Hyperpnea, Hyperventilation, and Brain Dysfunction

SINCE THE 19th century, when Cheyne (1818) first noted periodic breathing and Biot (1876) dubbed ataxic breathing "meningitic," perceptive clinicians have recognized that abnormal respiratory patterns can reflect serious dysfunction of the brain and often imply a poor prognosis. Rout, Lane, and Wollner (1) have recently refocused attention on these important principles in studies of patients with strokes, supplementing graphs of the abnormal breathing patterns with analyses of the respiratory gases and acid-base balance in the blood and cerebrospinal fluid. Patients with normal respiratory patterns and blood gases survived, while those with Cheyne-Stokes breathing or hyperventilation fared badly: out of 11 patients who had a P_{CO_2} of less than 35 mm Hg and a pH of more than 7.46 in the arterial blood, only 1 survived. Similar associations between hyperpneic hypocapnia and a poor outcome have also been noted after head injuries (2, 3). In the patients with stroke the cerebrospinal fluid of those with hyperpnea was usually more alkaline than normal, ruling out excess spinal fluid acidity as the cause of the respiratory change and leading Lane, Rout, and Williamson (4) to conclude that central neurologic damage caused the hyperpnea.

This conclusion is seemingly consistent with earlier clinical and postmortem observations (5, 6), which indicated that bilateral damage or dysfunction of the cerebral hemispheres or diencephalon usually was required before Cheyne-Stokes breathing developed, whereas neurogenic hyperventilation was associated with central lesions of the upper brain stem. Since only the more serious neurological injuries can cause breathing abnormalities (7), the damage alone could explain the frequently unfortunate outcome.

Perhaps that is all there is to it, but one should look further at what causes hyperpnea in seriously ill patients, whether or not they have brain injuries. If one starts by defining terms, *hyperpnea* describes increased breathing of whatever cause, whereas *hyperventilation* means that the volume of breathing is greater than required by the metabolic demands of the body; one cannot call overbreathing "hyperventilation" so long as a patient breathing room air has either an arterial P_{CO_2} above 40 mm Hg or an arterial P_{O_2} of less than 70 to 80 mm Hg. Thus, overbreathing patients with mild arterial hypoxemia may be considered to be hyperpneic but not truly hyperventilating. *Primary* or *central neurogenic hyperventilation* implies that the overbreathing arises in the absence of reflex stimuli originating in peripheral structures, including the chemoreceptors and chest-lung stretch receptors*, and that it persists during sleep, which eliminates a psychogenic cause. Such central neurogenic hyperventilation has never been produced experimentally, and clinically it is rare, even in patients with organic neurological disease. On a large neurological service with a considerable interest in the problem, we have examined many patients with hyperpneic hypocarbia during the past 8 years; in only one, a child with a primary brain stem neoplasm, could we be sure of central neurogenic hyperventilation, for in all the others the arterial oxygen tension was below normal, and the lungs and airways, by detailed clinical or postmortem studies, were seriously diseased, even when this had not been immediately obvious.

The combination of hyperpnea with a low arterial blood CO_2 tension, an elevated blood pH, and a subnormal or moderately low oxygen tension occurs in many serious illnesses that entirely spare the brain. These include the alveolar-capillary block of diffuse pulmonary carcinomatosis; heart failure; advanced cirrhosis, with or without hepatic coma; acute pulmonary infarction; and many others, including the cryptic pulmonary congestion that accompanies most serious disease in the obtunded or elderly.

In patients with a variety of acute brain lesions, including recent head trauma, it is being increasingly recognized that hypoxemia may develop in the absence of obvious pulmonary complications such as atelectasis, aspiration pneumonitis, or gross pulmonary edema. The mechanism of this effect is obscure, but it is presumed to derive from a ventilation/perfusion imbalance, possibly with a neurogenic orign (8). Its influence on respiration is to congest the lungs, provoking hyperpnea with consequent hypocarbia, and it thus becomes one of the many causes of the pseudohyperventilation syndrome. Whatever the cause, this syndrome calls for treatment of the underlying hypoxia, which, along with the pulmonary congestion (*see* footnote), is the drive to increased ventilation; if such treatment is delayed or never initiated, hyperpnea will inevitably correlate consistently with a poor prognosis. (FRED PLUM, M.D., *Department of Neurology, New York Hospital/Cornell Medical Center, New York, N.Y.*)

* Several papers in the sumposium cited in Reference 7 discuss these afferent pathways. See especially those by Guz, Widdicomb, Paintal, Godfrey, and their respective collaborators.

References

1. ROUT MW, LANE DJ, WOLLNER L: Prognosis in acute cerebrovascular accidents in relation to respiratory pattern and blood gas tensions. *Br Med J* 3:7-9, 1971
2. HUANG CT, COOK AW, LYONS HA: Severe cranio cerebral trauma and respiratory abnormalities. *Arch Neurol* 9:545-554, 1963
3. VAPALAHTI M, TROUP H: Prognosis for patients with severe brain injuries. *Br Med J* 3:404-407, 1971
4. LANE DJ, ROUT MW, WILLIAMSON DH: Mechanism of hyperventilation in acute cerebrovascular accidents. *Ibid.*, pp. 9-12
5. BROWN HW, PLUM F: The neurologic basis of Cheyne-Stokes respiration. *Am J Med* 30:849-860, 1961
6. PLUM F, SWANSON AG: Central neurogenic hyperventilation in man. *Arch Neurol Psychiat* 81:535-549, 1959
7. PLUM F: Neurological integration of behavioral and metabolic control of breathing, in *Breathing: Hering-Breuer Centenary Symposium*, Ciba Symposium, edited by PORTER R. London, J. & A. Churchill, Ltd., 1970, pp. 159-174
8. DUCKER TB, SIMMONS RL, ANDERSON RW: Increased intracranial pressure and pulmonary edema. Part 3: the effect of increased intracranial pressure on the cardiovascular hemodynamics of chimpanzees. *J Neurosurg* 29:475-483, 1968