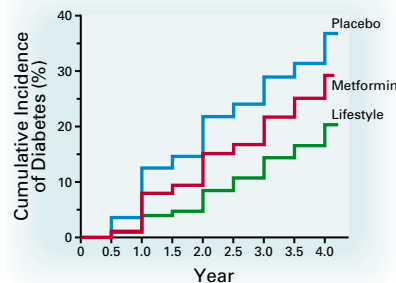




This Week in the Journal

February 7, 2002

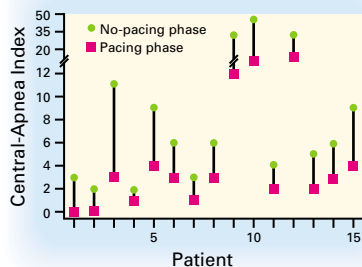


Prevention of Diabetes with Lifestyle Intervention or Metformin

This large clinical trial compared changes in diet and physical activity with metformin for the prevention of diabetes in persons at high risk for the disease. Although both interventions were effective in preventing diabetes, the lifestyle intervention was more effective than metformin.

Metformin is a biguanide that acts by improving sensitivity to insulin. Although it reduced the risk of diabetes in high-risk persons, weight loss through dietary change and regular exercise were even more effective. These observations are important for the 10 million persons in the United States who are at risk for diabetes.

see page 393



Benefit of Atrial Pacing in Sleep Apnea Syndrome

Both central sleep apnea and obstructive sleep apnea are characterized by episodes of apnea and hypopnea during sleep. Many patients also have associated arrhythmias and therefore receive permanent atrial pacemakers. This study found that, in such patients, atrial overdrive pacing at a rate 15 beats per minute above the base-line rate resulted in a substantial reduction in the frequency of episodes of apnea and hypopnea.

The mechanism of the beneficial effect of pacing is not clear but may involve a reversal of excess vagal tone. Whether or not atrial overdrive pacing would have a similar beneficial effect in patients with sleep apnea that is not associated with bradycardia cannot be determined from this study, but this question should be the subject of further investigation.

see page 404 (Perspective, page 390, editorial, page 444)

PERSPECTIVE

Sleep Apnea Syndrome

Breathing and sleeping are two very basic processes. If you stop breathing for more than a few minutes, life itself stops. Sleep is a little more forgiving, but if you stop sleeping, or fail to achieve a truly rejuvenating sleep, it is not long before life is pretty miserable. Since these two physiologic processes are so important, it has been somewhat surprising to discover over the past 25 years that disordered, even disrupted, breathing during sleep is a substantial medical problem.

The most common disorder of breathing during sleep, affecting more than 10 percent of the population over the age of 65, is obstructive sleep apnea. In this condition, the tone of the upper-airway musculature is inadequate to maintain airway patency. We associate the condition with obesity, as in Dickens's *Pickwick Papers*, but obesity, albeit common among patients with the disorder, is not one of the diagnostic criteria for it. In these patients, when the upper airway is floppy, the anatomical structures of the upper airway are drawn into the airstream as the diaphragm descends and obstruct inspiratory airflow (Fig. 1). In central sleep apnea, the second most common breathing disorder during sleep, there is also a loss of inspiratory airflow, but it occurs because of a loss of phasic diaphragmatic activity.

The consequence of both conditions is that normal ventilation does not occur during sleep. In either case, when there is inadequate breathing, a physiological fire alarm is sounded. The person is aroused from slumber, reinitiates the ventilatory process, and then tries to resume sleeping. The outcome is not good; what sleep there is is fragmented and not at all restful, and

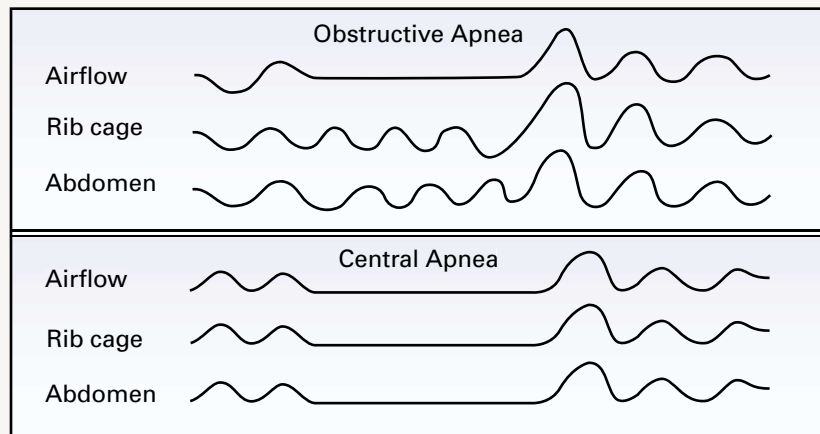


Figure 1. A Polysomnogram Showing Obstructive Apnea (Respiratory Motion of the Chest Wall with No Nasal Air Flow), Followed by Arousal from Sleep.

the patient is considered to have a sleep apnea syndrome. After months to years of sleep apnea, there may be severe physiological and psychological consequences, including hypertension, right heart failure, and death. Treatment to restore breathing during sleep can prevent these consequences.

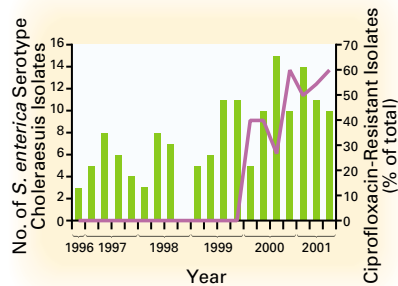
The most common treatment for patients with sleep apnea is to provide continuous positive airway pressure (CPAP) at the upper airway, usually through a nasal mask, during sleep. The mask is connected to an air pump that provides steady or phasic air pressure to the upper airway. This pressure creates a “pneumatic splint” of the upper airway and improves breathing in patients with obstructive or central sleep apnea. Although this approach is clinically effective, the treatment is cumbersome. Compliance with CPAP treatment is problematic, and the patient’s bed partner not uncommonly moves to a new sleeping place because of the noise and inconvenience. Better treatment for sleep apnea would be a boon for many.

Since sleep apnea tends to afflict older people, a substantial number have concomitant arrhythmias requiring cardiac pacemakers. In this issue of the *Journal*, Garrigue and coworkers (see pages 404–412) re-

port a fascinating observation. Patients with sleep apnea, either obstructive or central, who also had a sequential and programmable cardiac pacemaker had fewer and less severe episodes of apnea during sleep when their pacemakers were set to achieve atrial overdrive — that is, a heart rate 15 beats per minute faster than that measured on a night when their pacemakers were not active. Garrigue et al. documented the same effect regardless of whether the patients had heart failure. They speculate that the vagal tone that accompanies bradycardia also causes the sleep apnea, so that prevention of the enhanced vagal tone prevents the apnea, but they do not really know why this intervention worked.

If replicated, their observation could provide an entirely new way to think about the treatment of sleep apnea. If patients with this disorder have enhanced vagal tone and the enhanced tone inhibits normal ventilation, then prevention of enhanced vagal tone could offer a new treatment for this common condition. We, and the spouses of thousands of patients with sleep apnea, await the development of treatments less cumbersome than those currently available.

JEFFREY M. DRAZEN, M.D.



Fluoroquinolone Resistance in *Salmonella enterica* Serotype Choleraesuis

Salmonella enterica serotype choleraesuis is a cause of serious systemic infections. Data from a surveillance system in Taiwan document the rapid emergence of fluoroquinolone resistance in this serotype. The rate of resistance has reached 60 percent. Molecular typing indicates that the source of the resistant isolates is likely to be herds of swine raised for food.

This report provides further evidence of the spread of resistant bacteria from food animals to humans. Fluoroquinolone resistance is of major concern because fluoroquinolones are used for the treatment of severe salmonella infections, especially in areas where salmonella are resistant to many other antibiotics.

see page 413

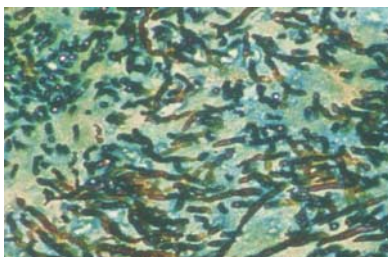
“Overexpression of p53 in malignant gliomas . . . is strongly associated with an adverse outcome.”

p53 and Outcome of Malignant Gliomas in Children

The clinical and histologic features of high-grade gliomas in children are not always useful prognostic indicators. This study investigated the prognostic usefulness of evaluating gliomas in children for the presence of p53, a protein involved in numerous aspects of the life and death of a cell. Children with tumors that contained many p53-positive cells had a much poorer outcome than children with tumors that contained few or no p53-positive cells.

The number of p53-positive cells in the tumor appears to be an independent prognostic marker in children with high-grade gliomas. This finding may contribute to better stratification of children who enter clinical trials of treatment for high-grade gliomas.

see page 420



Images In Clinical Medicine: Aspergilloma as a Complication of Pacemaker Implantation

see page 428



Current Concepts: **Community-Acquired Pneumonia in Children**

Pneumonia remains a common and potentially serious infection in children. This review summarizes the problems involved in making the diagnosis and establishing a cause and offers a practical guide to treatment. Decisions should be based first on the age of the child, then on clinical and epidemiologic considerations, and finally, on the findings on chest radiography.

see page 429



Clinical Problem Solving: **More Than Your Average Wheeze**

A 59-year-old man with a history of a nonproductive cough and wheezing presents with increasing shortness of breath. His symptoms have not responded to treatment with bronchodilators and inhaled corticosteroids or to treatment for sinusitis and esophageal reflux, but they improve when he takes oral prednisone.

see page 438

“If allowed to stand, federal interference with Oregon’s Death with Dignity Act will affect the ability of physicians . . . to prescribe drugs according to their best medical judgment.”

Oregon’s Death with Dignity Act — The Law and Challenges

This issue of the *Journal* contains two articles on Oregon’s Death with Dignity Act. In a Health Policy Report, Steinbrook provides an overview of the 1994 Oregon law legalizing physician-assisted suicide. He discusses the effects of the law on the care of terminally ill patients and the various legal challenges that have been made to the law. The most recent challenge is the directive issued by the attorney general of the United States, John Ashcroft.

In a Sounding Board article, Lowenstein and Wanzer discuss Ashcroft’s directive and their perceptions about its effect on medical practice. The authors make the case that the attorney general’s challenge to the Oregon law represents an inappropriate intrusion into medical practice and may have implications far beyond physician-assisted suicide.

see pages 447 and 460