

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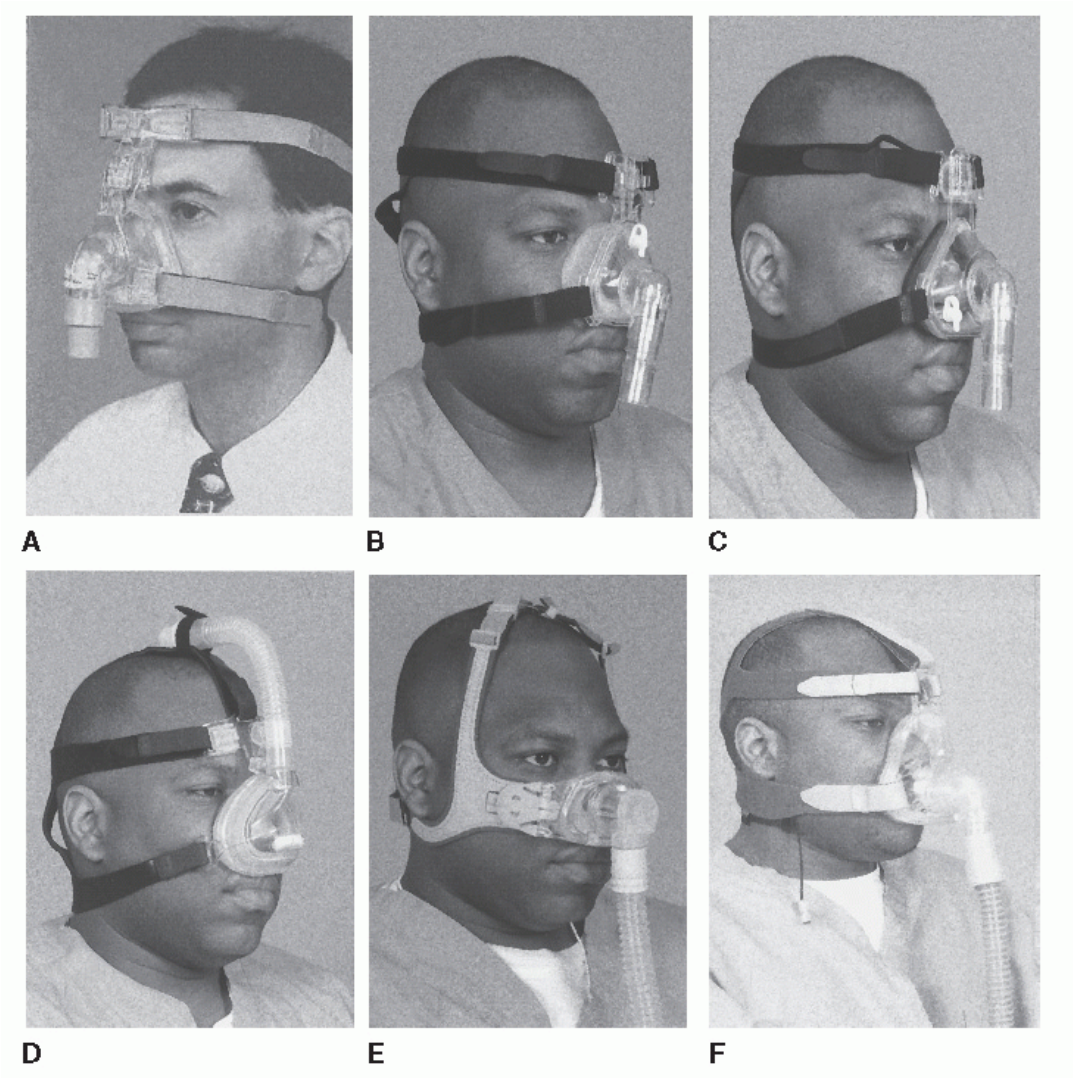

FIGURE 20-3 Six mask interfaces used for PAP treatment. (A) Ultramirage nasal mask (Res Med). (B) Comfort Classic (Respironics). (C) Profile Light (gel material) (Respironics). (D) Aclaim (Fisher-Paykel). (E) Vista (Res Med). (F) Full face Ultra Mirage Series 2 (Res Med). (A: From Berry RB. In: Johnson JT, Gluckman JL, Sanders MH, eds. *Management of obstructive sleep apnea.* United Kingdom: Martin Dunitz, 2001:95. With permission. F: From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia, PA: Hanley and Belfus, 2003:155, with permission.)

If patients have significant nasal congestion or obstruction, they may find breathing through a nasal mask with the mouth closed very uncomfortable. For this reason, oronasal or full-face masks covering both the nose and mouth (Fig. 20-3F) have been developed [23,24 and 25]. These masks incorporate valves that allow inspiration of room air should the pressure source fail. They also have head straps that allow quick removal as a precaution against vomiting or other events requiring rapid mask removal. One problem with these full-face masks is that they are required to form a good seal over a larger area of face. Thus, obtaining a good mask fit in all patients has been *(Print pagebreak 293)* a problem. The full-face mask can be particularly useful in patients with mouth leak and also tend to prevent the drying of the upper airway. In some patients initially requiring a full-face mask, intensive medical or surgical treatment of the nasal airway may allow eventual conversion to a nasal mask. Recently oral interfaces (Fig. 20-4C) have also been developed for PAP [26]. The nose is completely bypassed but aggressive humidification is required to prevent dryness. Nasal leak can be a problem with oral interfaces just as a mouth leak can complicate treatment with a nasal mask.

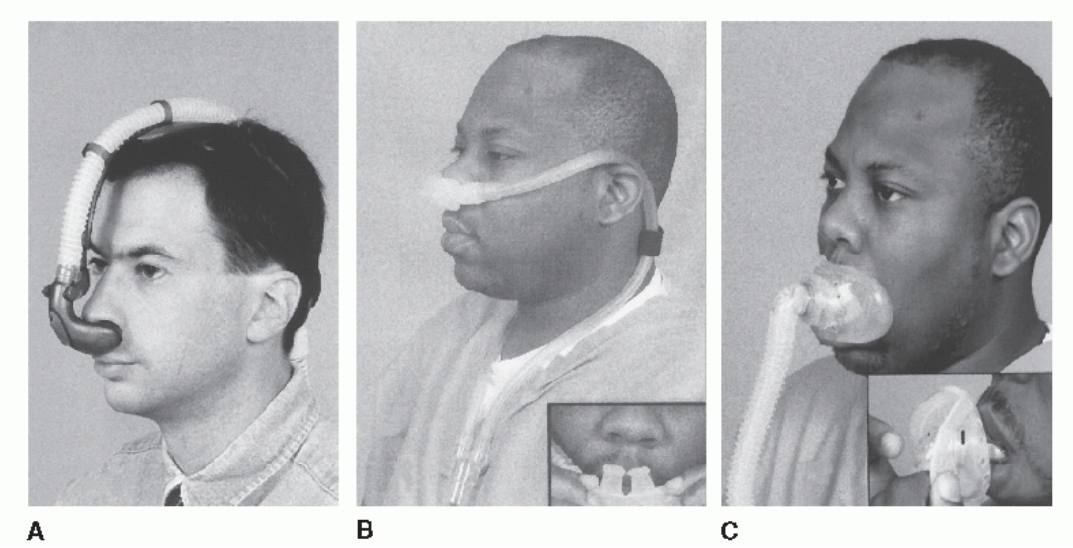

FIGURE 20-4 Three alternate interfaces for PAP treatment. (A) Breeze with nasal pillows (Mallinckrodt). (B) Nasal Aire (InnoMed). (C) Oracle (oral interface) by Fisher-Paykel. (A: From Berry RB. In: Johnson JT, Gluckman JL, Sanders MH, eds. *Management of obstructive sleep apnea.* United Kingdom: Martin Dunitz, 2001:95. With permission. B and C: From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia, PA: Hanley and Belfus, 2003:146,155, with permission.)

Because all modern CPAP equipment uses a single hose between blower and mask, some mechanism to wash out the exhaled CO_2 is needed. This is commonly performed by placing a small orifice or slit(s) in the nasal or full-face mask. Of note, the amount of leak (intentional leak) can increase considerably with increases in pressure. Although the possibility of rebreathing has been a concern if the mask is operating at lower pressures (less intentional leak), this does not appear to be a significant clinical problem. Most patients have some degree of unintentional leak, and the orifices are large enough to provide adequate washout at low pressures. On the other hand, the amount of intentional leak at high pressures can be up to 40 L/min with some masks.

ANCILLARY POSITIVE AIRWAY PRESSURE OPTIONS

The RAMP option is available on most CPAP and bilevel devices [4]. This allows the patient to select a "ramp time" during which the pressure slowly increases from a low initial value (typically 4 cm H_2O) to the prescription pressure. This provides a window of time during which pressure lower than the target pressure is applied and offers the patient an opportunity to fall asleep. The pressure from which a ramp may start to climb may be adjusted on some types of devices. This is a useful option because some patients prefer an initial pressure higher than 4 cm H_2O. Although the RAMP option makes sense, it has never been shown to increase adherence. Many PAP devices also offer mask-off alarms to alert the patient that the mask has been pulled off. The utility of this feature has never been systematically studied. Altitude compensation and adjustment for variable voltage sources are also available on many PAP units. Altitude compensation may be automatic or user selectable. This is a valuable feature because the same blower speed at higher altitudes delivers less pressure because of the decreased air density [51]. If the patient develops a complaint of the pressure "feeling different," the altitude adjustment should be checked to make sure that it was not inadvertently changed.

Currently, all but the lowest-priced PAP devices offer some method of objectively monitoring patient use (adherence) [52,53]. As will be discussed later, the capacity to objectively monitor PAP use is essential for optimal clinical care. The most basic method is a simple runtime meter (recording time the device is turned on). The average hours per night the machine is turned on can be calculated by the change in the meter values divided by the number of elapsed days. More advanced machines can monitor actual use ("time at pressure" or time with varying blower speed), and computer chip technology has allowed the recording of an electronic diary of the exact dates and times the machine was used (Fig. 20-5). This feature allows the physician to detect skipped days or early removal of the PAP device (the 4 AM trip to the bathroom). Some devices will also record estimates of persistent events or leak information. This stored machine information can be assessed through memory cards, modems, or direct transfer of information from the unit to a computer.

The use of humidification has been another frequently useful development. Initially, cold passover humidification (air simply blown across a water reservoir) was available. However, more moisture can be delivered with heated humidification and, currently, stand-alone heated humidifiers or models incorporated into the PAP device (integrated humidifier) are available. Studies have shown that nasal CPAP results in some drop in the relative humidity of air in the upper airway. Mouth leak causes a more dramatic drop in mask humidity via a unidirectional escape of water vapor out of the mouth [54,55] (Fig. 20-6). In fact, the symptom of mouth dryness usually implies some degree of mouth leak. Dryness of the nasal mucosa results in a large increase in nasal resistance [55].

This tends to cause more mouth opening and greater leak. In order to prevent this cycle, adequate humidification of air is required. One study found that heated but not cold humidity prevented changes in nasal resistance secondary to large mouth *(Print pagebreak 294)* leak [55]. Humidification by preventing dryness may also reduce the nasal congestion some patients experience when using CPAP. In one study, humidification increased average nightly use and patient satisfaction with CPAP treatment (heated > cool > none) [56]. Those patients who benefited the most were those with symptoms of nasal congestion or dryness at baseline. This study could be criticized for the fact that the subjects were not blinded to the fact that no humidity was used in the control arm. Medical devices can have an appreciable placebo effect. Another study found that prophylactic use of humidity to all comers did not improve satisfaction with the initial attended PAP titration in the sleep laboratory [57]. Thus, there is conflicting evidence on whether or not humidity should be used on every patient. It seems prudent to target humidification toward patients most likely to benefit (nasal congestion dryness and mouth leak). If there is a problem with condensation in the tubing, a tube insulator may be of some benefit. Certainly, care of humidifiers (cleaning and filling with water) requires some extra patient effort. Adherence data on the use of humidifiers is not available.

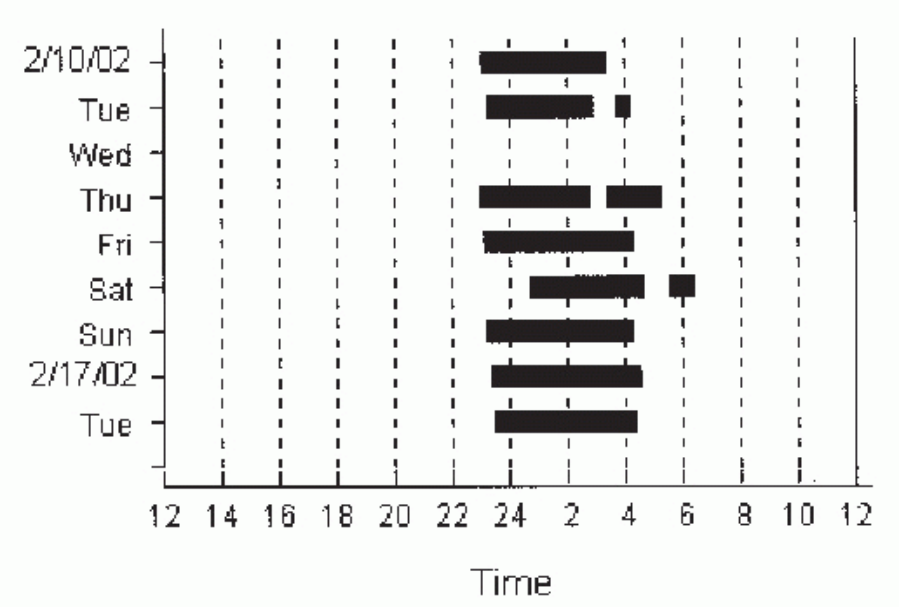

FIGURE 20-5 This is a typical graphical display of PAP device usage (time at pressure) over a period of time. The patient usually stopped using PAP after 4.00 AM. The electronic-use diary also shows that the PAP device was not used at all on February 12, 2002. On questioning, the patient admitted he stopped using the device after returning from the bathroom in the early morning hours. (From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia, PA: Hanley and Belfus, 2003:142, with permission.)

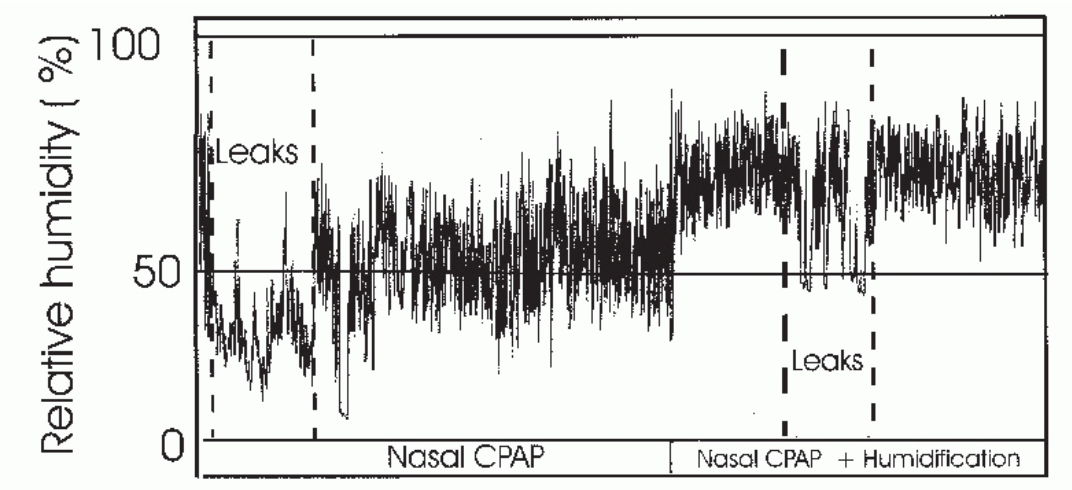

FIGURE 20-6 This tracing shows the fall in relative humidity at the nasal mask during mouth leaks (leak detected by an oral thermistor). Heated humidification minimized the fall in relative humidity when leak was present. (From Martins de Araujo MT, Vieira SB, Vasquez EC, et al. Heated humidification or face mask to prevent upper airway dryness during continuous positive airway pressure therapy. *Chest.* 2000;117:142-147, with permission.)

PATIENT SELECTION FOR POSITIVE AIRWAY PRESSURE

There are three major reasons to treat OSA [58]: (a) To decrease symptoms including excessive daytime sleepiness (EDS) [5] and associated morbidity such as an increased risk of auto accidents [59,60], (b) to prevent long-term cardiovascular and cerebrovascular consequences of OSA [61,62,63,64,65,66 and 67], and (c) to improve bed partner sleep (alleviate socially unacceptable snoring) [68]. Several controlled studies have demonstrated that PAP is effective in decreasing subjective and objective sleepiness and improving the quality of life in symptomatic patients with moderate to severe disease [5,6]. In general, although PAP can be effective in some patients with mild OSA (or those with isolated snoring), this group tends to be much less adherent to PAP treatment [7,8,9,10,11 and 12]. Patient preference should also be considered. Some patients with milder disease may not want upper-airway surgery or an oral appliance. In these cases, choices are limited to conservative treatment (weight loss, etc.) or positive pressure.

The indication for PAP treatment of asymptomatic patients is more controversial. In one 6-week study, there was no benefit with regard to sleepiness, quality of life, or cognitive test performance in moderate to severe cases of OSA (AHI of >30 per hour) when patients were not sleepy [69]. In this study, there was also no improvement in blood pressure, a finding that conflicts with the results of some other studies [66,67]. In addition, the severity of arterial oxygen desaturation was not specified. The results may then not be applicable to all patient groups. Social reasons for effective treatment can be very compelling for some patients. Some increased risk of developing cerebrovascular or cardiovascular disease exists even at low AHI levels [64,65]. However, no prospective controlled study has yet demonstrated that CPAP treatment will decrease the risk of long-term consequences. The risk of long-term consequences of untreated OSA in a given patient cannot be estimated with certainty. However, the presence of more severe arterial oxygen desaturation or comorbid conditions (coronary artery disease, CHF, prior cerebrovascular accidents [CVAs]) may well increase risk.

Medicare guidelines for the reimbursement of PAP treatment have recently been revised [70]. For patients with an AHI of 5 to 14 events per hour, symptoms or signs of significant impairment are required. The qualifying impairments include daytime sleepiness, insomnia, hypertension, prior CVA, or a mood disorder. For patients with an AHI of 15 events per hour or more, no associated findings are required. Of note, the Medicare definition of hypopnea is stringent. A hypopnea is defined as a ≥30% reduction in flow followed by a ≥4% desaturation. Arousals are not considered in this definition of hypopnea. No associated desaturation is required for an apnea.

In summary, one can argue that all patients with moderate to severe OSA, with or without symptoms, should be offered PAP treatment. Most would also offer PAP to symptomatic patients with mild OSA as an alternative to other treatments. For patients with moderate to severe *(Print pagebreak 295)* OSA without symptoms, the most compelling reasons for treatment would be social acceptance and prevention of long-term consequences. Scientific evidence (see later section) is accumulating that asymptomatic patients with significant cardiovascular comorbidity probably have the most to gain from PAP treatment.

TABLE 20-1 ESSENTIALS OF POSITIVE PRESSURE TITRATION

Patient education about positive pressure Mask fitting (before study)
CPAP training—acclimatization period (identify problems early)
Titration to eliminate apnea, hypopnea, snoring, desaturation, and RERAs in all body positions and sleep stages (including supine REM)
Reduction in the AHI: <5 per hour if possible or at least <10 per hour

POSITIVE PRESSURE TITRATION

The pressure used for PAP treatment is usually determined by a positive pressure titration (Table 20-1). Pressure is incrementally increased until an optimal pressure is reached. Standards for positive pressure titration have been published by a number of organizations [71,72]. Attended polysomnography (PSG) including electroencephalograph monitoring has been the standard of care for titration. This allows a determination of sleep stage and body position [42,43 and 44]. The sleep technologist is available for adjustments in mask seal and to minimize discomfort and patient complaints. Episodes of significant arterial oxygen desaturation that sometimes occur even when airflow is adequate (commonly during REM sleep) [73] or significant arrhythmias can be recognized and addressed. PAP titration is a labor-intensive process, and usually a technologist can titrate only one or two patients at a time.

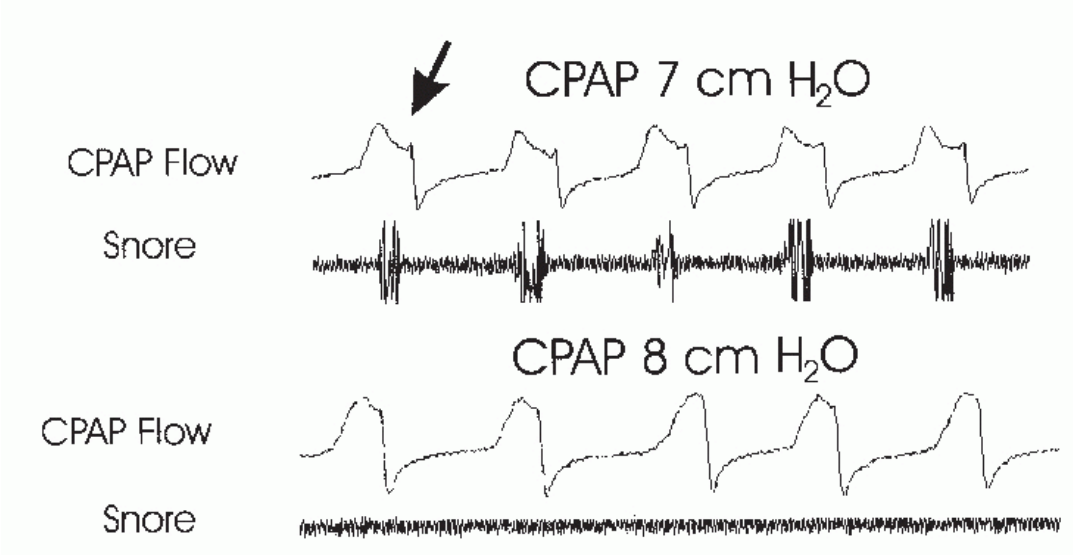

FIGURE 20-7 These tracings shows that an increase of only 1 cm H_2O in CPAP was needed to eliminate snoring. Notice that the increase in pressure also eliminated the subtle flattening in the inspiratory part of the flow signal from the CPAP device (arrow). (From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia, PA: Hanley and Belfus. 2003:125, with permission.)

Although airflow can be monitored with a thermistor or nasal pressure cannula under the mask, most sleep centers today monitor a flow signal generated by the positive pressure device (sometimes called machine flow, CPAP flow, Vest, or Cflow). This signal provides accurate information about the magnitude of flow and airflow limitation (flattened airflow profile). Some airflow signals may also provide snoring information, depending on the filtering and frequency response of the measuring device in the machine. An estimated leak signal as well as machine pressure are also available [74]. The use of the leak signal will be discussed in the following section.

It has been recognized that both snoring and airflow limitation usually imply persistent high upper-airway resistance [75,76] and are clues that a higher pressure may be needed. In Figure 20-7, a small increase in CPAP eliminates snoring and evidence of airflow limitation in the flow signal. The end point (goal) of titration varies somewhat but ideally includes elimination (or near elimination) of obstructive apnea, hypopnea, snoring, arterial oxygen desaturation, and respiratory effort-related arousals (RERAs), which are those events associated with arousals secondary to increased respiratory effort that do not meet criteria for obstructive hypopneas [77]. As esophageal pressure is not typically measured, RERAs are usually inferred from the evidence of airflow limitation or snoring preceding an arousal. Some centers also try to eliminate all evidence of airflow limitation [77]. Central apneas and mild airflow limitation may be acceptable as long as there is no associated sleep disturbance or significant oxygen desaturation. The goal of most centers is to have an AHI of <5 events per hour in all body positions and sleep stages. The highest pressures are usually needed during supine REM sleep. Unfortunately, supine REM sleep may not be recorded in every patient.

Bilevel pressure titration protocols vary, but two methods are popular [16]. One can increase IPAP-EPAP until obstructive apneas are abolished. Further increases in IPAP are administered until hypopnea/snoring is *(Print pagebreak 296)* eliminated. Alternatively, one could start with 6/4 to 8/4 and then sequentially increase IPAP and EPAP as needed. In general, apnea requires an increase in EPAP (Fig. 20-8). A common error is to attempt to stabilize the airway with EPAP that is too low or an IPAP-EPAP differential that is too high.

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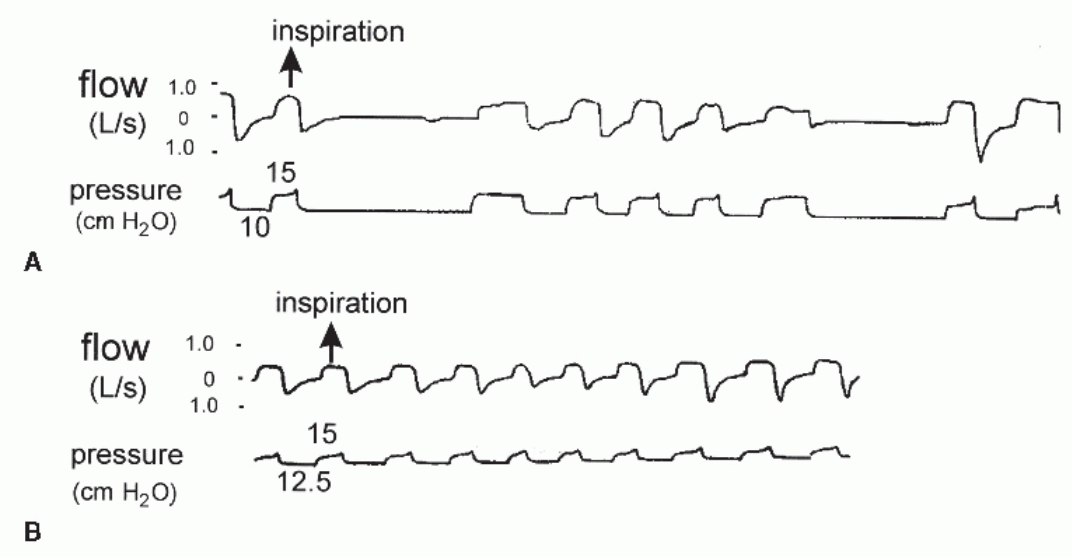

FIGURE 20-8 Bilevel PAP titration. (A) Apnea is still noted on a bilevel pressure of 15/10 cm H_2O. (B) An increase in EPAP to 12.5 cm H_2O apnea has resolved. (From Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. *Chest.* 1990;98:317-324, with permission.)

Initially, PAP titrations were performed during an entire night that followed a previous diagnostic study. This allowed an entire night for diagnosis and estimation of severity. Frequently, the patient could be educated by a physician about the nature of his problem, treatment alternatives, and the nature of PAP treatment before the PAP titration. However, because of limited resources and to expedite treatment, split- or partial-night studies were introduced [78,79,80,81 and 82]. The first portion of the night is for diagnosis, and the second part is for the PAP titration. Obviously, this approach allows less time for each goal, diagnosis, and PAP titration. Several studies have assessed the ability of a splitnight approach to determine an effective level of PAP, and guidelines for patient selection have been published by the American Academy of Sleep Medicine [71]. In general, around 60% to 80% of patients can be handled adequately by the split-night approach. Criteria for patients to have a split study are listed in Table 20-2. The rationale for these criteria is that severe patients usually do not require either REM sleep or the supine position to manifest the severity of their problem. The severity of mild to moderate cases may be underestimated when adequate amounts of supine or REM sleep are not included in the diagnostic portion of the study. In addition, there appears to be more uncertainty in the optimal level of PAP in milder cases studied for only part of the night. Certainly, enough time must be left for an adequate PAP titration once the diagnosis of OSA has been made. The split-study approach requires education, mask fitting, and optimally, some brief period of PAP adaptation before lights out. If a patient does not meet criteria during the first part of the night, the entire study is performed as a diagnostic one. Autotitrating devices offer an alternative to traditional PAP titration [18,19,83,84,85,86,87 and 88]. Information stored in the device memory can be analyzed, and a pressure can be chosen for fixed CPAP. A common method is to choose the 90th or 95th percentile pressure (pressure exceeded only 10% or 5% of the time, respectively) as the prescription pressure. This assumes periods of high leak have been eliminated from analysis. The devices could be used in an attended setting as a technologist extender. Interventions for mask leak, arterial oxygen desaturation, or arrhythmia would then be possible. In this setting, the ability of the devices to provide an adequate titration (low residual AHI) has been well documented [18,19,84,85]. Of note, most studies excluded patients with CHF or significant lung disease. The ability of APAP devices to perform in the unattended setting in CPAP naive patients [18,86,87 and 88] has been less well documented. Nevertheless, adequate titration can probably be obtained in many patients. Simply looking at a data summary can be misleading. Most devices allow the ability to look at single-night data in detail (pressure, leak, residual events vs. time) (Fig. 20-9). Periods of high leak and the frequently associated increase in pressure can be appreciated. High leak can result in many devices promptly increasing pressure until the upper pressure limit is reached. In Figure 20-9, a single-night tracing on APAP shows high leak (>0.4 L/s). Patients with suboptimal or inconclusive APAP titrations should have an attended lab PAP titration.

Other methods of determining a CPAP level for chronic treatment have been investigated. Hoffstein and *(Print pagebreak 297)* coworkers [89,90] developed a prediction equation for optimal CPAP based on the AHI and neck circumference (NC). CPAP pressure = -5.121 + 0.13 × body mass index (BMI) + 0.16 × NC + 0.04 × AHI. This equation incorporates the body mass index (BMI = weight in kilograms/[height in meters]^2), the NC in centimeters at the cricothyroid membrane, and the AHI. For example, a patient with a BMI of 27, an NC of 19 inches, and an AHI of 60 events per hour would be predicted to require a CPAP of 14.5 cm H_2O. This equation can be used to guide empiric treatment, but the confidence limits are fairly wide. Some protocols have also used patient- or spouse-adjusted pressure as an alternative to attended pressure titration [91] with good results.

TABLE 20-2 SUGGESTED CRITERIA FOR SPLIT TITRATION

2 hours of recorded sleep in the diagnostic portion (so that patient will qualify for Medicare payment of CPAP) AHI of >40 per hour
AHI of 20-40 per hour with significant desaturation or other factors
≥3 hours remaining for PAP titration

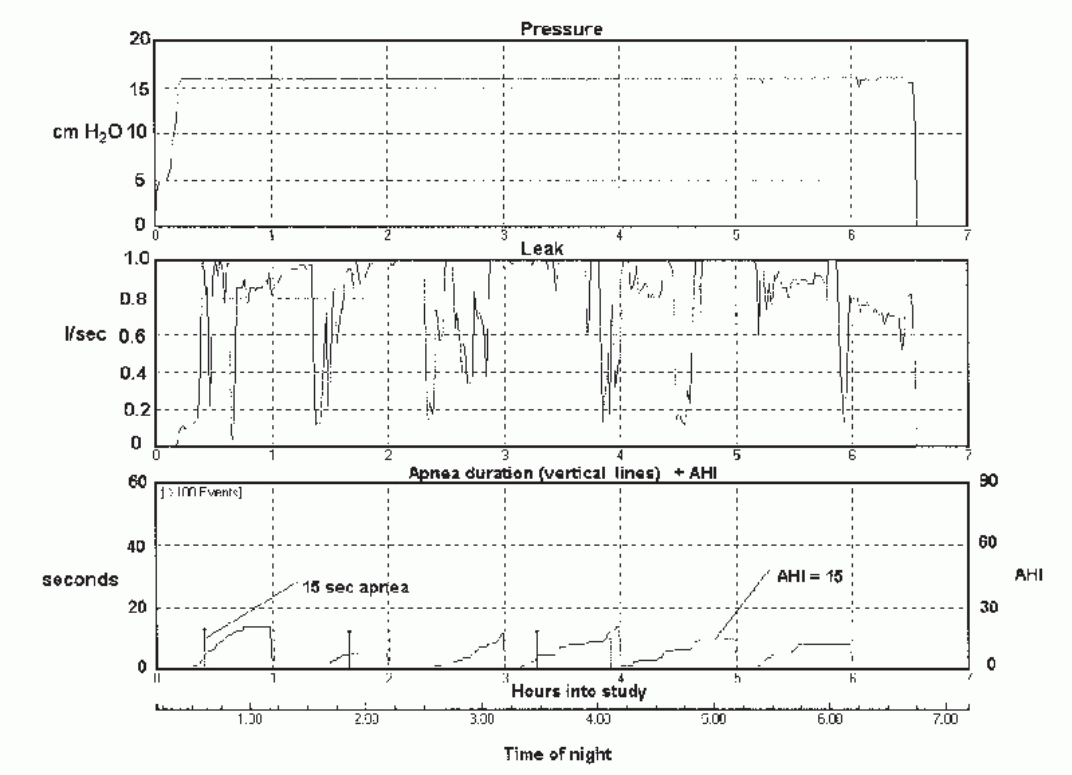

FIGURE 20-9 This is the tracing of a single night of inadequate APAP titration. There were very high leaks, and the machine titrated up to 15 cm H_2O (the clinician set upper pressure limit). In addition, one can see that there were appreciable residual events.

Common Problems and Decision Making in Positive Airway Pressure Titration

Although most sleep centers have established PAP titration protocols, the skill of the technologist is still important. PAP titration remains an "art as well as a science." Establishing a good patient-technologist relationship will help the patient relax and hopefully adapt to the discomforts of the study. Some of the common problems encountered during PAP titration are listed in Table 20-3, along with possible solutions. Education about OSA and PAP should always be performed before lights out. Most centers also have mask fitting and a period of PAP acclimatization while the patient is awake. This is very useful for identifying an inadequate mask seal, significant patient apprehension, pressure intolerance, and significant nasal obstruction. The technologist might change the mask, use humidification, use bilevel pressure/or a very slow upward titration of CPAP, based on the reaction to this brief trial of PAP. During titration, it may be necessary to temporarily reduce pressure to allow a return to sleep.

Mask or mouth leaks can cause difficulties during both attended manual and unattended autotitration of PAP. *(Print pagebreak 298)* As pressure is titrated upward during the night, mask or mouth leak may develop. If high leak is noted, the technologist can zoom in on the mouth area with the low light camera to see if the mouth is open. Widely fluctuating leak without pressure change or body movement also suggests that an oral leak is present. Mouth leak can mimic hypopneic events (Fig. 20-10A), prevent airway stabilization, or result in arousal from sleep. If mainly expiratory leak is present, the expiratory portion of the airflow signal may be truncated (Fig. 20-10B). If a leak is not recognized, the technologist may increase pressure in response to events rather than address the cause of the leak. A mask leak requires mask adjustment, and a mouth leak may be addressed by the use of a chinstrap or full-face mask. If nasal congestion is causing the mouth leak, heated humidity may also be useful.

TABLE 20-3 PROBLEMS DURING CPAP TITRATION AND TYPICAL SOLUTIONS

Claustrophobia	Desensitization Nasal pillows, nasal prong interface

	Anxiolytic medications
Mask leak	Careful mask fitting before study Adjust straps, change mask size or type Pressure adjustment/Cflex Wedge pillow
Nasal congestion	Full-face mask Heated humidity Decongestant
Pressure intolerance	Avoid rapid increase in pressure Temporary reduction in pressure to allow return to sleep Bilevel pressure Cflex Elevation of head of bed, side sleep position to decrease required pressure, wedge pillow

Central apneas may appear and are often a significant challenge. Some patients develop central apneas following arousals from high upper-airway resistance. An increase in pressure is indicated. Others develop central apneas following spontaneous arousals from pressure intolerance or leaks. In this case, a lowering of pressure may be attempted if central apneas persist.

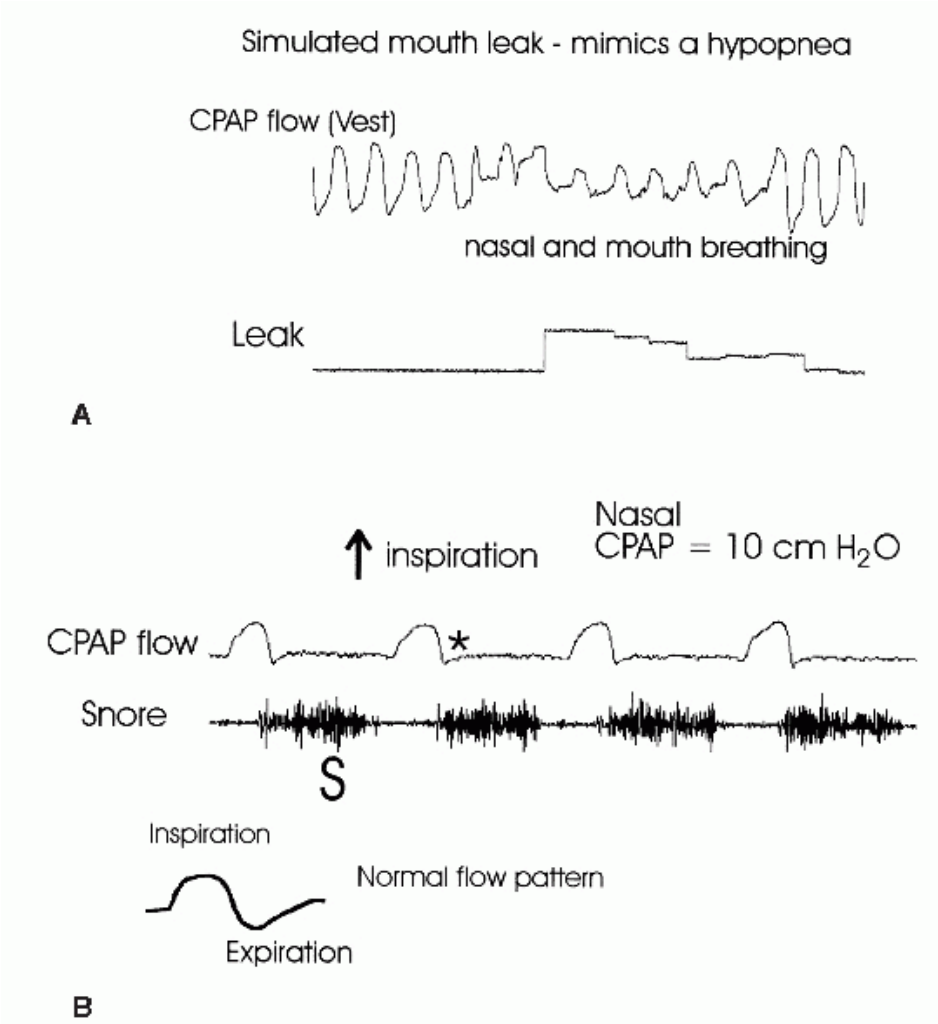

FIGURE 20-10 (A) This tracing was obtained when a patient breathing on nasal CPAP was asked to breathe partially through the mouth (nasal and mouth breathing). One can see what looks like a hypopnea. (B) This tracing shows airflow (inspiration up) with a truncated expiratory phase (*) compared with normal shape shown below. Expiratory leak was confirmed by evidence of expiratory snoring in the snore sensor tracing (S). The technician closely inspected the patient by zooming in on the face with a low-light camera. The patient's mouth was vibrating during exhalation. (From Berry RB. *Sleep medicine pearls.* 2nd edn. Philadelphia, PA: Hanley and Belfus, 2003:126,132, with permission.)

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Of note, some central apneas after treatment of OSA with tracheostomy were not uncommon and were resolved with continued treatment. Treatment-emergent central apneas may occur in some patients during CPAP titration if the PCO_2 is reduced to near the apneic threshold (the PCO_2 level required to stimulate respiratory effort during sleep). In this case, any brief increase in ventilation, such as that which occurs after an arousal, may trigger a central apnea. The treatment of Cheyne-Stokes type central apnea is discussed in later sections.

Factors Affecting Optimal Pressure

Because a single night or a partial night is utilized to establish an optimal pressure, the possibility of varying PAP requirements must be considered. Some studies have suggested a possible increase in upper-airway size [92] and decrease in the optimal pressure [93] with chronic CPAP treatment secondary to a reduction in upper-airway edema. However, others have found the pressure to be fairly constant [94]. Table 20-3 lists factors that have been demonstrated to alter the pressure required to keep the airway open. Posture has already been mentioned. One study found that elevation of the head of the bed or the lateral sleep position could alter the optimal pressure by up to 5 cm H_2O [44]. Weight loss/gain has also been demonstrated to alter pressure requirements [95]. Snoring at home on CPAP is a useful clue that higher pressure may be needed. Many authors have stated that ethanol use can also increase the pressure required. However, two studies have not found this to be the case [96,97]. Ethanol use is still to be discouraged as patients might fail to apply the mask or remove it during the night, although it does increase the arousal threshold to respiratory stimuli [98].

Nasal congestion also could conceivably alter the required pressure. One must remember that the pressure at the collapsible areas of the upper airway rather than at the mask is the critical pressure. It is also possible that increased mask or mouth leaks can render a given pressure less effective at keeping the airway open [99]. Mask pressure can be less than machine pressure (set pressure) when high leaks are present.

SIDE EFFECTS OF POSITIVE AIRWAY PRESSURE AND POSSIBLE SOLUTIONS

Studies have enumerated the many side effects associated with PAP treatment (100-108). If left untreated, side effects from PAP may cause a lower chance of acceptance and lower rates of adherence [104]. Side effects and possible interventions are listed in Table 20-4. Many side effects are secondary to the mask interface. In one study, intolerance of the mask was the most common reason for discontinuing CPAP treatment [102]. Obtaining an adequate mask fit may require trials of several different brands and types of masks. Adequate mask positioning is also essential, *(Print pagebreak 299)* as is the elimination of the overtightening of head straps. Often, moving the mask up or down slightly will produce a better seal than further tightening. Poor mask fit leads to leaks that are both uncomfortable (particularly into the eyes) and may result in an inadequate pressure. Overtightening of head straps can result in severe skin abrasion particularly on the bridge of the nose (CPAP divot). Turning in bed can also change mask position, resulting in loss of mask seal. Improvements in mask material and flexibility in the mask-hose connection have attempted to reduce these problems. Masks today use either a deformable gel material or thin material that balloons out against the face under pressure. Nasal prongs (nasal pillows) can sometimes provide a useful alternative for patients unable to get a good seal around the nasal bridge. Adequate care of masks (cleaning) and replacement of masks when old (and less flexible) are also necessary.

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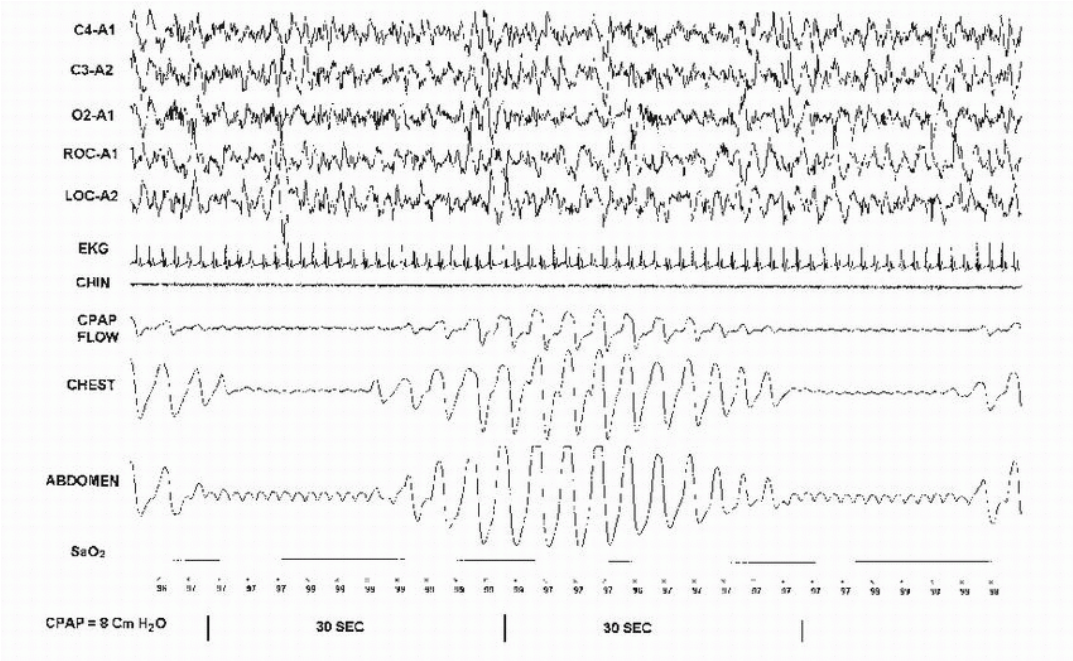

FIGURE 20-11 This tracing shows Cheyne-Stokes central apnea during treatment with CPAP of 8 cm H_2O. In this patient, no level of pressure reduced the AHI to below 20 events per hour. However, above 8 cm H_2O, all the persistent events were central apneas. Machine flow is the flow signal from the positive pressure device. Although these central apneas persisted, they did not result in significant desaturation or arousal.

Nasal symptoms including congestion, rhinorrhea, pain, dryness, and epistaxis are all potential problems with positive pressure treatment. Nasal congestion can often be improved with the use of heated humidification and/or treatment with nasal steroids, nonsedating antihistamines, or decongestants at bedtime. Some patients with intractable nasal congestion can be handled with the use of a fullface mask or oral interface [23,24 and 25]. If all else fails, referral for the surgical treatment of nasal obstruction is another approach [109,110]. Recently, less morbid procedures to reduce turbinate size have been used with some success. Although heated humidity generally is more effective in preventing dryness [55], an occasional patient will prefer cool humidification. A full-face mask may also prevent a loss of humidity from mouth leaks [54]. Rhinorrhea may develop during CPAP treatment or immediately following the cessation of treatment. This is usually controlled with intranasal ipratropium bromide or humidification.

Although PAP devices have the ability to compensate for leak, large mouth leaks may compromise the ability to deliver pressure and maintain an open airway [99]. Mouth leaks can also result in arousal and severe dryness, as noted above. Mouth leaks seem to be particularly problematic in patients with prior surgery of the palate [111]. To prevent mouth leaks, one can use chinstraps or full-face masks. The efficacy of chin straps has never been documented but may work in an occasional patient. Some patients may have less mouth leak with bilevel pressure (particularly those with expiratory mouth leak). In others, using APAP by lowering the average nightly treatment pressure may decrease the tendency for mouth leak. For patients with nasal congestion, treatment with nasal steroids or vasoconstrictors and using humidification may reduce the tendency for mouth leak.

Machine noise was once a common problem, but newer blowers are generally much quieter. One could recommend a longer tubing and removal of the blower unit from the bedroom. Another worrisome side effect is the noise or discomfort from the stream of air exiting from the controlled leak orifice in the mask or mask/hose interface. This intentional leak can sometimes also bother the bedmate. New designs in the controlled leak have addressed this problem.

(Print pagebreak 300)

TABLE 20-4 PAP SIDE EFFECTS AND POSSIBLE INTERVENTIONS

POSITIVE PRESSURE SIDE EFFECTS		INTERVENTIONS
Mask side effects		
Air leaks		Proper mask fitting
	Conjunctivitis	Proper mask application (education)
	Discomfort	Different brand/type of mask
	Noise	
		Avoid overtightening; intervene as above

Skin breakdown	for leaks Alternate between different mask types Nasal prongs/pillows Tape barrier for skin protection
Unintentional mask removal	Low pressure alarm Consider increase in pressure Anxiolytic medication
Nasal symptoms	
Congestion/obstruction	Nasal steroid inhaler Antihistamines (if allergic component) Night-time topical decongestants (oxymetazoline) Nasal saline Humidification (heated) Full-face (oronasal) mask
Epistaxis Pain Rhinitis/rhinorrhea	Nasal saline Humidification (heated) Nasal ipratropium bromide
Other problems	
Mouth leaks/mouth dryness	Humidification (prevent increased nasal resistance) Treatment of nasal congestion Chin straps (?) Full-face mask Oral mask Lower pressure/bilevel pressure Ramp
Pressure intolerance	Bilevel pressure Autotitrating device Lower prescription pressure; accept a higher AHI Lower pressure + adjunctive measures (elevated head of bed, side sleeping position, weight loss)

Intolerance to the level of positive pressure is also a common side effect, particularly at higher treatment pressures. There are several approaches to handle the problem. The RAMP option has already been described. Other approaches are to use bilevel PAP, autoadjusting CPAP, expiratory pressure relief, or simply to use a lower than optimal pressure for a few weeks. Patients who complain of difficulty exhaling or those with obstructive lung disease may find bilevel pressure more comfortable [40]. There has been conflicting evidence concerning the ability of APAP to improve adherence to treatment in unselected patients. Three studies found an increase in adherence with APAP compared with fixed CPAP [112, 113 and 114], whereas three other studies failed to do so [115, 116 and 117]. Perhaps this is not surprising when one considers that pressure intolerance is often not the biggest patient complaint. In addition, in some patients, there is relatively little variability in the pressure applied over a night. A patient with optimal pressure of 10 cm H_2O and an average pressure of 8 cm H_2O might not notice much difference on APAP. Series and Marc [118] found that the patients most likely to benefit from APAP were those with large variability in pressure over the night. In a recent study, Massie et al. [119] found that APAP used in patients requiring an optimal CPAP >10 cm H_2O had significantly better compliance on APAP. However, of note, the mean improvement in adherence was only about half an hour. In any case, individual patients may tolerate APAP much better than CPAP. Recently, the use of pressure relief during exhalation has been added to traditional fixed-pressure CPAP. The patient may select one of three levels of pressure relief. The amount *(Print pagebreak 301)* the airway pressure drops during exhalation depends on the amount of flow. The greater the flow is, the more the machine pressure is allowed to drop. The airway pressure returns to the set CPAP level at end expiration. Preliminary experience shows this approach may improve patient satisfaction. However, no data have yet been published to document an increase in adherence with this type of PAP.

Some patients find sensations of claustrophobia a severe problem when using PAP. Education and a period of CPAP adaptation prior to CPAP titration may help. Using nasal pillows or nasal prong interfaces may also reduce the feeling of claustrophobia in a

few patients.

A systematic program of desensitization can also be effective [120], although it usually requires the assistance of counselors trained in the technique, as well as a motivated patient.

FACTORS DETERMINING ACCEPTANCE AND ADHERENCE

Acceptance is usually defined as patient willingness to take a PAP device home and use it for at least 1 week [121]. The term "adherence" has become preferred over "compliance" and is used in much of the recent literature. The methods that have been employed to quantify adherence vary considerably, as does the definition of adequate adherence. However, one commonly used definition of an adherent patient is one using PAP for more than 4 hours per night for over 70% of days [52,108]. This definition is unsatisfactory because it is likely that a significant proportion of patients require >4 hours of use per night for maximal benefit from treatment [122]. Estimates of acceptance vary from 5% to 50% and of those initially using PAP, up to 12% to 25% discontinue PAP within 3 years [121,123]. Estimates of adherence have varied widely, with the highest figures of 70% to 80% reported by programs with a systematic program for PAP treatment [108].

Rational design of a system to improve acceptance and adherence to PAP requires understanding the factors that determine why patients either do not accept or adhere poorly to PAP treatment [121]. Not all studies agree but, in general, more disease severity, more symptoms, self versus spouse referral, and more perceived benefit for PAP predict success [124,125]. In one study, prior uvulopalatopharyngoplasty and problems with the nose or pharynx were more common in patients who stopped CPAP treatment than in those who were adherent [126]. In other types of disease with demanding treatment regimens, cognitive constructs have been useful in determining adherence. Patients who place a high value on health, feel they are in control, do not believe that chance rules their life, and have high self-efficacy are better treatment risks. One study of psychological correlates of adherence found that patients who by nature engaged in active coping strategies with new and difficult situations used CPAP more [127].

Studies of the pattern of adherence have also provided valuable information. Early intervention is important. Weaver and coworkers [128] found that a difference in the pattern of use by compliant and noncompliant patients is noted as early as day 4 of treatment. Patients complying over the first 1 to 3 months tend to continue to accept positive pressure treatment.

METHODS TO INCREASE ADHERENCE

Some procedures that have been recommended to increase adherence are listed in Table 20-5. Of note, most systematic evaluations of interventions to improve adherence have not studied individual components but rather have a "package" approach. The monitoring of objective adherence is now recommended as several studies have demonstrated that patients overestimate their actual usage [52,53]. Time at pressure or time of actual usage is preferred, although there appears to be good correlation between machine usage time and time at pressure for the majority of patients.

Education about OSA and CPAP is now a standard part of most programs (by staff, video, printed material, group sessions) [129]. Involvement of the spouse in education and follow-up appointments has also been recommended [125]. In many European centers, patients actually spend several extra nights in the hospital during the initial CPAP use [108]. Although this is not practical in fee-for-service healthcare systems, early follow-up and interventions to handle side effects are suggested. If the initial choice of mask and headgear are not satisfactory despite adjustments, a different size or type should be tried. Unfortunately, there continues to be some resistance to this intervention by home healthcare agencies because they may be only reimbursed for one mask every 6 months. Regular attendance at PAP clinics, where objective adherence is checked and education is repeated, has been *(Print pagebreak 302)* shown to be effective. Even simple telephone follow-up has been shown to increase adherence [130]. Today, many PAP devices have the ability to store information on memory cards that can be mailed in or that transmit data via modem. A significant portion of PAP training and follow-up can be performed by nurses or respiratory therapists. However, physician involvement is particularly important with respect to convincing the patient of the need for treatment and the benefits of adequate adherence.

TABLE 20-5 METHODS TO IMPROVE PAP ADHERENCE

Education about OSA and PAP by Staff
Video
Printed information
Involvement of significant other/spouse
Extended hospital (2-3 nights) stay

Subsequent mask and headgear adjustment or change
PAP helpline
Unsolicited telephone follow-up
Early interventions for side effects and concerns
Objective monitoring of adherence
Early and regular clinic visits

BENEFITS OF POSITIVE AIRWAY PRESSURE TREATMENT TO OBSTRUCTIVE SLEEP APNEA PATIENTS

There are many benefits and changes that occur after the successful PAP treatment of OSA (Table 20-6). On the first night of PAP titration, some patients exhibit a large increase in both slow-wave and REM sleep (rebound from prior deprivation) and often will note improvement in sleepiness after only one night of CPAP [131]. However, in 1997, Wright et al. [132] challenged the effectiveness and widespread use of PAP treatment of OSA because of the lack of placebo-controlled evidence that PAP improved symptoms and quality of life. Since that time, placebo-controlled studies have documented that PAP improves subjective and objective sleepiness and quality of life [5,6]. Improvements in subjective sleepiness (Epworth sleepiness scale), maintenance of wakefulness test, and sleep latency are more robust than improvements in the multiple sleep latency test at detecting improvements after PAP [133,134 and 135]. The Epworth sleepiness scale quantifies a patient's propensity to fall asleep in eight commonly encountered situations [133]. Many clinicians find it a useful tool to follow the symptomatic response to PAP treatment [134]. Improvement in sleepiness [5,131] and neurocognitive function [136] can occur quickly, although many patients require up to 6 months for the peak benefit [137]. Studies of the quality of life have usually found improvements in vitality scales on PAP [138].

TABLE 20-6 EFFECTS AND BENEFITS OF PAP TREATMENT

Improved sleep quality	
Decreased subjective and objective daytime sleepiness	
Improved cognitive function (some studies)	
Improved quality of life measures (vitality)	
Decreased sympathetic tone	
Increased heart rate variability	
Decreased nocturnal and daytime blood pressure (most studies)	
Decreased nocturnal and daytime pulmonary arterial pressure	
Changes in possible mediators or markers of vascular disease	
	Decreased fibrinogen level
	Decreased white blood cell and platelet activation
	Decreased C-reactive protein
Improved symptoms of anxiety and depression	
Improved insulin resistance	
Decreased nocturnal gastroesophageal reflux disease	

PAP treatment reverses many of the effects of OSA that are believed to increase the risk of coronary artery disease or CVAs or worsen coexisting heart failure. Reductions in nocturnal systemic and pulmonary arterial pressures on PAP have been well documented. It has been known for some time that many patients with OSA do not have the normal nocturnal fall in blood pressure because blood pressure rises at each event termination (nondippers). PAP reduces this effect by preventing apnea and hypopnea [139,140]. Of even greater importance is the finding that PAP can reduce daytime blood pressure as well [65,66,141]. For example, Becker and coworkers [66] found that CPAP treatment resulted in a mean drop in nocturnal and daytime blood pressure of about 10 mm Hg. The authors contended that similar long-term changes in blood pressure are believed to reduce coronary heart disease event risk by 37% and stroke risk by 56%. The failure of some studies to detect a drop in daytime blood pressure with PAP [142,143] may have been secondary to inadequate adherence, too short treatment time, inadequate ambulatory blood pressure—monitoring methods, or selection of patients with mild intermittent hypoxia.

Patients with OSA also have nocturnal increases in pulmonary arterial pressure secondary to hypoxic vasoconstriction. It has been said that patients with OSA with normal daytime blood gases usually have normal or only mildly increased daytime pulmonary pressures [144,145]. However, studies have shown that PAP reduces both nocturnal and daytime pulmonary arterial pressure [146,147

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). The improvement is not necessarily secondary to the improvement in daytime oxygenation. One study found a decrease in pulmonary vascular reactivity to hypoxia with PAP use (147).

Patients with OSA have daytime as well as nocturnal increases in sympathetic tone. Several studies have shown that PAP can reduce daytime sympathetic activity (148,149 and 150). The increased sympathetic activity is believed to be one reason that patients with OSA have reduced heart rate variability. PAP treatment has also been shown to increase heart rate variability OSA (151).

A growing number of studies show changes in blood components or indicators of inflammation in OSA that may be associated with an increased risk of atherosclerosis or thrombosis. PAP treatment reduces the early morning hematocrit (152) and fibrinogen levels (153). The levels of vascular endothelial growth factor (154), amount of neutrophil (155,156), and platelet activation (157) are also reduced with PAP. Inflammation is now believed to play a role in *(Print pagebreak 303)* atherosclerosis or plaque rupture. The level of C-reactive protein (a marker of inflammation) is reduced with PAP treatment (158,159). Untreated OSA is associated with nocturnal natriuresis probably due, at least in part, to an increased secretion of atrial natriuretic peptide (160). PAP also decreases the natriuresis and, clinically, patients may report a decrease in nocturia. PAP may also influence the distribution of fat. One study found a reduction in leptin (a hormone secreted by adipose tissue) and a reduction in visceral fat on PAP treatment (161). Increased visceral fat is associated with an increased risk of cardiac disease.

Recently, there has been tremendous interest in the effects of PAP on patients with heart failure. In patients with CHF and OSA, treatment with PAP increased the ejection fraction and reduced the level of dyspnea in patients with stable but severe failure (162,163). The use and benefits of PAP in patients with CSB and central sleep apnea (CSA) will be discussed later.

Adherence to PAP therapy can also result in significant improvement in morning headaches, chronic daily headache, and migraine. Such symptomatic improvements can be used as an incentive to pursue therapy.

POSITIVE AIRWAY PRESSURE IN OBSTRUCTIVE SLEEP APNEA—SPECIAL CIRCUMSTANCES

Hypoventilation with Obstructive Sleep Apnea

The two groups of patients with OSA who have daytime hypoventilation are those with OHS (hypoventilation not secondary to lung disease) and those with coexistent OSA and obstructive airways disease (OSA + COPD), the so-called overlap syndrome (164). These patient groups are also likely to have more severe arterial oxygen desaturation (165). Chronic treatment with CPAP can reduce the daytime arterial carbon dioxide tension ($PaCO_2$) in these groups (166,167 and 168). The ventilatory response to CO_2, typically shifts to the left without a change in slope (167). This suggests a change in set point. Although chronic CPAP treatment will improve the daytime $PaCO_2$ in some of these patients, most physicians treat patients with OSA and hypoventilation with bilevel PAP. This treatment augments ventilation as well as maintains upper-airway patency during sleep. However, if the IPAP—EPAP gradient is narrow, as might occur when the EPAP required to prevent apnea is very high (≥18 cm H_2O), the pressure support, which is available to augment ventilation (the amount IPAP exceeds EPAP), is reduced for devices delivering a maximum pressure of 20 cm H_2O. There are bilevel pressure devices capable of delivery pressures up to 30 cm H_2O, but mask and mouth leak may be problematic at these high pressures.

Patients with OSA and hypoventilation can present with acute hypercapnic respiratory failure (acute on chronic respiratory acidosis). Treatment with mask PAP and oxygen can often avoid the need for intubation (169). In very severe patients, one group reported on the use of volume-controlled ventilation with a mask (170). One problem with this approach is that many volume ventilators are not leak tolerant. The addition of supplemental oxygen to PAP is usually required for adequate oxygenation in acutely ill patients. Patients with coexistent OSA and obstructive lung disease and those with OHS (low daytime PO_2) may also require supplemental oxygen, as well as PAP, for chronic treatment (171). The challenges of using supplemental oxygen with PAP are discussed later.

Supplemental Oxygen and Positive Airway Pressure

During CPAP titration, some patients will exhibit significant arterial oxygen desaturation despite what appears to be adequate airflow (73). This is more common during REM sleep and in patients who are obese or have abnormal awake arterial blood gases. Presumably, desaturation is present because of hypoventilation and/or ventilation—perfusion mismatch. Hypoventilation may be related to a fundamental abnormality of ventilatory control or neuromuscular/chest wall abnormality (including obesity) sometimes complicated by a persistently high upper-airway resistance. Hypoxemia persisting despite maintenance of upper-airway patency during sleep may also be associated with ventilation—perfusion mismatch due to underlying lung disease or low FRC (severe obesity). If hypoxemia persists despite apparently normal airflow, one can try the following interventions. CPAP can be increased to eliminate unrecognized residual high upperairway resistance, CPAP can be changed to bilevel pressure to increase tidal volume, or

supplemental oxygen can be added. As noted, certain patient groups are more likely to require supplemental oxygen as well as PAP. When adding supplemental oxygen, one must remember that high flow from the device will dilute the added oxygen. Thus, a patient with an adequate saturation of 2 L/min of oxygen by nasal cannula when awake may require a higher oxygen flow on PAP. High flows (and low effective oxygen concentration [FiO_2]) are particularly likely when there is a high degree of unintentional leak (mask and mouth). One must also remember that the intentional leak devices built into masks have fixed orifices. Increases in pressure will increase the intentional leak and possibly mask leak and thus the total flow delivered (reduced effective concentration of oxygen). Thus, increases in pressure may require an increase in the flow of supplemental oxygen to maintain a satisfactory arterial oxygen saturation in some cases.

POSITIVE AIRWAY PRESSURE FOR CENTRAL SLEEP APNEA

CSA syndrome is usually diagnosed when the majority of events are central in nature. The group is heterogeneous but can be classified according to the presence or absence *(Print pagebreak 304)* of daytime hypercapnia [172]. In the hypercapnic CSA syndrome (central hypoventilation, chest wall disease, neuromuscular disease), there may be discrete central apneas or simply nocturnal hypoventilation. The daytime elevation in $PaCO_2$ worsens with sleep. In the past, negative-pressure ventilators (cuirass, body wrap) were frequently used. Unfortunately, obstructive apnea may occur with these devices as upper-airway muscle contraction and ventilation assistance may not be synchronized. Today, nasal or full-face mask bilevel PAP is more frequently used [173,174]. The EPAP is adjusted to maintain upper-airway patency. Some patients may require a timed backup rate (ST mode). In more severe cases, volume-cycled ventilation with a mask or tracheostomy may be necessary.

Nonhypercapnic CSA includes CSB and the idiopathic CSA syndrome. Both groups develop central apnea because the sleeping $PaCO_2$ is below the apneic threshold ($PaCO_2$ level triggering ventilation). CSB is the most common form of CSA (CSB-CSA). It occurs in 30% to 40% of patients with moderate to severe CHF [175,176]. These patients have periods of central apnea or hypopnea alternating with hyperventilation in a crescendo-decrescendo pattern. Patients with CSB-CSA have lower daytime and nocturnal $PaCO_2$ levels than patients with similar cardiac function but without CSB. The lower $PaCO_2$ levels are thought secondary to higher pulmonary capillary pressure (stimulation of J receptors). The lower the cardiac output is, the longer is the ventilatory phase between apneas. Patients with CSB-CSA may not complain of daytime sleepiness but often complain of disturbed sleep and nocturnal dyspnea. The goals of treatment include improved sleep (reduced events, arousals, and desaturations), improved cardiac function [177], and increased survival [178]. Treatment of CHF-associated CSB always begins with the optimization of CHF treatment (beta blockers, ACE inhibitors, and diuretics). If CSB persists, successful treatment of CSB with both PAP [177] and oxygen [179] has been reported. Of note, CPAP titration may reduce events acutely but rarely to the low levels usually seen in OSA. One randomized trial of 3 months of CPAP treatment [177] found a reduction in the AHI (43.2 ± 4.9 events per hour to 14.7 ± 4.8 events per hour) and improvement in the ejection fraction (21.2% ± 3.8% to 28.9% ± 4.2%). Neither the AHI nor the ejection fraction improved in the control group. In this study, CPAP was started at 5 cm H_2O and increased slowly over several nights to a mean of 10.1 ± 0.5 cm H_2O. Of note, studies of shorter duration have not always shown a clear benefit with CPAP treatment. Another study suggested a benefit for transplant-free survival in patients with CHF and CSB-CSA who were treated with CPAP [178]. A large multicenter trial is in progress to confirm this finding [180]. In some patients, a reduction in CSB may occur only after several weeks of treatment. CPAP appears to work acutely by inducing a mild increase in $PaCO_2$ and improving oxygenation. Chronically, CPAP may improve CSB by improving cardiac function. A recent acute study [181] compared one night of oxygen, CPAP, bilevel PAP, and a new form of ventilation (adaptive servoventilation [ASV]). ASV uses a fixed level of EPAP and a varying level of IPAP. The IPAP-EPAP difference increases during periods of low ventilation and decreases during periods of high ventilation. The bilevel PAP in this study included a backup rate (spontaneous rate -2 breaths per minute). The results are shown in Table 20-7. Only treatment with ASV reduced the AHI to levels commonly seen with PAP treatment of OSA, although all improved CSB.

TABLE 20-7 SUMMARY OF ACUTE TREATMENT STUDY FOR CSB-CSA

	ACUTE STUDY				
	CONTROL	*OXYGEN*	*CPAP*	*BILEVEL*	*ASV*
AHI (per hour)	44.5 ±3.4	28.2 ± 3.4	26.8 ± 4.6	14.8 ± 2.3	6.3 ± 0.9
Treatment mean values and ranges (-)	—	2 L/min	9.25 (7.5-10) cm H_2O	IPAP (11,12,13,14 and 15) EPAP (5 and 6)	EPAP 4-6
				Mean: IPAP-EPAP 13.5/5.3 cm H_2O	IPAP-EPAP difference was 4-10 cm H_2O
				Backup rate 13-18 per minute	

Adapted from Teschler H, Dohring J, Wang YM, et al. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure. *Am J Respir Crit Care Med.* 2001;164:614-619, with permission.

CSB-CSA can coexist with OSA. These patients often have mixed apneas with a long central portion. The nadir in desaturation following the mixed apneas is typically delayed because of an increased circulation time. During PAP titration, pure CSB-CSA often appears once pressure is high enough to eliminate the obstructive component. In *(Print pagebreak 305)* Figure 20-11, a tracing shows CSB on a CPAP of 8 cm H_2O. During the diagnostic portion of the study, mixed apneas were seen.

In summary, there is no consensus on the best way to treat CSB—CSA or to titrate PAP for this disorder. A reasonable approach is to increase pressure until obstruction is abolished. If further increases in pressure do not eliminate CSB, then a reasonable goal would be treatment with 10 to 12 cm H_2O (or higher if needed to maintain airway patency). If persistent significant arterial oxygen desaturation secondary to central apneas persists on PAP, some physicians add oxygen as well.

PAP has also been used as a treatment for idiopathic CSA [182,183]. This syndrome is diagnosed when a majority of events are central but no disorder such as neurologic disease or CHF is present. These patients usually have a low daytime $PaCO_2$ and increased ventilatory responses. The mechanism by which PAP decreases central apnea in these patients is unknown. In some patients, upperairway stabilization may prevent RERAs that are followed by hyperventilation and a central apnea on returning to sleep. In others, PAP may induce a mild increase in the $PaCO_2$, which may stabilize ventilation. In one case report, CPAP helped but bilevel worsened events in patients with idiopathic CSA [184].

POSITIVE AIRWAY PRESSURE IN CHILDREN

Adenotonsillectomy is the most common treatment for OSA in children. This surgery is effective in the majority of cases. In cases where this treatment is not effective, where only minimal adenotonsillar tissue is present, if there are specific surgical contraindications, or for those who prefer nonsurgical alternatives, PAP has been used with success [185,186]. Children with craniofacial malformations, severe obesity, and those with hypoventilation are the most frequent candidates for PAP. Older children generally tolerate PAP. Young children or older children with learning or behavioral problems may require desensitization or behavior techniques to accept this treatment. Letting children play with the mask, try it on during the day, and wear it for short periods of time for several days to a week prior to the initial titration is an important technique for improving acceptance. The involvement of a dedicated caregiver and close attention to adherence is essential. The side effects of PAP treatment are similar to those in adults. One case of midface hypoplasia has been reported [187]. Therefore, chronic overtightening of the mask should be avoided and attention to facial development is required. As pressure requirements may change with growth, periodic assessment of pressure requirements is also prudent. Some centers use bilevel PAP, rather than CPAP, routinely in an attempt to improve acceptance. Use of bilevel PAP would definitely be preferred in patients with hypoventilation.

FUTURE CHALLENGES FOR POSITIVE AIRWAY PRESSURE TREATMENT

Not long ago, the sleep medicine community was called upon to demonstrate the clinical value of CPAP [132]. During the subsequent years, data have accumulated that demonstrate objective and meaningful benefits conferred on noteworthy subsets of patients with OSA in terms of quality of life, daily function, specific measures of performance, and physiologic measures of cardiovascular function and health. In addition, data have been provided demonstrating public health benefits reflected by reduced motor vehicle accidents [59,60]. Untreated OSA in the community is associated with an increased healthcare burden [188]. Much remains to be learned, however, regarding long-term outcomes of this therapy and, in a similar vein, optimal identification of those patients who are most likely to accrue health benefits. In considering the utility and future of PAP therapy, healthcare providers and administrators must consider the five “C's” of PAP:

1. Compliance (aka Adherence). The common dialog in which clinicians engage regarding patients with poor versus adequate compliance might lead one to the erroneous conclusion that we know what constitutes acceptable utilization of PAP modalities. However, further reflection on the poorly understood nature of the relationship between sleep and function will lead to the conclusion that we are currently not in a position to precisely define a duration or frequency of usage that alleviates symptoms, normalizes function, and prevents poor outcome. For example, recent data suggest that the modest degrees of sleep restriction that are prevalent in society are associated with meaningful functional impairment [122]. Thus, assuming little or no value in “sleep” without PAP (and this is by no means currently known), it may be inappropriate to accept 4 hours of PAP use as adequate. Before we can confidently demand a requisite usage of PAP by our patients, we must first ourselves obtain compelling, evidence-based information to support our recommendations and expectations. It is also essential to define the complex elements and interactions that determine whether an individual patient will use PAP in the prescribed manner. Only with knowledge of these factors can we identify patient-specific issues that promote suboptimal adherence and, having identified the problem, only then can we begin to develop a solution.

2. and 3. Comfort and Convenience. Anyone who has slept with a PAP device will recognize that it engenders encumbrance and inconvenience. It will probably never be as easy to put an interface on one's nose, mouth, or both as it is to simply go to bed. It is nonetheless imperative that the technologies continue to improve to reduce the size and noise of devices to reduce the burden on bed partners as well as patients. Similarly, the interfaces must continue to evolve in *(Print pagebreak 306)* order to provide a wide range of choices for patients. It is likely that a positive attitude is important. This includes the healthcare provider as well as the patient and family. If the healthcare provider appears unconvinced of the merits of PAP, the patient is unlikely to be a believer and is, therefore, a poor risk for successful home therapy.

4. Consequences. Considerable information regarding the cardiovascular and neurocognitive consequences of OSA has become available in the last decade. We have begun to learn how PAP interacts with cardiovascular physiology but, at present, can only infer how this might translate into long-term outcomes. Such data, as well as those related to the long-term impact on relevant neurocognitive functions, are essential if we are to make a justifiable argument for CPAP therapy to many of our patients (particularly those with minimal symptoms).

5. Cost. The issue of healthcare costs spans a wide spectrum of considerations. Certainly, it is important to maintain the cost of PAP devices within a range of affordability. However, we must learn more about the healthcare costs of untreated OSA and the impact of PAP therapy. We must assess the cost savings, if any, with regard to fewer hospitalizations, provider visits, and productivity. It is important to continue to explore innovative ways to minimize the costs associated with diagnosing and managing OSA in a manner that will maximize the utilization of resources and patient satisfaction.

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