## **Current Comments**

Sleep Disorders. Part 2.
Sleep Apnea—When Snoring Is the Symptom, Not the Disease

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Last week we published an essay on snoring, its causes, varying degrees of severity, and the types of remedies people have sought. I observed that there is very little literature in scientific and medical journals on snoring and that, until recently, it was not treated as a medical problem at all. However, this picture is beginning to change due to the recent interest in a breathing disorder known as sleep apnea, which afflicts only very loud, "heroic," or "obnoxious" snorers, and which, left untreated, can seriously undermine their health.

Sleep apnea is only one of many sleep disorders now recognized as posing potentially serious threats to people's physical and mental well-being. Table 1 lists some of the sleep abnormalities which are currently being studied and treated. The table was prepared from a special supplemental issue of the journal Sleep. That issue is devoted to the "diagnostic classification of sleep and arousal disorders."2 These disorders range from the inability to stay awake to the inability to sleep, and from organic problems such as neurological, cardiovascular, and motor disorders, to emotional or psychological problems which interfere with normal sleep patterns.

"Apnea" comes from the Greek term meaning "want of breath." People with sleep apnea have difficulty sustaining breathing during sleep and often stop breathing for intervals of up to two minutes throughout the night. Some sleep apnea sufferers have as many as 600 to 800 apneic episodes in a single night, taking only two or three normal breaths

at a time between episodes.<sup>4</sup> Thus, as Mark Pressman, Sleep Disorders Center, Medical College of Pennsylvania, Philadelphia, points out, they may spend as much as 75 percent of the time they are sleeping without getting oxygen.<sup>5</sup> This places a strain on the cardiovascular system and may lead to a number of complications, some of which can be fatal. But because the condition is only obvious while a person is asleep, the majority of people with sleep apnea do not realize they have a medical problem and do not seek help.<sup>4</sup>

Sleep apnea sufferers are typically overweight males over the age of 40. Men are thought to be between ten and 60 times more likely to develop the disorder than females.<sup>6</sup> Although sleep apnea in young women is virtually unknown, the disease can occur in women, particularly if they are postmenopausal or obese.<sup>7</sup> Children too can develop sleep apnea, usually due to a throat obstruction stemming from enlarged tonsils or adenoids.<sup>8</sup>

There are two basic types of breathing defects which can cause sleep apnea. "Central sleep apnea" results from a failure in the breathing reflex which controls the respiratory muscles in the chest and diaphragm. This form of sleep apnea rarely becomes a problem in adults. It is seen more frequently in infants, and may be responsible for many cases of "crib death." "Obstructive sleep apnea" is far more prevalent among adults and is the type of sleep apnea associated with snoring. 4.7 During episodes of obstructive sleep apnea, the throat closes and

Disorders of insomnia and excessive daytime sleepiness-

caused by a number of psychological and physiological conditions; these include sleep apnea, sleep-related myoclonus (involuntary jerking of the legs), and others.

Disorders of excessive somnolence-

in which a person sleeps an excessively long time per day; organic conditions which cause it include narcolepsy ("sleep attacks"), Kleine-Levin syndrome (intermittent excessive sleepiness marked by aberrant behavior, sometimes including gluttonous eating, apathy, and/or loss of sexual inhibitions), and sleep drunkenness (prolonged, exaggerated confusion and/or antisocial behavior while waking up).

Disorders of the sleep-wake schedule-

the inability to keep to a sleep-wake schedule which is conventional or desirable may result from jet lag, changing work shifts, or organic causes.

Dysfunctions associated with sleep, sleep stages, or partial arousals-

a wide variety of disorders which include sleepwalking, sleep terror arousal (awakening screaming), bed-wetting, nightmares, bruxism (teeth grinding), headbanging (rocking head or body at sleep onset), and a variety of gastrointestinal, neurological, and vascular problems brought on or exacerbated by sleep.

prevents air from entering the lungs, despite repeated attempts to inhale. Some adults have "mixed" apneic episodes which typically involve brief central sleep apnea, followed by a longer period of obstructive sleep apnea. 10,11 The exact incidence of sleep apnea is not known, but based on a large study conducted in Israel, Peretz Lavie and colleagues, Israel Institute of Technology, Haifa, estimate that 1.5 percent of the total adult male population may be affected by the disorder. 12

Obstructive sleep apnea, like snoring, occurs most often in those who are overweight, or who have a small, crowded upper airway. Air must rush through such an airway quickly in order for sufficient quantities to reach the lungs. But according to a physical principle known as the Bernoulli effect, after the eighteenth-century Swiss physicist Daniel Bernoulli, 13 the greater the velocity of air inside the throat, the lower the air pressure in the throat cavity becomes relative to the air pressure outside. 14 This partial vacuum may cause the flexible walls of the rear portion of the throat, or oropharynx, to collapse. It may also suck the tongue back into a position where it totally blocks the entrance to the oropharynx.14

In most people, the muscles of the tongue and oropharynx keep the upper

airway open regardless of the Bernoulli effect. These muscles even stiffen slightly each time you inhale. <sup>14</sup> But people with obstructive sleep apnea seem to lose their muscle tone during each episode of apnea. <sup>14,15</sup> For this reason, researchers believe that sleep apnea may be related to a defect in the portion of the central nervous system responsible for regulating muscle tone. <sup>10</sup>

Virtually all people afflicted with obstructive sleep apnea snore and have done so for years. Many adult patients recall snoring as far back as their teens. 10.15 Also, they are "legendary," "heroic," or "obnoxious" snorers. 16 Their snoring usually makes it impossible for anyone else to sleep in the same room with them. In addition to producing explosive snores and snorts when they are breathing, they thrash around violently when they are not. Thus, anyone who does try to sleep with them may be punched or kicked at intervals throughout the night. 6,15

Despite all this activity, and despite becoming partially aroused each time they struggle for breath, people with sleep apnea do not remember their apneic episodes in the morning. Unless someone else has witnessed their behavior, they may not know that they have a problem. Indeed, apneic episodes which are very brief and occur less than five

times per hour may not constitute a threat to health.<sup>17</sup>

However, mild sleep apnea may grow worse if left untreated, because a cascade of changes may occur in the respiratory center of the nervous system. The breathing reflex depends on feedback from chemoreceptors which monitor oxygen tension and carbon dioxide levels in the blood and spinal fluid. If these chemoreceptors chronically detect inadequate respiration, their sensitivity to these signals and their ability to stimulate the necessary breathing effort can be blunted. As a consequence, the patient may gradually react less vigorously to clear apneic obstructions. 14

When breathing interruptions occur frequently and last long enough to cause a drop in blood oxygen levels, a number of complications may result. One of the most common of these is "excessive daytime somnolence" or excessive sleepiness during the day. According to Bashir A. Chaudhary, Medical College of Georgia, Augusta, "Excessive daytime somnolence is present in 80 percent of adult patients with obstructive sleep appea and is the usual reason they seek medical treatment." These people fall asleep while driving, having conversations, even while having sex.6 One reason for daytime hypersomnolence among sleep apnea sufferers may be their inability to sleep soundly or experience normal sleep patterns. Although they do not become fully conscious during apneic episodes, they may spend the night in a state of semiarousal, never reaching deep sleep. 15 William C. Orr and colleagues, University of Oklahoma, Oklahoma City, have suggested that daytime hypersomnolence could also be a result of chronic oxygen deprivation, which could trigger complications in the central nervous system and disrupt the chemical balance in the brain. 18

Whatever its cause, excessive daytime somnolence, particularly when accompanied by sporadic bursts of heavy snoring and excessive motor activity during sleep, is a good indication of sleep apnea. A recent cooperative study of patient records at 11 sleep disorders clinics found that 45 percent of patients complaining of excessive daytime somnolence went on to be diagnosed as having sleep apnea.<sup>19</sup>

In addition to continual drowsiness, some people with severe sleep apnea experience personality changes, intellectual deterioration, depression, headaches, irritability, impotence, and bed-wetting. Sometimes these symptoms are so pronounced that a person will be unable to hold down a job or maintain relations with family or friends.<sup>4</sup>

Another serious consequence of sleep apnea is the strain that it places on the cardiovascular system. In many instances it causes pulmonary hypertension, that is, high blood pressure in the blood vessels which transport blood to the lungs. This occurs because the blood vessels in the lungs constrict when the lungs chronically fail to yield oxygen. The right side of the heart must then pump harder to force blood into these constricted blood vessels. As a result it eventually becomes enlarged. During apneic episodes the heart must work without oxygen. Lactic acid builds up in it, causing it to slow down or begin to beat irregularly. In some cases these cardiac arrhythmias may lead to a heart attack. In addition, people with sleep apnea frequently have systemic hypertension. For this reason, too, their risk of heart attack is high.4

Among sleep apnea patients there is often an abnormal proliferation of erythrocytes, or red blood cells.<sup>20</sup> When the erythrocytes cannot carry as much oxygen as the body needs, we compensate by producing more of them. But these extra erythrocytes may cause the blood to thicken and become sludgy. This prevents it from moving easily through narrow blood vessels, a situation which can lead to blood clots, resulting in strokes, heart failure, or a general decline in mental function.

Obstructive sleep apnea was not recognized as a medical problem until the late-1960s.4 But as early as 1906, William Osler observed, "An extraordinary phenomenon in excessively fat young persons is an uncontrollable tendency to sleep—like the fat boy in Pickwick."21 Osler was referring to a character in Charles Dickens's The Posthumous Papers of the Pickwick Club.22 By the 1950s, the correlation between obesity, daytime hypersomnolence, and heart disease had been established. In 1956, C. Sidney Burwell and colleagues, Harvard Medical School, Boston, Massachusetts, described a case in which heart disease was caused by insufficient respiration, which in turn resulted from obesity.23

In the mid-1960s, researchers began observing sleep patterns in "Pickwickian" patients and discovered that they occasionally had apneas. H. Gastaut and colleagues, National Institute of Health and Medical Research, Marseilles, France, demonstrated that these apneas were due to airway obstruction in the throat.<sup>24</sup> Since that time it has become apparent that sleep apnea is not directly caused by obesity, but rather, is aggravated by it.<sup>10</sup>

Only in the mid-1970s did sleep apnea begin to receive widespread attention in the medical and scientific community.6 This was partially because of growing scientific interest in sleep disorders in general and in the proliferation of sleep disorders clinics where sleep apnea could be diagnosed with electronic sleep monitors and its possible complications assessed.14 Whereas a few years ago there were only a handful of sleep disorders centers in the US.25 the Association of Sleep Disorders Centers, the accrediting organization in the US, now has 23 full members and another 25 provisional members. The fully accredited members are listed in Table 2.

Although awareness of sleep apnea is growing, and diagnosis is more commonly made, researchers suspect that many cases never come to the attention of a physician. Sometimes, when the condition is not recognized, people will obtain sleeping pills as a remedy for what

Table 2: Location of Sleep Disorders Centers accredited by the Association of Sleep Disorders Centers.

Sutton-Cooper Green Hosp., Birmingham, AL Good Samaritan Hosp., Phoenix, AZ Holy Cross Hosp., Mission Hills, CA Univ. California, Irvine Med. Ctr., Orange, CA Stanford Univ. Med. Ctr., CA Mt. Sinai Med. Ctr., Miami Beach, FL Rush-Presbyterian-St. Luke's Hosp., Chicago, IL Univ. Chicago, IL Baltimore City Hosp., MD Henry Ford Hosp., Detroit, MI Hennepin Co. Med. Ctr., Minneapolis, MN Deaconess Hosp., St. Louis, MO Dartmouth Med. Sch., Hanover, NH Montefiore Hosp., Bronx, NY SUNY, Stony Brook, NY Univ. Cincinnati Hosp., OH Ohio State Univ., Columbus, OH Presbyterian Hosp., Oklahoma City, OK Western Psychiat. Inst., Pittsburgh, PA Crozer-Chester Med. Ctr., Upland-Chester, PA Baptist Memorial Hosp., Memphis, TN Baylor Coll. Med., Houston, TX Metropolitan Med. Ctr., San Antonio, TX

they suppose to be insomnia.<sup>25</sup> Sleeping pills and other depressants, such as alcohol, add to the sleep apnea victim's problems by slowing down the breathing reflex and increasing both the frequency and duration of apneic episodes.<sup>26,27</sup>

For this reason, some researchers believe that sleep apnea may be a "hidden killer" responsible for some of the thousands of unexplained deaths which occur each year during sleep, particularly among overweight males and elderly females who drink or take sleeping pills.<sup>25,28</sup>

The most common remedy for severe cases of sleep apnea is a tracheotomy, 4 a surgical procedure similar to the one performed in emergencies where patients are in danger of suffocation. A hole is cut in the throat below the site of obstruction so that air can be taken in directly through the windpipe. During the day, the hole is plugged with a stopper so that patients can speak normally. Although this procedure may seem severe, people with sleep apnea are usually happy with the result, finding this preferable to perpetual drowsiness and the other problems they had to live with. 6

A recent innovation in the treatment of sleep apnea is an alternative surgical procedure called an "uvulopalatopharyngoplasty" (UPPP), sometimes called "palatopharyngoplasty" (PPP). The basic purpose of UPPP is to widen the throat. This is usually accomplished by removing the tonsils, if they are still there, the faucial pillars, and the posterior edge of the soft palate, including the uvula, and then stitching the remaining flaps of tissue together so that they no longer sag into the airway.

The operation was first attempted in sleep apnea patients three years ago by Shiro Fujita and colleagues, Henry Ford Hospital, Detroit, Michigan.<sup>29</sup> Since then other researchers, including F. Blair Simmons and colleagues, Stanford University Medical School, California, 30 and David N.F. Fairbanks, George Washington University Hospital, Washington, DC,31 have performed the operation on patients with sleep apnea, and on problem snorers who have a high likelihood of developing it. The operation appears to benefit about 50 percent of sleep apnea patients who receive it, by reducing the frequency and duration of apneic episodes and preventing dangerous drops in blood oxygen levels.<sup>30</sup> It also has the pleasant side effect of alleviating snoring. However, the UPPP is not generally recommended as a treatment for "simple" or "garden-variety" snoring.

In instances where sleep apnea has been diagnosed as mild and non-life-threatening, less radical forms of therapy are usually prescribed. In some cases, a rigorous weight-loss program will cure sleep apnea, by removing the excess tissue that obstructs the throat. <sup>15</sup> It is often difficult for sleep apnea sufferers to lose weight, however, because they are in the habit of eating to stay awake or combat depression.

Some cases of sleep apnea have been treated with pharmaceutical agents. Tricyclic antidepressants, drugs which are often used to combat depression,<sup>32</sup> also seem to prevent sleep apnea in some patients. In part, these antidepressants

seem to work by decreasing the amount of time spent in rapid eye movement sleep, the portion of the sleep cycle in which apneas are most common and severe. Unfortunately, in some patients, drug tolerance sets in after several months.<sup>33</sup> For this and other reasons, the drugs are used only on an experimental basis.

Another class of compounds under investigation are those related to the female hormone progesterone. Young women, who have an abundance of this hormone, are the least susceptible to sleep apnea, suggesting that the hormone might play a role in preventing the disease. One analogue of progesterone, medroxyprogesterone acetate, may stimulate breathing and reduce daytime hypersomnolence in some sleep apnea patients. 6,15 But more research is needed before this and other drugs can replace other forms of therapy.

Another experimental treatment for sleep apnea involves filling the upper airway with slightly pressurized air in order to keep it open. In 1981, Colin E. Sullivan and colleagues, University of Sydney. New South Wales, Australia, found that air piped into the nostrils through a nose mask allowed five patients with severe sleep apnea to get a night of uninterrupted sleep. As they explained, the positive air pressure acted as a "pneumatic splint," eliminating the vacuum which would otherwise form in the upper airway of these patients during inhalation.<sup>34</sup> The continuous positive airway pressure technique is currently under investigation in several laboratories, but has not vet been developed for home use.

A different type of appliance for holding the upper airway open has been invented and tested by Rosalind D. Cartwright and Charles F. Samelson at the Sleep Disorders Center, Rush-Presbyterian-St. Luke's Hospital, Chicago, Illinois. It is a tongue-retaining device, not unlike the appliances which have been patented to curb heavy snoring. By pulling the tongue forward and increasing the dimensions of the upper airway, the researchers believe that the device can

Table 3: Core papers for the ISI/BIOMED® research front #81-0736, "Oxygen desaturation of hemoglobin (Hb) during sleep."

Block A J, Boysen P G, Wynne J W & Hunt L A. Sleep apnea, hypopnea and oxygen desaturation in normal subjects. N. Engl. J. Med. 300:513-7, 1979.

Flick M R & Block A J. Continuous in-vivo monitoring of arterial oxygenation in chronic obstructive lung disease. Ann. Intern. Med. 86:725-30, 1977.

Guilleminault C, Tilkian A & Dement W C. The sleep apnea syndromes.

Annu. Rev. Med. 27:465-84, 1976.

Wynne J W, Block A J, Hemenway J, Hunt L A & Flick M R. Disordered breathing and oxygen desaturation during sleep in patients with chronic obstructive lung disease (COLD). Amer. J. Med. 66:573-9, 1979.

reduce the number and severity of apneic episodes, and that it may constitute an alternative to a tracheotomy.<sup>35</sup> But a tongue retainer may not work well in cases where the obstruction begins in the oropharynx.<sup>36</sup>

Sleep disorders specialists and researchers in other areas such as pulmonary medicine and otolaryngology are continuing to investigate the causes, complications, and possible cures for sleep apnea. A number of papers published on the subject can be found in ISI/BIOMED® research front #81-0736. "Oxygen desaturation of hemoglobin (Hb) during sleep." I have explained research front searching in previous essays.<sup>37</sup> Table 3 lists the core documents of this research front. These are papers most frequently cited in the current sleep apnea literature. Some deal primarily with sleep apnea, while others discuss it in conjunction with other breathing disorders or with monitoring and diagnostic techniques. More recent papers by authors identified through this core cluster have, of course, been cited in this essay.

Although an increasing number of researchers are turning their attention to the problem of sleep apnea, many more questions remain. We still do not understand the relationship between sleep apnea and systemic hypertension, a major health problem in the general population. Although there is some evidence

that sleep apnea may be hereditary, we do not know how much it is affected by genetic, as opposed to environmental, factors. Mild sleep apnea is relatively common in older men, and Mary A. Carskadon and colleagues, Sleep Disorders Center, Stanford University, have pointed out that there may be a relationship between this breathing disorder and insomnia, depression, mental deterioration, and daytime sleepiness among the elderly.<sup>38</sup> In addition, asymptomatic apnea may be more widespread among snorers than we presently realize, and may have subtle complications which masquerade as a variety of other health problems. For these reasons researchers will probably continue to work toward better understanding and treatment of the disease, 11,39

As we've seen, snoring, a condition that society has accepted as normal, may actually be a symptom of an important medical problem. Perhaps people like Senator Proxmire would have us continue to ignore the snore. But thanks to some persevering souls there may yet be relief in sight for those whose lives are disrupted by this phenomenon.

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