Respiratory Pattern Disturbances in Ischemic Cerebral Vascular Disease

BY M. C. LEE, M.D., A. C. KLASSEN, M.D., AND J. A. RESCH, M.D.

Abstract:
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Impedance pneumography was used to monitor respiratory rates and patterns in 49 patients with acute ischemic cerebral vascular disease. Nine patients had clinical evidence of bilateral ischemic cerebral disease. In one of these, normal respiratory pattern was present at all times; in five, there was intermittent Cheyne-Stokes respiration; in two, there were variants of Cheyne-Stokes pattern, and one patient eventually developed sustained tachypnea with probable hyperpnea. Twenty-eight patients had unilateral cerebral infarct. In five of these, normal respiratory pattern was present at all times; in 15, there was intermittent Cheyne-Stokes respiration; six had a variant of Cheyne-Stokes respiration; two had sustained tachypnea with probable hyperpnea. In 12 patients with brainstem infarcts, Cheyne-Stokes respiration was intermittently present in four, Cheyne-Stokes variant patterns were observed in two, and sustained tachypnea with probable hyperpnea developed in six. Abnormalities of respiratory patterns occurred more frequently during sleep, in the presence of a depressed sensorium, and in patients with severe neurological deficits. Respiratory alkalosis of variable degree was present in all patients with Cheyne-Stokes respiration or sustained tachypnea with probable hyperpnea. Cheyne-Stokes respiration was not always related to bilateral cerebral lesions. Intermittent Cheyne-Stokes respiration was not closely related to immediate prognosis. Sustained tachypnea with respiratory alkalosis was associated with the highest mortality rate among patients with respiratory pattern abnormalities.

Additional Key Words
tachypnea impedance pneumography hyperventilation Cheyne-Stokes respiration respiratory alkalosis

Introduction
Cerebral vascular disease may be associated with a variety of alterations in respiratory patterns. These changes include Cheyne-Stokes respiration, ataxic, cluster, and apneustic respirations and central neurogenic hyperventilation.14 The mechanisms underlying these changes of respiratory pattern are not well understood.

Impedance pneumography is a simple andatraumatic method for continuous monitoring of respiratory patterns. Changes in transthoracic impedance are proportional to changes in tissue/air volume ratios, and provide estimates of rate and, less reliably, of volume of respiration. The method has been used to detect abnormal respiratory patterns associated with lesions of the central nervous system.7-9

In the present study the respiratory rates and patterns were investigated in patients with acute cerebral or brainstem infarcts. The frequency and types of respiratory pattern abnormalities were related to the clinical localization of the lesions and, where possible, with the pathological findings. In some patients respiratory pattern changes were related to changes in arterial gas values. The prognostic significance of respiratory pattern changes also was considered.

Methods
Forty-nine patients with acute cerebral or brainstem infarcts admitted to the University of Minnesota Hospitals Neurological Intensive Care Unit within 72 hours after the onset of symptoms were studied during the first two weeks of hospitalization (table 1). On the basis of the clinical examination, the patients were classified as having unilateral or bilateral infarcts in the cerebral hemispheres or infarcts in the brainstem.

A Beckman "Apnea Monitor" Model RM-10 was used to provide continuous oscilloscopic monitoring of respiratory patterns as well as to obtain permanent recordings. Permanent records of respiratory patterns were obtained with a chart recorder for approximately ten minutes per hour during the duration of the patients' stay in the intensive care unit. Arterial blood gas samples for pH, Pco2, and PO2 were obtained in 25 patients soon after admission and occasionally thereafter. The paper records of respiratory patterns were reviewed by the authors without knowledge of the presumed clinical localization of the lesions in these patients. Records were reviewed for the presence or absence of Cheyne-Stokes respiration, Cheyne-Stokes variant patterns and tachypnea. Other types of
respiratory pattern changes were not included because of frequent difficulties in distinguishing them from artifactual changes using this method. Respiratory pattern abnormalities were not quantitated, although in individual patients, the trend of the changes was studied. Cheyne-Stokes respiration was used to designate periods of hyperpnea regularly alternating with a period of apnea. The term Cheyne-Stokes variant was used to designate respiratory patterns in which phasic variations in depth of respiration without definite apneic periods occurred. Patients who showed both Cheyne-Stokes respiration and Cheyne-Stokes variant patterns were classified as having Cheyne-Stokes respiration. Rapid, regular respiratory rates greater than 30 per minute were designated as tachypnea.

Results
Figure 1 shows examples of various respiratory pattern changes studied in these patients.

In the majority of patients who showed abnormal respiratory patterns, the abnormality was usually intermittent and tended to occur more frequently in the presence of severe neurological deficit and especially when there was marked depression of sensorium. As the neurological status of the patient improved, respiratory pattern abnormalities tended to become less frequent and sometimes disappeared.

No abnormal patterns were detected in five of 28 patients with unilateral cerebral infarcts and in one of nine patients with bilateral cerebral infarcts (fig. 2). This absence of any observed abnormalities in respiratory patterns occurred in patients with mild neurological deficit and minimal or no depression of sensorium. Typical Cheyne-Stokes respiration was present intermittently in 15 of 28 patients with unilateral cerebral infarcts, in five of nine patients with bilateral cerebral infarcts, and in four of 12 patients with brainstem infarcts. Cheyne-Stokes variant patterns were present intermittently in six of 28 patients with unilateral cerebral infarcts, in two of nine patients with bilateral cerebral infarcts, and in two of 12 patients with brainstem infarcts. Sustained tachypnea with probable hyperpnea was observed in two of 28 patients with unilateral cerebral infarcts, in one of nine patients with bilateral cerebral infarcts, and in six of 12 patients with brainstem infarcts.

In 42 patients there was evidence of cardiac, pulmonary or other systemic disease. There were only seven patients (four with unilateral cerebral, two with bilateral cerebral and one with brainstem infarcts) in whom there was no clinical evidence of other significant systemic disease.

Ten patients died during the observed period. These patients consisted of two with unilateral cerebral, four with bilateral cerebral and four with brainstem infarcts. Autopsy was performed in two
patients with bilateral cerebral infarcts and in three with brainstem infarcts.

Of the seven patients without evidence of other systemic disease, four patients with unilateral cerebral infarcts had normal respiratory patterns, while two patients with bilateral cerebral infarcts and one with brainstem infarct had intermittent Cheyne-Stokes respiration. None of these seven patients died during the observed period.

Of the 25 patients who had one or more arterial gas studies performed (fig. 3), patients with normal respiratory patterns had arterial gas values within normal range. Patients with Cheyne-Stokes variant patterns had normal values or mild respiratory alkalosis. Respiratory alkalosis was present to a similar degree in both unilateral and bilateral infarct groups but was more severe in patients with sustained tachypnea with probable hyperpnea. PaO₂ was less than 66 mm Hg in four patients with unilateral cerebral infarcts, three patients with bilateral cerebral infarcts and three patients with brainstem infarcts. All of these patients with low PaO₂ values had Cheyne-Stokes respiration and in four of them sustained tachypnea with probable hyperpnea eventually developed.

In three patients with cerebral infarcts (two unilateral, one bilateral) the development of sustained tachypnea was preceded by Cheyne-Stokes respiration and respiratory alkalosis. The clinical course in these three patients appeared to be compatible with the transtentorial herniation syndrome and associated upper brainstem dysfunction. However, it is of interest that postmortem examination in one of these cases did not reveal evidence of significant transtentorial herniation syndrome and associated upper brainstem lesions. Furthermore, in two patients with extensive pontine infarction involving both the basal and tectal portions as confirmed at autopsy, tachypnea was not observed at any time, whereas typical Cheyne-Stokes respiration was noted in both. In a third autopsied patient with a similar extensive pontine infarct, Cheyne-Stokes respiration preceded the development of sustained tachypnea.

Discussion

In agreement with others, this study demonstrates the frequent occurrence of respiratory pattern abnormalities and arterial gas changes in patients with acute ischemic cerebral vascular disease. Whether or not these respiratory pattern abnormalities are directly related to the neurological lesion in these patients is difficult to ascertain. Other systemic factors such as old age and cardiopulmonary or metabolic dysfunction also may contribute to changes in respiratory patterns and arterial gas values. Such causes of respiratory dysfunction may be expected to be present in a large proportion of patients in the “stroke” age group. However, our study showed that Cheyne-Stokes respiration occurred in three patients (two with bilateral cerebral infarcts, one with
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brainstem infarct) without associated cardiac or other systemic disease. This confirms the observations by Brown and Plum who reported on Cheyne-Stokes respiration in humans. This confirms the observations by Brown and Plum that Cheyne-Stokes respiration may occur in the absence of cardiac or other circulatory abnormalities, and that extracerebral abnormalities, although they may increase the severity of periodic breathing, are not usually the primary cause of Cheyne-Stokes respiration.

Previous studies have suggested that specific respiratory pattern changes may be correlated with the anatomical site of the central nervous system lesion. When due to cerebral lesions, Cheyne-Stokes respiration in humans has usually been considered to be indicative of bilateral cerebral dysfunction. In our series, however, Cheyne-Stokes respiration was also frequently observed in patients with unilateral cerebral and brainstem infarcts. However, Cheyne-Stokes respiration in patients with unilateral cerebral infarct occurred only in association with cardiac or pulmonary abnormalities. Thus, while the presence of bilateral cerebral lesions may not be essential for the development of Cheyne-Stokes respiration, systemic factors may contribute to the development of Cheyne-Stokes respiration. Moreover, it is possible that additional unrecognized lesions were present in the other cerebral hemisphere, or that unilateral cerebral infarct resulted in transtentorial herniation with subsequent bilateral midbrain compression. An alternative explanation would be that unilateral cerebral lesions may result in bilateral cerebral dysfunction manifesting as altered respiratory sensitivity to CO2 and subsequent Cheyne-Stokes respiration. This may be analogous to other bilateral changes in central nervous system function such as depression of sensorium, bilateral electroencephalographical abnormalities and bilaterally decreased cerebral blood flow which may occur in patients with unilateral cerebral infarct.

In support of this is the observation that in some patients in our series Cheyne-Stokes respiration became less frequent or disappeared as the level of sensorium and neurological status improved.

Other studies have demonstrated that hyperventilation attributed to the presence of central nervous system lesions, often referred to as "central neurogenic hyperventilation," is usually associated with midline lesions in the area of midbrain and upper pontine tegmentum. To be considered "primary" or "central" in origin, such "hyperventilation" must be accompanied by normal levels of Pao2 (greater than 80 mm Hg) and by a volume of breathing which is increased beyond the necessity of body demands. Reflex hyperpnea due to hypoxic drive could easily be mistaken for "central neurogenic hyperventilation." For example, in all four patients with sustained tachypnea and probable hyperpnea in whom arterial gas determinations were obtained, low Pao2 values were present. It thus seems likely that true "central neurogenic hyperventilation" occurs very rarely, if ever. Therefore, tachypnea alone, even when combined with respiratory alkalosis, is not a satisfactory indicator of the presence of "central neurogenic hyperventilation." In the absence of accurate measurements of volumetric alveolar ventilation, it can be speculated that the presence of tachypnea in many of our cases might have been due to reflex hyperpnea rather than due to "central neurogenic hyperventilation."

Other investigators have suggested that the presence of either Cheyne-Stokes respiration or "central neurogenic hyperventilation" in combination with respiratory alkalosis is associated with a very high mortality rate. In our study, the mere presence of intermittent Cheyne-Stokes respiration or Cheyne-Stokes variant patterns did not necessarily indicate a poor immediate prognosis. Transient periods of Cheyne-Stokes respiration or Cheyne-Stokes variant patterns were frequently observed in patients with relatively mild neurological deficits, especially during sleep. In these patients, as mentioned earlier, the intermittent respiratory pattern abnormalities usually disappeared as the neurological status improved. The presence of severe sustained tachypnea and probable hyperpnea with respiratory alkalosis in our series indicated a grave prognosis. The development of such tachypnea in patients with massive cerebral infarction was associated with a fatal outcome in all three cases. Three out of six patients with brainstem infarcts in whom severe tachypnea with respiratory alkalosis was present died during the observed period.

All cases with respiratory pattern abnormalities except for Cheyne-Stokes variant showed varying degrees of respiratory alkalosis regardless of the site or the extent of the infarct. The underlying mechanism for the development of respiratory alkalosis is not known. Peripheral chemoreceptors are much less sensitive to changes in Pao2 than in Paco2, and reflex hyperpnea secondary to hypoxic drive probably does not occur unless Pao2 becomes less than 40 to 45 mm Hg. In our series, however, all of the ten patients who had Pao2 values less than 66 mm Hg showed respiratory alkalosis and respiratory pattern abnormalities. It is possible, therefore, that in these patients respiratory alkalosis and respiratory pattern abnormalities were related to hypoxemia and the subsequent hypoxic drive of respiration.

Impedance pneumography appears to be useful for detecting respiratory pattern abnormalities which would otherwise often not be detected in the usual clinical setting. The method permits constant monitoring of respiratory patterns although it does not provide accurate information on volumetric pulmonary changes. However, in conjunction with intermittent measurements of total pulmonary ventilation and arterial gas studies, this technique may prove to be helpful in further elucidating complex neurogenic influences on respiration. The prognostic
and therapeutic significance of the respiratory pattern changes seen in patients with cerebral vascular or other central nervous system lesions requires further elucidation.

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