of medicine and health care are ever to be dealt with efficiently or effectively.

This is a challenge to our leadership in both the public and private sectors—whether at the local, state or national levels. It seems unlikely that much will be accomplished until there is a new approach. If there is a lesson from nature, or a model from nature, it would seem that collaboration and cooperation with efficient use of energy and resources and each contributing to the success of the whole is the key. This will require a number of relatively autonomous sources of power, not only in government and in the organizations and institutions of the private section but perhaps even including physicians, patients and individual citizens, to pull together in a spirit of good will and direct their energies and resources to the accomplishment of agreed upon solutions to agreed upon problems in the common interest of all.

This appears to be a needed next step in health care—and there could be a lesson in nature.

—MSMW

Of Sleep and Seals and Many Things: Pickwickians—1978

THE REVIEW by Morgan and Zwillich elsewhere in this issue provides a lively and timely summary of the problems of hypoventilation in the obese, especially during sleep. Their review stands on its own and this editorial will emphasize some additional nuances not covered in the review and will consider nosology and human culture, an animal model, pathogenesis, the heart in obese persons and therapy.

Nosology and Human Culture

The choice of the term obesity-hypoventilation syndrome (OHS) is logical, but it has limitations. It is not as appealing, culturally, as the term Pickwickian syndrome. Medicine needs all the ties to the broad stream of human culture that it can develop. OHS deprives Charles Dickens of the priority that is correctly his. Whether Joe the Fat Boy was derived from Dickens' imagination or was originally a real-life person is immaterial. Dickens' description is still the single most accurate description and is marvelously fashioned as well. OHS does not emphasize the pathologic somnolence and appetite found in many of the patients which usually persist despite loss of weight. As a result, OHS is a less complete and satisfactory designation.

The Seal as an Animal Model

Knowledge of the syndrome has been handicapped by lack of an appropriate animal model. An animal model may now be available. Professor Kooyman of the Scripps Oceanographic Institute has recently studied ventilation and blood gases during sleep in Weddell seals. This aquatic mammal is certainly obese. An adult weighs about 1,500 pounds, much of which is blubber. To maintain this body mass, Weddell seals must have substantial hyperphagia. Seals generally have depressed respiratory centers while awake, presumably as an adaptation which subserves prolonged diving. Seals are polycythemic to a pronounced degree, like human Pickwickians. While sleeping on the ice floes of their native Antarctica, Weddell seals develop apnea of seven to eight minutes duration. When the animal awakes, apnea is abolished. During seal sleep apnea, arterial oxygen pressure (Pa_{O_2}) drops to as low as 20 torr; arterial carbon dioxide pressure (Pa_{CO_2}) rises only to about 50 to 60 torr (mm of mercury) (J. Kooyman—personal communication). This indicates that as in human Pickwickians, sleep is associated with altered ventilation-perfusion abnormalities as well as accentuated respiratory depression and alveolar hypoventilation. Quickly after waking, blood gas values return to normal.

One interesting sidelight of this comparative model relates to the relation between substrate utilization and the control of breathing. In human Pickwickians but not in normal persons, hypocaloric ketogenic diets significantly increase the respiratory response to carbon dioxide. This improvement correlates with ketone body concentrations and dietary manipulation leading to ketosis and has been suggested as a possible therapeutic manipulation.[1] This might represent an additional mechanism by which weight reduction improves Pickwickians, independent of a direct effect on

pulmonary mechanics. Seals often subsist for long periods on endogenous substrate (starvation); however, without the development of significant ketosis.[2] Thus seals may be especially appropriate for pursuing this fascinating metabolic aspect of depressed respiratory control in Pickwickians.

Pathogenesis

It is now generally accepted that Pickwickians represent a subset of a larger group of patients with sleep apnea. This subset is made up of patients with massive obesity, alveolar hypoventilation awake and accentuated during sleep, with reversal of alveolar hypoventilation with simple weight reduction. It is conventional to classify sleep apnea into three groups: (1) patients with upper airway obstruction during sleep (obstructive type) in which apnea results from obstruction of upper airways during sleep because of neurologic abnormalities, or occasionally because of structural lesions of the airways, (2) patients with pure depression of the respiratory center which is accentuated during sleep (central type) and (3) mixed sleep apnea (both obstructive and respiratory center depression present). It appears that most Pickwickians represent a combination of depressed central respiratory drive and mechanical and blood gas abnormalities caused by obesity.

The major gap in this theory of pathogenesis is that neither nervous system structural lesions nor precise neurophysiological abnormalities have been reported in Pickwickians or in many patients with sleep apnea. Therefore, the evidence provided in the review for either central depression or carotid body depression is indirect. This critical deficiency will not be remedied until precise neurophysiological techniques are applied to these patients. Studies based on peripheral changes (ventilation, gas exchange) can provide only indirect evidence. As recently *quoted by* an eminent neurophysiologist:

> Fundamentally the control of ventilation is neuronal in nature. Therefore, ventilatory control must ultimately be described in acceptable neurophysiologic terms.
>
> Because of the diverse connections, the problem of determining mechanisms of abnormal ventilatory control is quite complex. Given an abnormality in ventilatory response, the abnormality may reside in any segment of the total neuronal connections subserving a given function. For example, a blunted hypoxemic drive could arise from direct abnormality of the carotid body itself; from changes in arrival time in afferent nerves; from increased inhibitory stimuli or decreased activating stimuli from a variety of central neurons, or from inadequacy of the peripheral ventilatory mechanism.
>
> Classic approaches to the study of ventilatory control, say during exercise, which measure variables based on effect or function such as ventilatory volume or gas exchange parameters, must be cautiously interpreted. At the very least, these studies will require reinterpretation in neurophysiologic terms.[3]

In furthering such neurophysiologic studies, the use of seals as animal models might be particularly useful.

The Heart

Abnormalities of cardiac function frequently play an important role in Pickwickians. Charles Dickens described Joe the Fat Boy as "young Mr. Dropsy." His edema may have been related to cor pulmonale (although venous insufficiency of the obese cannot be excluded as the cause). Pickwickians commonly show reversible pulmonary hypertension and right ventricular failure. Alexander and co-workers showed that massively obese patients, even in the absence of alveolar hypoventilation, showed impairment of left ventricular function.[4] This was attributed to the increased volume work of the left ventricle because of the increased blood flow required by excess fat. Tilkian and associates showed severe intermittent pulmonary hypertension and a substantial incidence of bradyarrhythmias and tachyarrhythmias during episodes of obstruction in obstructive sleep apnea.[5] Thus careful evaluation and management of cardiac factors is an important aspect of patient management.

Therapy

Morgan and Zwillich suggest an aggressive approach, especially in obese patients with obstructive sleep apnea associated with serious bradyarrhythmias and tachyarrhythmias and profound desaturation which is life-threatening. The difficulty is in defining life-threatening. Two important aphorisms may be worth remembering: (1) Not all that snores is obstructive sleep apnea and (2) if you tracheostomize in a hurry, the patient may repent in leisure. Sleep apnea has been so widely publicized in the medical and lay press that large numbers of patients, often obese and almost invariably snorers, are referred to hospitals for "definitive" therapy (tracheostomy). A number of these patients do not, in fact, have clinically important sleep apnea and will not be benefited by tracheostomy. Documenting signifi-

cant upper airway obstruction and relief by intubation should be a precondition before surgical operation is undertaken. Careful physiologic measurements during sleep and a trial of weight reduction together with measurements following reversible airway intubation should precede tracheostomy. A careful search for anatomical causes of upper airway obstruction should be conducted. For example, in young patients, tonsillar-adenoid obstruction should be specifically investigated. In adults, upper airway tumors should be ruled out. It is necessary to emphasize the fact that in central sleep apnea, tracheostomy is contraindicated.

Aside from weight reduction, either long-term or intermittent (patients with pathologic hyperphagia find long-term dieting intolerable), progestational drugs have been recommended. No careful clinical trial of these has been done, but their use entails relatively low toxicity and this form of therapy is at least logical in patients with almost pure "central" alveolar hypoventilation.

Summary

Joe the Fat Boy was described by Dickens in 1837. The first scientific description was provided by Sieker and associates in 1953. The Pickwickian name was first applied and the role of alveolar hypoventilation, central respiratory depression, and the independent nature of hypersomnolence and hyperphagia were first described by Burwell and co-workers in 1956. Since then, as indicated in the review, substantial information has been accumulated. As indicated in this editorial, much, however, remains to be learned and therapy continues to be pragmatic and anecdotally based. In similar fashion, the operation of disease, during the third of our lives that we spend sleeping, is not well understood.

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Plague on Us

SINCE ANCIENT TIMES bubonic plague has been the subject of intense dread, a rich stimulus for literature and at times a major influence on the course of history.[1] Characteristically, the disease has occurred in cycles with major pandemics at irregular intervals and with intervening epidemics in various parts of the world. Over the past 1,500 years, four plague pandemics have been documented. The first was recorded in the sixth century AD, beginning in Egypt, speading to Constantinople and then to Europe and persisting for about 60 years. The second occurred in the 14th century and was carried from Asia Minor and Africa to Europe by merchants and other travelers, where, known as the Black Death, it decimated the population. It is estimated that millions died in Asia, and in Europe. About a fourth of the population—at least 25 million people—fell victim to the pestilence. The third pandemic, again involving Europe, occurred during the period of the 15th to 18th centuries, finally subsiding to be succeeded by the fourth pandemic, beginning in China about 1860 and continuing to the present.

That plague is still with us, even in the United States, is effectively illustrated in the case presented and discussed by Connor and associates in the Speciality Conference elsewhere in this issue. The case was that of a 3-year-old child who became ill while vacationing with her family at California's Lake Tahoe. The family returned home to San Diego where, despite rapid diagnosis and appropriate therapy, the child died—the only fatality and the only recorded case of plague in San Diego.

The California "connection" in this case is of interest because California figured prominently in the importation of the disease into the United States during the worldwide pandemic still in progress.[2] Although apparently reemerging in the Chinese province of Yunnan in about 1860, the disease attracted worldwide concern in 1894 when it reached Hong Kong.[3] The means for rapid widespread transmission was now at hand through extensive ocean commerce, and by 1899 it had reached the Americas with the first New World case in Santos, Brazil. The plague bacillus, Yersinia pestis, had been identified by Yersin in 1894. (Yersin's contribution was recognized recently by changing the name of the genus from