The syndrome of obesity, hypersomnolence, and hypercapnia, known as the "Pickwickian" syndrome, has remained the focus of much physiologic and clinical interest since its first description by Burwell et al. Most prior reports have shown a low minute ventilation to be characteristic of the hypercapnia. However, the reasons for this chronic hypoventilation and an accurate definition of the patterns of breathing associated with it remain incomplete. Initial speculation with respect to its etiology focused on diminished central responses to ventilatory stimuli and mechanical chest wall abnormalities of the obese. More recently, it has become clear that patients with the "Pickwickian" syndrome usually also have sleep-related periodic functional obstruction of the upper airway—the obstructive sleep apnea phenomenon. While the occurrence of obstructive apnea provides for a potential reduction of ventilation while asleep (and thus for acute hypercapnia), chronic waking hypercapnia remains unexplained by this mechanism. Furthermore, hypercapnia is not present in most patients with the obstructive sleep apnea syndrome while they are awake. This dilemma is highlighted by previous results from our laboratory demonstrating that patients with severe obstructive sleep apnea and chronic hypercapnia need not differ from eucapnic patients with the syndrome in number of apneas, their duration, the degree of obesity, or the clinical severity of their hypersomnolence. Thus, the mechanism of the chronic hypercapnia in the "Pickwickian" patient with obstructive sleep apnea remains to be fully elucidated.

The present study was designed: (1) to define the contribution of apnea to the etiology of chronic hypercapnia in eight "Pickwickian" patients with the obstructive sleep apnea syndrome by following the response of their chronic hypercapnia to correction of the apnea phenomenon, and (2) to characterize other mechanisms of their hypercapnia before and after therapy of the apnea.

METHODS

Eight chronically hypercapnic patients with obstructive sleep apnea syndrome were evaluated before and after therapy for their apneas. Therapy consisted of permanent tracheostomy in seven patients; one patient was successfully treated with nightly use of a nasal mask which delivered continuous positive airway pressure (nasal CPAP). In each case, the patient was able to reduce his arterial Pco₂ below 40 mm Hg by voluntary hyperventilation. All patients were obese and hypersomnolent. Six of the eight had had multiple...
hospitlizations characterized by cardiorespiratory failure and edema. Two patients had additional symptoms of chronic bronchitis. Each patient was in a clinically stable state for at least two months at the time of pretherapy study.

All patients had standard polysomnographic sleep monitoring to establish the diagnosis of obstructive sleep apnea. This included EEG, EOG, and chin EMG for sleep staging, nasal PC02, and oral thermistor to document air movement, detection of chest and abdominal movement by inductance plethysmography, ECG, and measurement of arterial O2 saturation by ear oximetry. Ear oximeter saturations below 50 percent were reported as 50 percent due to the known alinearity of the instrument in this range. In two patients, an esophageal balloon was used to document persistent respiratory effort during apneas. Obstructive apnea was defined as a cessation of air movement lasting more than 10 seconds associated with persistent respiratory efforts. Apneas which began without respiratory efforts but during which efforts developed (mixed apneas) were also classified as obstructive. Central apnea was defined as cessation of both air movement and respiratory effort for more than 10 seconds.

Pulmonary Function

All patients had standard tests to determine pulmonary function both before and after therapy for the obstructive sleep apnea. These included lung volumes by spirometry and body plethysmography, maximal expiratory flow volume loop, and multiple arterial blood gas determinations while awake. In addition, minute ventilation and pattern of respiration were determined while awake in the supine position using a three minute collection of expired gas in a Tissot spirometer. From analysis of the mixed expired gases, CO2 production (VCO2) and physiologic dead space were calculated. In the patients with tracheostomy, posttherapy testing was performed with a plugged tracheostomy button which restored the upper airway anatomy to its pretracheostomy state. All tests were repeated one, six, and 12 months after therapy.

Ventilatory Responses to Hypercapnia and Hypoxia

Ventilatory responses and pressure generated in the first 100 msec of an occluded breath (P0.1) were measured during duplicate runs of progressive hypercapnia induced by rebreathing CO2 on a modified circuit as described by Reed and Whitlow et al. Responses are reported as the slope of the best fit linear regression of ventilation and occlusion pressures to end tidal PC02 (ΔVE/ΔPC02 and ΔP0.1/ΔPC02, respectively). Ventilatory response to isocapnic progressive hypoxia was measured in duplicate using the rebreathing circuit of Rebuck and Campbell and is reported as the slope of the best fit linear regression of ventilation to O2 saturation, measured by ear oximetry (ΔVE/AO2sat). Tests were repeated before therapy and on at least two occasions separated by at least one month. Because results differed by less than 10 percent they were averaged for each patient. Tests were then repeated one, six, and 12 months after therapy. After tracheostomy, tests were always performed through a mouthpiece, with the tracheostomy plugged using a tracheostomy button.

Sleep Ventilatory Monitoring

In addition to the diagnostic sleep study, a one hour daytime sleep study was performed with a canopy ventilation monitor. This allowed non invasive quantitative measurement of ventilation, tidal volume, and frequency, both during wakefulness and sleep. No effort was made to sleep deprive the patients, as all were severely hypersomnolent and slept easily during testing. The canopy study was performed in association with sleep stage monitoring as above, ECG, inductance plethysmography, and ear oximetry.

Sleep ventilatory studies were again performed four to six weeks after treatment. In the seven patients with tracheostomy, an all night sleep study was performed using a cuffed tracheostomy tube connected to a pneumotachograph to quantitatively monitor ventilation. The one patient treated with nightly home use of nasal CPAP necessarily had a slightly modified followup study: variations in the pressure and flow through his mask were used as markers of apnea. Quantitative sleep ventilatory measurements were not possible while he was receiving therapy because of the mask.

All ventilation measurements (awake and asleep) were expressed as liters/minute/meter2 of body surface area (BSA) in order to normalize for the differing body size of the patients. This normalization was not applied to CO2 and hypoxic rebreathing ventilatory responses.

Treatment

Seven of the eight patients underwent creation of a permanent tracheostomy with an H-shaped incision in the trachea and skin to create overlapping flaps of epithelial tissue lining the stoma. After two weeks of healing, a plastic cannula was inserted which did not extend past the stoma track, and which could be plugged during the daytime. The patients were instructed to remove the plug at night and during any naps to bypass the functional upper airway obstruction; they left the plug in during waking hours, which allowed them to speak and cough normally. In one case, a stricture developed above the tracheostomy site due to a wound infection; this patient was unable to use a button after an initial period of success and has continued to use a standard metal tracheostomy tube open at all times.

Posttreatment Interventions

Posttreatment residual chronic hypercapnia was evaluated six months after treatment by temporarily returning the patient's arterial PC02 and serum bicarbonate to normal values. This was accomplished either by elective mechanical ventilation with a respirator attached to a cuffed tracheostomy tube for 48 hours, or by administering an oral dose of 250 mg of acetazolamide once daily for one to two weeks. Arterial blood gas values, ventilation, and ventilatory response to rebreathing CO2 were then retested.

At a separate time, also at least six months after definitive treatment of the obstructive sleep apnea, medroxyprogesterone (20 to 40 mg sublingually three times daily for one to two months) was given to the same patients in an attempt to produce central respiratory stimulation.

Table 1 lists anthropometric data and arterial blood gas levels of the patients before treatment, establishing the degree of chronic hypercapnia. Data from the pretreatment all-night sleep studies are also shown, documenting that each patient had severe obstructive sleep apnea.

Tracheostomy and nasal CPAP resulted in relief of hypersomnolence and disappearance of snoring in all cases. Peripheral edema disappeared or decreased in those in whom it was present.

Sleep pattern before treatment was severely fragmented in all eight patients. Short periods of predominantly stage 2 sleep ("microsleeps") were interrupted continuously every 30 to 120 seconds by arousals. These "microsleeps," defined as 10 to 60 second EEG evidence of sleep (ie, dropout of alpha waves and/or appearance of sleep spindles), usually occurred in...
association with an obstructive apnea; both apnea and sleep were terminated by an EEG arousal. Virtually no stage 3 to 4 non-REM or sustained REM sleep was present in any patient in the eight hours of monitoring. During the daytime nap studies, the EEG pattern was identical to the all-night studies in each patient, showing stage 1 to 2 sleep interrupted by arousals. For this reason, the quantitative measurements of ventilation during the nap were felt to be representative of events whenever "sleep" was present prior to treatment. After treatment (tracheostomy or on nasal CPAP), sleep showed prolonged uninterrupted periods of all stages including stages 3 to 4 and REM.

Response of Hypercapnia to Treatment

The response of the patients' chronic hypercapnia to therapy defined two clearly separable groups (Fig 1). Four of the eight patients, including the one treated with nasal CPAP, showed a return to eucapnia documented within two weeks by a normalisation of waking PCO₂ and return of the elevated serum bicarbonate to normal (correctors). This has persisted for the period of follow-up (28 to 60 months). The other four patients remained hypercapnic, despite a similar degree of improvement in the symptoms of sleep apnea (noncorrectors). This hypercapnia has persisted to the present (follow-up of 16 to 48 months).

Analysis of Mechanisms of Hypercapnia Pretreatment and Posttreatment

Transient weight loss occurred in two noncorrectors and three correctors, who lost 2.3 to 13.6 kg acutely with tracheostomy, reflecting a spontaneous posttherapy diuresis and/or anorexia. The weight loss was not sustained and did not relate to correction of hypercapnia. In fact, the greatest weight loss (13.6 kg) occurred in one of the noncorrectors.

Sleep-Related Apneas: Figure 2 shows the apnea

![Graph](image-url)
index and lowest $O_2$ saturations during a night before and after therapy. Apnea index before treatment did not differentiate the correctors from the noncorrectors. Apnea index dropped dramatically after treatment in all patients (from 40 to 130 per hour to 0 to 15 per hour; $p<0.0001$). The residual apneas were short and central and occurred almost exclusively at sleep onset. They were not more frequent in the noncorrectors. Periods of oxygen desaturation still occurred following treatment in both groups; however, the lowest saturation seen during the night of monitoring was markedly improved in all patients from the value seen before therapy ($<50$ percent in all patients to 75 to 92 percent, $p<0.0001$). The desaturations seen were not associated with apneas but rather with shallow respiration and were most frequent in REM sleep.

Thus, differences in the apnea phenomenon pretreatment or persistence of apnea posttreatment did not provide a mechanism for persistence of hypercapnia in the noncorrectors.

**Pulmonary Function:** Table 2 shows values for representative pulmonary function tests before and after treatment in both groups. Six of the patients showed abnormalities characteristic of obesity (mildly reduced vital capacity characterized by reduced expiratory reserve and mildly reduced functional residual capacity). Two of the patients had obstructive airway disease (reduced forced expiratory volume in 1 second/forced vital capacity and increased functional residual capacity). No change in pulmonary function occurred after therapy in any patient acutely or long term. Both patients with airways disease were correctors. In one of these patients, the physiologic dead space was elevated. It remained elevated after treatment despite his return to eucapnia. In the other seven patients, dead space was normal, confirming the clinical impression that significant lung disease did not play a role in their hypercapnia.

Thus, improvement in pulmonary function did not account for return to eucapnia in the “correctors,” nor did intrinsic lung disease or worsened pulmonary function after treatment account for persistent hypercapnia in the noncorrectors.

**CO$_2$ Production and Anatomic Dead Space:** CO$_2$ production measured in the basal resting state did not change in the patients after therapy (277 ml/min vs 290 ml/min, $p = NS$). This is in accord with the lack of consistent weight change and excludes a change in CO$_2$ production as the cause of the change in chronic arterial Pco$_2$ at the same level of awake ventilation in the “correctors.” This change in arterial Pco$_2$ without change in CO$_2$ production implies that a change in alveolar ventilation must have occurred.

The measured physiologic dead space was not changed from the preoperative value in the seven patients with tracheostomy as long as their tracheostomy button was plugged and they breathed

### Table 2—Pulmonary Function Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Vital Capacity (%) predicted</th>
<th>Funct Resid Cap (%) predicted</th>
<th>FEV/FVC</th>
<th>Physiologic Dead Space (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correctors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>82</td>
<td>137</td>
<td>.61</td>
<td>256</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>81</td>
<td>.85</td>
<td>116</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>58</td>
<td>.81</td>
<td>108</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>84</td>
<td>.42</td>
<td>167</td>
</tr>
<tr>
<td>Mean</td>
<td>71.5</td>
<td>90.0</td>
<td>.67</td>
<td>161.8</td>
</tr>
<tr>
<td>SD</td>
<td>8.2</td>
<td>33.4</td>
<td>.20</td>
<td>68.0</td>
</tr>
<tr>
<td>Noncorrectors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>89</td>
<td>.73</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>103</td>
<td>91</td>
<td>.77</td>
<td>151</td>
</tr>
<tr>
<td>7</td>
<td>112</td>
<td>104</td>
<td>.84</td>
<td>144</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>76</td>
<td>.72</td>
<td>174</td>
</tr>
<tr>
<td>Mean</td>
<td>87.8</td>
<td>89.2</td>
<td>.77</td>
<td>140.5</td>
</tr>
<tr>
<td>SD</td>
<td>23.3</td>
<td>10.3</td>
<td>.05</td>
<td>34.2</td>
</tr>
<tr>
<td>P value*</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*For statistically significant difference between correctors and noncorrectors.
through their upper airway (pretreatment mean 154 cc to posttreatment mean 137 ml, p = NS by paired Student's t-test). Allowing these patients to breathe through their tracheostomy lowered the measured dead space by 70 ± 10 cc (mean ± SD), which was attributed to a change in anatomic dead space. To further assess the significance of this change, each of the seven patients had 70 ml of dead space tubing attached to his tracheostomy for 60 hours to increase the total dead space approximately to its preoperative value. At the end of this period, arterial blood gas levels showed no change in PCO₂. In particular, the correctors had not redeveloped hypercapnia.

Thus, variability in the change in the dead space due to tracheostomy did not explain changes in alveolar ventilation, and the change in anatomic dead space did not account for correction of hypercapnia in the correctors.

Ventilatory Responses: Figure 3 shows the ventilatory responses to CO₂ rebreathing (ΔVE/ΔPCO₂, ΔP.1/ΔPCO₂) and to hypoxia (ΔVE/ΔO₂sat) of the patients before and after treatment. The ventilatory response to CO₂ was low in all but one patient and was associated with a low occlusion pressure response, indicating low central drive was present. The noncorrectors did not have lower responses to either CO₂ or hypoxia than the correctors. Furthermore, the correctors showed no improvement in ventilatory responses after treatment despite their improvement in arterial blood gas levels. Repeat testing up to four years (range 16 to 48 months) after therapy has shown no late improvement in CO₂ or hypoxic responses in these patients.

Thus, differences in ventilatory responses pretreatment or changes in responses posttreatment did not account for the differing resolution of hypercapnia after therapy in the two groups.

Ventilation: Figure 4 shows representative tracings from a patient studied before treatment. The tidal volume was obtained quantitatively with a ventilation monitor.

If care was taken to measure ventilation only during EEG evidence of the sustained awake state (persistent alpha wave activity for at least two minutes and no microsleeps), a distinct pattern and level of ventilation was defined for each patient, which was not periodic (see representative tracing in Fig 4B). The numerical value of this ventilation was calculated and called the sustained awake ventilation.

Whenever these severely hypersomnolent patients
were left unstimulated, they assumed a state of consciousness characterized by continuously alternating EEG evidence of microsleep and wakefulness. This pattern is illustrated in the EEG tracing in Figure 4A and is essentially identical to the pattern of EEG seen during the all-night recording of sleep. Ventilation during this state was always periodic in all eight patients. The periodic ventilation was associated with the EEG arousals between microsleeps: unobstructed respiration occurred during the part of the EEG cycle when there was a momentary arousal; obstructive apnea occurred during the microsleep part of the EEG cycle.

Figure 5 summarizes the results of these pretreatment ventilatory measurements and demonstrates the relationship between the two ventilatory patterns seen in each patient. In the spontaneous relaxed state (with periodic breathing), ventilation was low in both “correctors” (range 2.1 to 3.1 L/min/m²) and noncorrectors (range 1.7 to 2.4 L/min/m²). Although the average ventilation was lower in the noncorrectors, there was significant overlap with the correctors. In contrast, the level of ventilation in the sustained EEG-documented awake state (when periodicity was not present) clearly differed between the two groups: in the normal range in the “correctors” (range 3 to 3.8 L/min/m²); and low in the noncorrectors (range 2.1 to 2.9 L/min/m²). Thus, the ventilation in the sustained awake state distinguished the correctors from the noncorrectors before treatment and anticipated their return to eucapnia after treatment.

After treatment of the OSAS, the relaxed state was one of sustained wakefulness as the patients were no longer hypersomnolent, and microsleeps did not occur. Furthermore, periodic ventilation did not occur.
during wakefulness nor regularly during sleep as before. Figure 6 examines this posttreatment awake ventilation and compares it to the sustained awake ventilation seen before treatment. For each patient, the posttreatment awake ventilation was identical to the pretreatment sustained awake ventilation.

Thus, the ventilation in the sustained awake state was characteristic for each patient. It distinguished the correctors from the noncorrectors by being higher even before therapy. Furthermore, this ventilation remained unaffected by treatment of the OSAS and was independent of the effect of treatment on hypercapnia.

Posttreatment Interventions

Eucapnia was transiently induced in three noncorrectors: in two by the use of 48 hours of elective continuous mechanical ventilation until arterial Pco2 and serum bicarbonate were normalized; in one by the use of acetazolamide for one week. Results are shown in Figure 7. All three patients had returned to the control level of chronic hypercapnia within one week of discontinuation of mechanical ventilation or acetazolamide.

Medroxyprogesterone (given to three patients) resulted in no change in arterial Pco2 (mean 53 mm Hg vs 52 mm Hg), awake minute ventilation (mean 2.8 L/min/m2 vs 2.9 L/min/m2), or response to CO2 rebreathing (0.4 L/min/mm Hg vs 0.3 L/min/mm Hg) while the patients were receiving the drug.

Thus, neither imposed eucapnia nor medroxyprogesterone succeeded in permanently correcting chronic hypercapnia in the noncorrectors.

DISCUSSION

In the present study, tracheostomy or chronic nocturnal use of nasal CPAP produced complete correction of the obstructive sleep apnea syndrome in all eight hypercapnic patients. However, correction of the chronic hypercapnia occurred in only four of the eight. The association of chronic hypercapnia with obstructive sleep apnea is now well recognized, and a variable response of this hypercapnia after correction of the upper airway obstruction has been observed by others. Possible explanations for this variability in return to eucapnia include the effects of nonuniform changes in weight, pulmonary function, or level of ventilatory chemoresponsiveness after therapy for the OSAS. In our eight patients, weight loss, change in pulmonary function, and dead space effects did not account for the variability in return to eucapnia after therapy for OSAS.

All patients had CO2 responses in the low range prior to therapy, and those who reversed their chronic hypercapnia (the correctors) did so without improvement of their CO2 response. Improved CO2 responsiveness has been suggested as a mechanism for the improvement of hypercapnia in several other stud-
ies. However, the published data supporting this concept remain unconvincing as responses in these studies either were not measured posttherapy, demonstrated only a shift in intercept without a change in slope, or were reported as changing only within the normal range without ever being low. In contrast, and in accord with our results, an earlier study demonstrated low CO2 responses in previously hypercapnic patients long after correction of the upper airway obstruction. The implications of these observations and our results are that low CO2 response per se did not cause hypercapnia pretreatment, and that increased CO2 responsiveness is not the mechanism of improvement in hypercapnia posttreatment. Low CO2 responsiveness, however, may still play a permissive role in the development of chronic hypercapnia under the stress of untreated apnea by blunting respiratory compensations to the apnea phenomenon in the interapnea periods.

In the absence of intrinsic lung disease, the degree of hypercapnia must be related to the overall level of ventilation. Our data on the ventilatory patterns seen before and after therapy suggest at least two different mechanisms may exist for low ventilation and chronic hypercapnia in the "Pickwickian" patient prior to treatment for obstructive sleep apnea.

The first mechanism (demonstrated by the correctors) consisted of an unfavorable balance between ventilation during time awake—which was normal—and hypoventilation during periods containing apnea. This mechanism is thus clearly dependent on the presence of the apnea phenomenon itself; these patients present a form of the "Pickwickian" syndrome that is due to an identifiable cause other than sustained hypoventilation in the waking state. The second mechanism (demonstrated by the noncorrectors) consisted of sustained hypoventilation present even when fully awake. This hypoventilation was independent of the apnea phenomenon. The noncorrectors thus appear to represent a true "Pickwickian" syndrome. They can be identified before therapy for obstructive sleep apnea by demonstrating a low ventilation even in the fully awake state, and this low ventilation appeared to be characteristic of these patients in that it persisted after treatment of the apnea. Furthermore, their posttreatment hypercapnia could not be reversed by correction of their elevated serum bicarbonate or by temporary hyperventilation, indicating that this state represented an intrinsic abnormality of ventilatory homeostasis, and emphasizing the fundamental difference between these patients and the correctors.

Chronic hypercapnia is dependent on a critical balance between the time spent over the 24 hour period in three distinct states and on the ventilation in each state: the fully awake state, the sleeping state, and the intermediate state associated with periodic breathings due to microsleeps and apneas. If all of these ventilations are low, then the time spent in each is no longer critical, and hypercapnia is explained by classic alveolar hypoventilation. This appeared to be the mechanism of both pretreatment and posttreatment hypercapnia in the noncorrectors in the present study. If the ventilation during periodic breathing is low but ventilation during the sustained awake state is normal, then hypercapnia is dependent on the relative amount of time spent in the two states. This appeared to have been the mechanism of pretreatment hypercapnia in the correctors, where the pretreatment balance must have been in favor of the low periodic ventilation due to the severe hypersomnolence. It should be noted, however, that while the value of the ventilation in the awake and the apnea-containing states was defined for each patient in the present study, the actual percentage of time over 24 hours spent awake vs the time in periods of apnea containing ventilation has not been measured in this or other studies.

In contrast to the patients of this study, most patients with obstructive sleep apnea remain chronically eucapnic. Although less apnea may explain eucapnia in less severely affected individuals, a previous study from this laboratory showed that eucapnic patients with severe obstructive apnea may have the same number and duration of apnea as hypercapnic patients. The eucapnic patients in that study did however, show a "big breath" after their apneas and had higher CO2 rebreathing responses than the hypercapnics. A normal CO2 response may thus play a protective role against the development of chronic hypercapnia under the stress of apnea by stimulating respiratory compensation for each apnea in the interapnea period.

Figure 8 shows a proposed overview of the relationship of hypercapnia in the absence of intrinsic lung

**Figure 8. Schema summarizing the mechanisms which determine the level of chronic arterial PCO2 in patients with obstructive sleep apnea.** The groups shown in the upper panels are conceptual. Whether the alveolar hypoventilation schematized on the right is congenital, acquired, or related to the longstanding obstructive apnea remains to be determined.
disease (the “Pickwickian” syndrome) and the obstructive sleep apnea syndrome. It incorporates observations from our previous study and the present data. The upper left of the schema shows a eucapnic individual at risk of developing obstructive sleep apnea. When the stress of intermittent airway obstruction is imposed, these eucapnic patients can be subdivided according to their response. The majority will tend to compensate for each apnea with an increase in ventilation just after that apnea, yielding a net ventilation which is maintained in the normal range even during the periodic breathing, independently of the number of apneas. This ventilatory compensation during periodic breathing may be related to the normal CO\textsubscript{2} rebreathing responses seen in these patients.\textsuperscript{7} In the second group of eucapnic patients, compensation for the stress of apnea is inadequate: they will not raise their ventilation between each apnea sufficiently to normalize their net ventilation. A low CO\textsubscript{2} response may be permissive for this lack of compensation.\textsuperscript{7} These patients thus develop prolonged periods of hypoventilation during their periodic breathing. Since ventilation in this group remains normal in periods free of apnea, successful treatment of the obstructive sleep apnea results in a return to eucapnia.

On the right of the schema is shown a subset of the population with sustained hypoventilation and hypercapnia independent of apnea. The hypoventilation can only be worsened by the additional mechanical stress of obstructive apnea. The patients in this group appear to have a defect in control of ventilation independent of the apnea phenomenon and a lower set-point for ventilation; they are the true “Pickwickians” in that they represent a syndrome of chronic alveolar hypoventilation of unknown etiology in the obese patient without intrinsic lung disease. The significance of delineating this subset from other hypercapnic patients with OSAS lies in that they represent a different abnormality of ventilatory control from the latter, whose hypercapnia is a direct consequence of the recurrent apneas. Whether the defect of the true “Pickwickian” is acquired (perhaps due to some aspect of obesity or to years with severe apnea in some patients), whether it results from a congenital abnormality of ventilatory control, or whether it merely represents an extreme in the spectrum of the normal population remains to be determined.

REFERENCES