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Methods to Stabilize the Upper Airway Using Positive Pressure

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Summary: Nasal CPAP has become the treatment of choice for obstructive sleep apnea because of its predictable physiologic effect over the full spectrum of disease. The physiology of the upper airway during sleep mimics the behavior of a collapsible tube; CPAP prevents the negative intraluminal pressure thought to cause apnea, hypopnia and increases in airway resistance. Titration of CPAP for optimal therapy is not well standardized. However, treatment algorithms should aim to eliminate apneas, hypopneas, snoring, significant O_2 desaturations, and EEG arousals. Flow limitation (recognized from the shape of the flow tracing) may also need to be eliminated. Once prescribed, CPAP is effective but compliance with therapy is not uniform or optimal. Attention to details of comfort and various enhancements to CPAP may improve results but need to be validated. Automatically adjusting CPAP may provide a new therapeutic option, but again needs to be carefully evaluated to define improvements possible in ease of titration, effectiveness, and ultimate compliance. **Key Words:** CPAP—Obstructive sleep apnea—Upper airway—Flow limitation.

Nasal continuous positive airway pressure (CPAP) has become the treatment of choice for obstructive sleep apnea (1–3). In large part, this is because this form of therapy has the most predictable physiologic effect on upper airway collapse during sleep. The major limitation of CPAP is that there is suboptimal patient compliance (4,5), but the past several years have seen improvements in blowers and in interfaces to the patient. In addition, a series of refinements on the concept of CPAP as a form of upper airway splint have been proposed. This review will describe the present state of CPAP use.

CPAP systems

The concept of using positive pressure applied via the nose as a splint to prevent collapse of the upper airway was first proposed by Sullivan et al. (6). The success of this therapeutic intervention in obstructive apnea derives from the effect of positive intraluminal pressure at the site(s) of airway collapse. Typically, this is either in the hypopharynx at the level of the posterior soft palate or in the oropharynx at the level of the base of the tongue. CPAP provides a positive intraluminal pressure which acts by opposing the collapsing force created during inspiration by a negative intraluminal pressure (Fig. 1). Intraluminal positive pressure also opposes constant or expiratory extraluminal/tissue forces (e.g. gravitational effects on the tongue). Finally, positive intraluminal pressure applied during expiration and/or the pre-inspiratory pause provides a dilating effect on the airway prior to the start of inspiration, which may further contribute to the therapeutic effect of CPAP (7).

The technology to apply CPAP is conceptually simple—all that is necessary is to maintain pressure in the airway that is positive. Current devices all include at least the following components (Fig. 2) (8).

1) A source of pressurized airflow, usually a blower. Typically the blower characteristics and its speed or power control the pressure in the CPAP circuit. Although originally a separate pressurizing valve was used, this is no longer usually necessary in most systems.

2) A tight-fitting nasal or full-face interface. The most common devices are either a mask or a variation on nasal prongs. These are held on with some type of

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Page 1 of 8

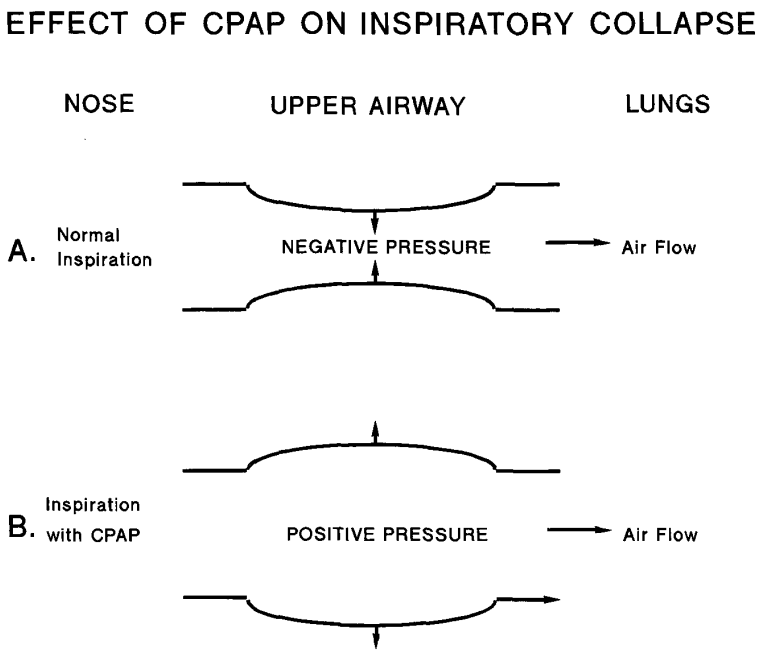

FIG. 1. Effect of CPAP on inspiratory collapse of the upper airway. a. During a normal inspiration, negative pressure is generated in the lumen of the upper airway by the contraction of the diaphragm acting through the resistance of the nose. This pressure favors collapse to the extent that the luminal walls are not rigid. b. With CPAP applied, intraluminal pressure is always positive with respect to the outside and thus the airway is prevented from collapsing during inspiration. Actual dilatation may also occur.

headgear and may be the most important determinant of patient comfort.

3) A hose connecting 1) and 2) with an intentional leak port positioned near the nose to provide a continuous washout of the dead space in the system. This leak port has replaced the non-rebreathing valves present in most ventilator circuits.

Current systems have evolved to a point where they are quiet, reliable, and sufficiently varied to accommodate most patients' requirements for comfort. Systems are portable and some have the ability to adapt to 110–220 V AC or even to 12 V DC for use with a car battery.

Titration of CPAP pressure

Obstructive apnea is virtually always obliterated by some level of CPAP < 20 cm H_2O (2,3). It is intuitive-

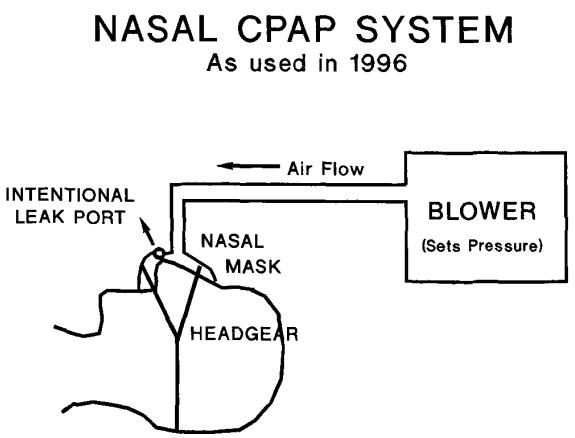

FIG. 2. Schematic of nasal CPAP systems as currently used. See text for details.

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Page 2 of 8

ly believed by most authorities that the lowest pressure that achieves a therapeutic result during an entire night is the desirable prescription pressure. Excessive pressure is thought to be less comfortable and to reduce patient compliance with therapy, although this has not been proven. Determination of the prescription pressure, or "CPAP titration", has traditionally been done by a technician in the sleep laboratory during full polysomnography (3), but, other than elimination of apnea, the actual endpoint of titration has not been well defined or even described in many published reports. Recently, attention to effects of CPAP on airway physiology has suggested more specific algorithms to be followed for CPAP titration (3,9). It is now common for the sleep technician to titrate CPAP first to the abolition of frank apneas and hypopneas, then to the elimination of snoring, intermittent O_2 desaturations, and microarousals on EEG (10) thought to be due to partial obstruction. In our laboratory, we use an additional criterion for an "optimal CPAP"—the elimination of all evidence of an elevated upper airway resistance as judged from the shape of the inspiratory flow waveform recorded directly from the CPAP circuit (see description of flow limitation below) (9).

Until recently, CPAP titration was always done in the sleep laboratory. However, some recent reports have suggested that it is possible to move CPAP titration to an outpatient setting. Approaches proposed and being evaluated include empiric settings of CPAP with subsequent monitoring, attended home titration (11), unattended titration, and the use of "automatic" titrations.

While it is generally assumed that careful adjustment of CPAP is essential to produce the best result and compliance, there are a few proponents of the "one size fits all" approach (12). Until now, this has generally been limited to situations in which an empirically chosen single pressure (e.g. 10 cm H_2O) is used indiscriminantly for an interim period prior to a definitive titration study confirming the efficacy of therapy. This approach may have use in patients who are in desperate need of therapy when a titration study is not immediately available, but it exposes the patient to the possibility of both under- and over-treatment. As an alternative to the single pressure prescription approach, a variety of equations have been proposed that attempt to predict the therapeutic pressure using indices of weight, apnea severity, etc. (13). These formulae have been applied to only small samples of patients and data on their validity and the long-term outcomes of patients so treated are still pending. Yet another non-technician based approach that has been used proposes titration of CPAP performed in the home by the spouse based on simple observation and auditory cues such as persistent snoring (14).

Despite the practical appeal of the above approaches, most clinicians base their CPAP prescription on an attended monitored study. There is, however, little published uniformity to the criteria used by the technician to decide on the "optimal" pressure. Most protocols stress the abolition of apnea, but include reference to hypopnea (variably defined), snoring, and periodic oxygen desaturation. Some laboratories also titrate CPAP to try to abolish periodic electroencephalogram (EEG) arousals (which suggest mild intermittent upper airway obstruction not producing detectable hypopnea or desaturation reminiscent of the recently described upper airway resistance syndrome [10]). Similarly, an additional approach proposed is to use esophageal pressure monitoring to titrate the level of CPAP to that pressure which minimizes intrathoracic pressure swings indicative of high resistance, thus fully correcting any elevated upper airway obstruction. Our own approach is to use the non-invasive index of airway abnormality available from the inspiratory flow contour (flow limitation) to effect the CPAP titration (9).

Flow limitation

In the past four years, our laboratory has utilized the concept of identifying flow limitation as a technique for both the diagnosis of abnormal upper airway behavior indicating the need for therapy and in titrating the optimal pressure to be applied to a CPAP mask for treatment of patients with OSAS (9).

Flow limitation is defined as the behavior observed when increasing effort applied to a system produces no increase in flow. This situation is typical of collapsible tubes subjected to negative intraluminal pressures. This model applies well to the human upper airway during sleep, where inspiration creates a collapsing pressure that has a roughly sinusoidal contour. When the airway is relatively rigid, the inspiratory contour is also sinusoidal because flow is proportional to driving pressure. In contrast, if the airway becomes more collapsible, as during sleep in patients with OSAS, flow limitation occurs and a characteristic plateau develops on the flow tracing (Fig. 3). We have also shown that there is a high likelihood of subsequent arousal whenever this contour is seen (15). Flow limitation is obliterated when CPAP is applied, as positive intraluminal pressure opposes airway collapse during inspiration. We have shown that if airway resistance is monitored, as with an esophageal pressure transducer, there is a close correlation between periods of high airway resistance and the appearance of the characteristic flow contour indicative of inspiratory flow limitation (9). Small changes up and down in CPAP (sometimes as small as 0.5 cm H_2O) produce

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Page 3 of 8

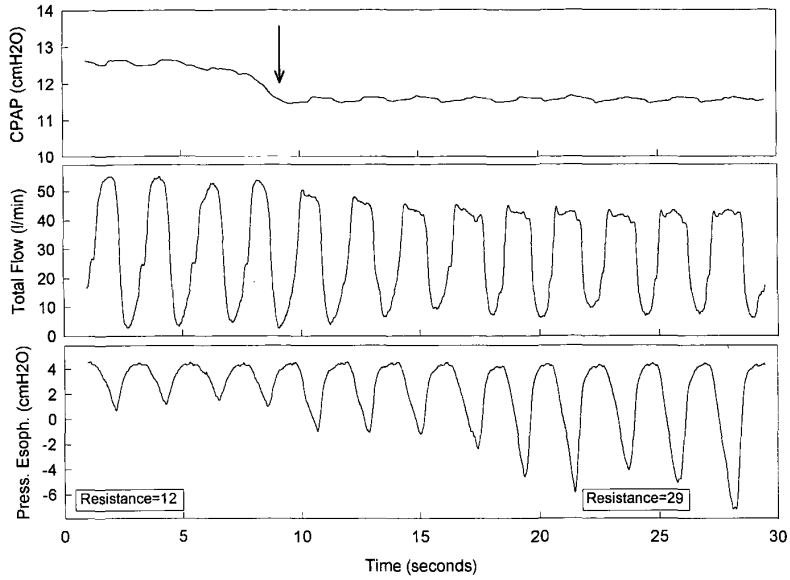

FIG. 3. Tracing of CPAP (top channel) and flow through the CPAP circuit (middle tracing) in a patient with obstructive sleep apnea syndrome (OSAS). Lower channel shows exophageal pressure. At the arrow, CPAP was reduced by 0.5 cm H_2O. Note nasal contour changes from sinusoidal to flattened, indicating flow limitation has developed. Also note that esophageal pressure swings increase markedly when CPAP is lowered indicating an increase in airway resistance at the same time as flow limitation develops. [Reprinted from Condos et al. (9) with permission.]

dramatic changes in the shape of the flow. This is readily and non-invasively monitored by recording the shape of the total flow in the CPAP circuit and subtracting the baseline "leak" flow. An analog flow signal is directly available as an output on some CPAP systems and can be used for this purpose.

Titration of CPAP by the sleep technician to the point where the flow-limited contour disappears and the inspiratory flow becomes sinusoidal has been our standard of determining the "optimal CPAP". Automation of this process underlies one version of automatic CPAP titration (see below).

Two caveats to this approach have been raised. First, there appears to be some hysteresis in the pressure at which flow limitation disappears (generally, during upwards titration of CPAP, it requires about 2 cm H_2O more CPAP to eliminate flow limitation than the pressure at which it disappears during downwards titration) (9). Thus, both upwards and downwards titrations (as well as titrations during all stages of sleep and in all body positions) contribute to the evaluation of CPAP therapeutic pressure. Secondly, it has been suggested by at least one abstract that flow limitation can occur without impeding the quality of CPAP prescription and thus may represent too stringent a criterion (16). This remains to be further tested. In our hands, however, residual flow limitation during CPAP generally coincides with increased patient complaints of residual fatigue associated with excessive numbers of arousals on EEG study.

Compliance with CPAP

Fitting of the mask, choice of the minimal pressure needed to abolish apnea, and attention to patient discomfort and concerns probably play a significant role in determining ultimate patient compliance. Despite the intuitive logical appeal of this statement, it has been difficult to document this in published studies. Perception of symptomatic improvement by the patient may be the most important factor in long-term compliance (4,5).

In order to maximize CPAP compliance, a series of training steps are used by most clinicians. Thus, it is important to fit the patient with the most comfortable mask/strap before the sleep study begins. Overtightening the head strap is perhaps the most common mistake patients and therapists make, believing they can overcome leakage around the mask. In fact, most current masks work best when fit somewhat loosely. Claustrophobia is a frequently described complaint (4). This may contribute to lack of compliance and on occasion may preclude the use of CPAP entirely. On rare occasions, we have found the judicious use of anti-anxiety agents during the initiation of CPAP to be of

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Page 4 of 8

some use (buspirone is particularly safe in this regard as it is not a respiratory depressant [17]).

The presentation of the reason for using CPAP to the patient may also play some role in improving the outcome of the initial trial. Whereas some patients readily accept the need for therapy, in other cases review of the diagnostic tracing with the patient may help convince them of the need for therapy. In addition, we have found utility in presenting the initial use of CPAP as a "therapeutic trial" to the patient, with the endpoint being dramatic relief of the symptoms the patient himself can judge, rather than as a physician-imposed requirement.

The prescription of nasal CPAP settings, and the initial patient training in use of the device is generally performed in, or directly under, the supervision of the sleep disorders laboratory and is an integral part of the laboratory's function. Our general practice is to do a full separate night of in-laboratory CPAP titration on all patients previously diagnosed with obstructive apnea (unless, as occurs in less than 5% of cases, the patient's first contact with the mask is so negative as to preclude even trying it for a night). If the patient tolerates the device for the full night in the laboratory, CPAP therapy is prescribed for home use and therapeutic results are reevaluated after several weeks. If the patient is resistant to use of CPAP, alternate therapies may be tried. Even then CPAP may provide a temporary treatment, as during weight loss, pre- and post-operatively for uvulopalatopharyngoplasty (UPPP) or during the workup and treatment of coincident disease (e.g. hypothyroidism). Furthermore, the CPAP titration and therapeutic trial can be used to provide the patient with a preview of the "best" symptomatic outcome possible. This can then be used to evaluate the potential benefits to be realized by surgical approaches, etc.

Despite an initial preference for tracheostomy, most practitioners now agree that severe apnea is not a contraindication to use of CPAP (3). When used conscientiously by the patient, CPAP is as successful as tracheostomy in even the most severe cases of obstructive apnea. At the other extreme of severity, the symptoms of a patient with even very mild apnea may respond dramatically to a trial of CPAP. Thus, our present approach is to try CPAP whenever the diagnosis of apnea is clear, provided symptoms of daytime impairment motivate the patient. The one exception to this rule would be the (rare) patient with life-threatening cardiac symptoms which might not allow for the occasional non-use of CPAP generally observed in even the most compliant patient. In this case, tracheostomy may need to be considered more strongly.

The major limitation of CPAP therapy relates to discomfort or other factors leading to incomplete compliance with the necessary use of the device (generally thought to be required during all periods of sleep, at night or otherwise). Several recent studies suggest that patients tend to use CPAP less than might be expected given their reported sense of improvement on therapy (4,5). These studies show an average use of 4–5 hours per night with as many as one-third of patients using CPAP only 4–5 nights per week. It is, therefore, not unexpected that some patients on CPAP continue to be sleepy by objective (multiple sleep latency tests [MSLT]) testing, but the exact relationship to compliance has not been demonstrated. Postulated therapeutic interventions include attempts at behavior modification to achieve better CPAP compliance and changes in the way CPAP is prescribed (see above) aimed at improving comfort. The possibility has also been raised that there is an independent or acquired disorder in some patients with obstructive apnea which causes hypersomnolence to persist even when apnea is optimally treated, but this remains entirely speculative at this time.

A variety of "gadgets" have been added to conventional CPAP, and have been alleged to contribute to improved compliance.

Heat/humidification. One of the most frequently reported complaints during initiation of CPAP therapy is that of nasal dryness, pain, and nasal congestion. This is particularly true in patients who experience a large leak through the mouth. The first line of therapy for this complaint should be to condition the inflowing airstream to reduce the drying effect of large volumes of air passing over the nasal mucosa. With the advent of the current blowers (as opposed to the original compressor CPAP systems), the inflowing air is not desiccated, but ambient air, especially in the winter, may be relatively dry. It has been our experience that about 25% of patients benefit from humidification. This can be achieved with a moderately effective simple pass-over humidifier, available as an "add-on" for most CPAP systems, through humidification of the air taken in by the blower, as by an ultrasonic room nebulizer placed 4–6 feet from the blower or with a heated humidifier placed in line with the CPAP circuit to the patient. This last option is the most efficient at humidification and raises the relative humidity significantly. The disadvantages are added cost and the possibility of fostering bacterial colonization in the tubing. Thus, heated humidification is best reserved for the minority of patients who cannot be handled otherwise.

A factor which interacts with the need for humidification is mouth leak. In the absence of a mouth leak, the actual flow over the nasal mucosa is no greater than the volume of air normally breathed in by that route, no matter what the flow through the CPAP circuit. Thus, it is a misconception that the high flow

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Page 5 of 8

generated by CPAP blowers necessarily causes desiccation of the nose. In contrast, when there is a mouth leak, flows through the nose can approach 40–60 l/minute with consequent discomfort. While not a problem in the majority of patients, this does occur in 10–15% of cases, and a recent report suggests it is more common after palatal surgery. The mouth leak can usually be handled by a variety of "chin straps", whose function is to keep the mouth closed. When prescribing these, attention should be paid to showing that they work at keeping mouth airflow down and to adjusting them so that they do not add unduly to discomfort.

Ramp. CPAP pressure is sometimes perceived as uncomfortable when a patient is awake, but well tolerated when he/she is asleep. To overcome the lack of compliance proposed to occur in this setting, a "ramp" feature that slowly increases pressure after the machine is turned on has been introduced on several machines. This may allow the patient to fall asleep at lower, and perhaps more comfortable, settings. No data exist on the effectiveness of this approach, but intuitively it is attractive and may be appropriate for a subset of patients. It is our impression that this approach plays its largest role in the early weeks of CPAP use, as most patients who continue to use CPAP rapidly become adapted to the sensation of pressure while awake. In fact, we have seen several long-term users of CPAP who cannot fall asleep when the CPAP is not present, as they have come to rely on this feedback that the mask and system are functioning correctly.

Bi-level CPAP. Bi-level CPAP (BiPAP® and others) is a modification of the CPAP concept which provides independent adjustment of inspiratory and expiratory pressures, whose alternative application is triggered by the patient (18). It was originally proposed that this might address the complaint of some patients who experience CPAP as uncomfortable due to the impediment to exhalation that the pressure causes (similar to pursed lip breathing). Since it is believed that to treat obstructive apnea the greatest need for pressure is during inspiration, it was hypothesized that bi-level systems would allow the pressure to be set somewhat lower during expiration. Unfortunately, it has generally proven to be the case that when the expiratory pressure is dropped significantly below the CPAP needed to abolish apnea, evidence of airway obstruction rapidly reappears (19). Thus, the EPAP (expiratory pressure) needed is usually set very close to the CPAP pressure needed for a one-pressure machine. When this is done, the major advantage of a bi-level device is lost unless it is desirable to provide an inspiratory pressure boost above CPAP. This does not clearly play a role in obstructive apnea, but may be important in subjects with alveolar hypoventilation syndromes and can be likened to pressure support ventilation. Although bi-level CPAP is widely prescribed by some clinicians, there is little evidence to date that this improves compliance with therapy (19), and there has been some retreat from this mode of therapy due to its added cost.

The use of ventilatory assistance (in contrast to airway maintenance) is not relevant to simple obstructive apnea, as the typical apneic makes adequate respiratory efforts. Ventilatory support is applicable to the small number of patients with alveolar hypoventilation syndromes (although these may overlap with obstructive apnea in 5–10% of cases), as well as to the patient with central (i.e. non-obstructive) apneas and non-obstructive hypoventilation during sleep. A full discussion of the issues of assisted non-invasive ventilation is beyond the scope of this review. The same patients needing ventilation, and some others, will occasionally also need the use of supplemental O_2 to correct residual hypoxia despite successful stabilization of the airway with CPAP, but this should be reserved as a last resort for the special case due to its added cost and potential complications. In our opinion, the first attempt at treatment should be ventilatory assistance as above to augment alveolar ventilation or increase the tidal volume. This may, however, not reverse the hypoxemia in all cases. At this point, additional O_2 can be added to the CPAP/ventilation circuit by bleeding it into the mask. The absolute concentration of O_2 being delivered is difficult to regulate as the variable leak of the mask and changing pressure in the circuit cause non-constant dilution of the supplemental O_2 by the supply of air from the blower. Generally, a somewhat empiric setting of 2–10 l/minute of O_2 can be titrated in the sleep laboratory to produce an acceptable, but not excessive, oxyhemoglobin saturation (e.g. ~90%). It is our policy to do this only after other manipulations have excluded all apneas and after failure of a trial of ventilation as a means of improving hypoxemia because of both safety and cost concerns.

Self-adjusting CPAP. Until recently it had been assumed that the amount of positive pressure needed to overcome obstructive apnea in a given patient was constant. It is now clear that changes in position, sleep stage, and nasal patency all can have profound effects on the tendency of the airway to collapse; similarly, these changes in physiology may result in different therapeutic requirements for CPAP (20–22). Although the usual clinical approach to these variations (which become apparent on an all night laboratory study as the re-occurrence of apnea or snoring at a previously therapeutic pressure) is to choose the highest pressure needed as the therapeutic prescription pressure, an evolving concept is to apply a continuously self-adjusting CPAP. To achieve this, one needs a signal

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Page 6 of 8

which is interpreted by the "smart" device as indicating the "need" for CPAP. Current research and commercial efforts have resulted in a variety of approaches to this problem (23–28). Available signals on which the feedback has been based include: apneas, reductions of peak flow (hypopnias), snoring, and flow limitation. Although data are limited so far, it is clear that such machines are technologically possible and will respond to changes in the patient. The remaining question is whether this will advance the therapy of patients. From a theoretical point of view this could occur through several very different means.

1. An automatically adjusting machine could reduce the technician effort needed to do titration to a single prescription pressure by reducing the need to have a technician and a supervised setting for the titration night. This approach is being actively investigated with several machines.

2. Automatically adjusting machines, used on a continuous basis, could improve the outcome of therapy by providing a system capable of responding to the occasional high levels of pressure that were previously undertreated with a single constant prescription pressure. This could improve the residual sleepiness so often seen in apnea patients who do use their CPAP regularly.

3. Automatically adjusting machines, used on a continuous basis, could result in overall lower pressures as they would drop the pressure when it was not needed (as during periods prior to sleep and arousals from sleep), possibly making the CPAP system more tolerable. It is generally assumed (but not proven) that a lower overall CPAP means greater likelihood of compliance.

4. Automatically adjusting CPAP also provides a unique opportunity to track "physiologic need" for CPAP and, thus, may provide new research insights.

Whatever the goal chosen, it is clear that the automatically adjusting CPAP machines need to be assessed to see if they provide any advantage. It also needs to be kept in mind that the mode of operation of each machine (e.g. the feedback signal for "CPAP need" chosen) has a large role in determining how the machine functions, and, thus, it will be difficult to extrapolate advantages (or failures) of one machine to another.

In summary, since first proposed in 1981, CPAP has become an established and successful way to stabilize the upper airway in patients with the obstructive sleep apnea syndrome. Further improvements in mask and blower technology may add to the percentage of successes. However, most clinicians currently agree that this non-invasive and reversible therapy should be the first line of therapy in symptomatic cases of apnea.

REFERENCES

1. Sullivan CE, Issa FG. Obstructive sleep apnea. *Clin Chest Med* 1985;6:633–50.
2. American Thoracic Society. Indications and standards for the use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. *Am Rev Respir Dis* 1994;150:1738–45.
3. Kryger MH. Management of obstructive sleep apnea. *Clin Chest Med* 1992;13:481–92.
4. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993;147:887–95.
5. Waldhorn RE, Herrick TW, Nguyen MC, O'Donnel AE, Sodero J, Potolicchio SJ. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. *Chest* 1990;97:33–8.
6. Sullivan CE, Berthon-Jones M, Issa FG, Evese L. Reversal of obstructive sleep apnoea by continuous positive airway pressure. *Lancet* 1981;1:862–5.
7. Rapoport DM, Garay SM, Goldring RM. Nasal CPAP and obstructive sleep apnea: mechanisms of action. *Bull Europ Physiopath Resp* 1983;19:616–20.
8. Rapoport DM. Techniques for administering nasal CPAP. *Respir Manage* 1987;17:17–21.
9. Condos R, Norman RG, Krishnasam I, Peduzzi N, Goldring RM, Rapoport DM. Flow limitation as a non-invasive assessment of residual upper airway resistance during CPAP therapy of obstructive sleep apnea. *Am Rev Respir Dis* 1994;150:475–80.
10. Guilleminault C, Stoohs R, Clerk A, Simmons J, Labanowski M. From obstructive sleep apnea syndrome to upper airway resistance syndrome: consistency of daytime sleepiness. *Sleep* 1992;15:S13–6.
11. Waldhorn RE, Wood K. Attended home titration of nasal CPAP therapy for OSA. *Chest* 1993;104:1707–10.
12. Ramos R, Nahmias J, Karetsky MS. Determinants of the magnitude of CPAP required in OSAS. *Sleep Res* 1989;18:291.
13. Hoffstein V, Mataka S. Predicting nasal continuous positive airway pressure. *Am J Respir Crit Care Med* 1994;150:486–8.
14. Flemmons WW, Whitelaw WA, Remmers JE. Setting the level of continuous positive airway pressure for sleep apnea patients by untrained observers—is it safe? *Am J Respir Crit Care Med* 1994;149:A492.
15. Rapoport DM, Norman RG. Inspiratory flow limitation and sleep fragmentation in normal subjects. *Am J Respir Crit Care Med* 1995;151:A153.
16. Meurice JC, Paquereau J, Series F, Denjean A, Patte F. Influence of correction of flow limitation on CPAP efficiency in sleep apnea hypopnea syndrome. *Am J Respir Crit Care Med* 1996;153:A772.
17. Rapoport DM, Greenberg HE, Goldring RM. Differing effects of the anxiolytic agents buspirone and diazepam on control of breathing. *Clin Pharm Therap* 1991;49:394–401.
18. Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. Physiologic and clinical implications. *Chest* 1992;98:317–24.
19. Reeves-Hoche MK, Hudgel D, Meck R, Wittman R, Ross A, Zwillich CW. Continuous vs bilevel positive airway pressure for obstructive sleep apnea. *Am J Respir Crit Care Med* 1995;151:443–9.
20. Cartwright R. The effect of sleep position on sleep apnea severity. *Sleep* 1984;7:100–14.
21. Olsen DD, Dern EB, Westbrook PR. Sleep and breathing disturbance secondary to nasal obstruction. *Otolaryngol Head Neck Surg* 1981;89:804.
22. Schwartz AR, Smith PL, Gold AR, Wise RA, Permutt S. Induction of upper airway occlusion in sleeping normal humans. *J Appl Physiol* 1988;64:535–42.
23. Berton-Jones M. Feasibility of a self-setting CPAP machine. *Sleep* 1993;16:S120–1.

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Page 7 of 8

24. Sadrnoori B. Evaluation of recently released self-adjusting nasal CPAP (DPAP). *Sleep Res* 1996;25:528.
25. Burke EA, Burk JR, Axe JR, Behbehani K, Yen F-C. Auto-CPAP in the treatment of obstructive sleep apnea. *Sleep Res* 1996;25:281.
26. Grunstein RR, Willson GN, Lawrence S, Flynn W, Piper AJ, Sullivan CE, Berthon-Jones M. Automatically adjusting nasal CPAP—one year experience in a sleep laboratory. *Sleep Res* 1996;25:249.
27. Teschler H, Berthon-Jones M, Thompson AB, Henkel A, Henry J, Konietzko N. Automated continuous positive airway pressure titration for obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 1996;154:734–40.
28. Meurice JC, Paquereau J, Series F, Neau JP, Patte F. Evolution of sleep and breathing characteristics during ventilation with autocpap Morphee + in sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 1996;153:A872.

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