

## Cheyne-Stokes Respiration in Congestive Heart Failure

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Cheyne-Stokes respiration is an abnormal breathing pattern which commonly occurs in patients with decompensated congestive heart failure and neurologic diseases, in whom periods of tachypnea and hyperpnea alternate with periods of apnea. In the majority of these patients, the ventilatory patterns may not be recognized, and the clinical features are generally dominated by the underlying disease process. Cheyne-Stokes respiration may, however, have profound effects on the cardiopulmonary system, causing oxygen desaturation, cardiac arrhythmias, and changes in mental status. Treatment of Cheyne-Stokes respiration in congestive heart failure with supplemental oxygen or nasal continuous positive airway pressure, in addition to conventional therapy, may improve the overall cardiac function and perhaps the patient's prognosis.

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### INTRODUCTION

Cheyne-Stokes respiration (CSR) is a form of periodic breathing in which episodes of hyperpnea alternate with periods of apnea (Fig. 1). This abnormal respiratory pattern was originally described in patients with congestive heart failure, first by Cheyne in 1818 [1] and then by Stokes in 1854 [2]. CSR can occur, however, as a part of normal sleep in healthy individuals and those at high altitude [3,4]. It may also be present in 20–30 percent of otherwise healthy elderly persons [5,6]. Nevertheless, when present, it usually indicates the presence of congestive heart failure, neurologic disease, prematurity, and uremia (Table 1) [7–11].

In this review, we have focused on CSR in congestive heart failure with a search of literature dating back to the original description of the entity by Cheyne and Stokes in the early and middle 1800s. When congestive heart failure is associated with CSR, it generally carries a poor prognosis [11]. The apneas are associated with worsening of oxygenation and fluctuation in  $PCO_2$  and pH, which may have adverse effects on an already compromised cardiovascular system. Alterations in the breathing pattern are often difficult to detect clinically, and thus the condition may remain undetected. The advent of continuous noninvasive ventilatory and oxygenation monitoring techniques should make the detection of this breathing disturbance easier. This review covers the literature in English on the subject since 1818 and describes the pathophysiology of CSR, its associated clinical entities, and its effect on the cardiovascular system. We also review the different modalities in the management of CSR.

*Abbreviations:* CPAP: continuous positive airway pressure CSR: Cheyne-Stokes respiration NYHA: New York Heart Association functional class PCWP: pulmonary capillary wedge pressure REM: rapid eye movement sleep  $SO_2$ : arterial oxygen saturation SWS: slow-wave sleep TST: total sleep time

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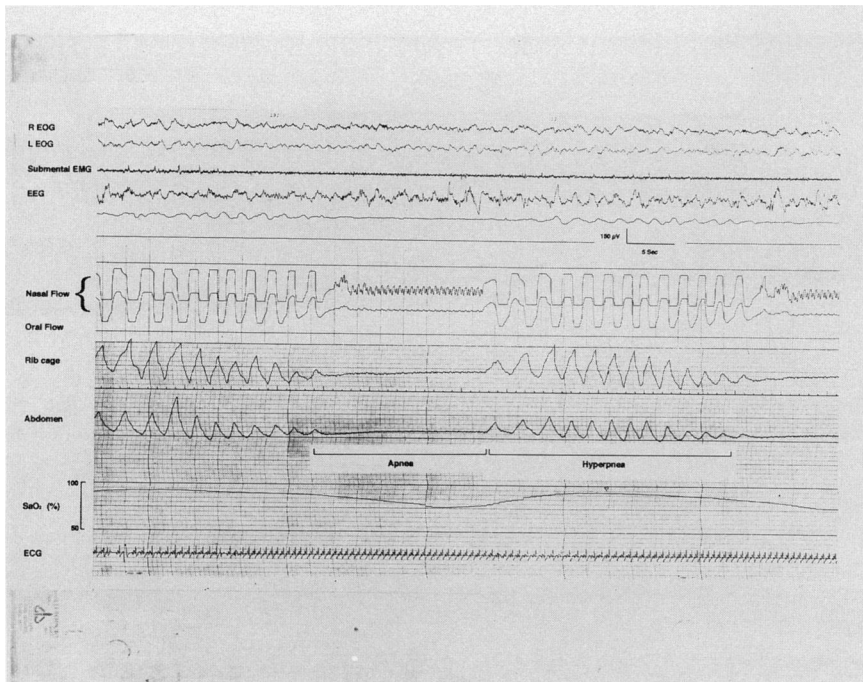


FIG. 1. Ninety-two seconds of polygraphic recording during sleep in a patient with congestive heart failure. Twenty seconds of central apnea characterized by absence of abdominal and rib cage efforts and no nasal airflow are followed by 28 seconds of hyperpnea. The cycle of apnea-hyperpnea repeats every 48 seconds in this patient. A decrease in oxygen saturation to 75 percent is present after apnea. **R/EOG**, **L/EOG**, right and left electrooculograms, respectively; **EMG**, submental electromyogram; **EEG**, electroencephalogram; **SaO<sub>2</sub>**, arterial oxygen saturation; **ECG**, electrocardiogram.

TABLE 1  
Conditions Associated with Cheyne-Stokes Respiration

*Cardiovascular:*

- Congestive heart failure
- Coronary heart disease
- Hypertensive cardiovascular disease

*Neurologic:*

- Cerebrovascular disease
- Subarachnoid hemorrhage
- Trauma
- Cerebral tumor
- Meningitis
- Encephalitis
- Narcolepsy

*Miscellaneous:*

- High altitude
- Sleep
- Prematurity
- Elderly status
- CO<sub>2</sub> narcosis
- Uremia

## RESPIRATORY CONTROL SYSTEM IN NORMAL SUBJECTS

It is currently thought that two separate anatomic pathways are responsible for the voluntary and the automatic control of breathing [12]. In the waking state, automatic and behavioral influences interact to establish the level and pattern of breathing. During sleep, voluntary control is lost, the effects of environmental stimuli are diminished, and breathing is believed to be governed almost exclusively by automatic mechanisms. The automatic or metabolic control system consists of the chemoreceptors (carotid body for hypoxia, and carotid body, aortic body, and central medullary chemoreceptors for hypercapnia), vagal intrapulmonary receptors, and numerous brainstem mechanisms that both process information from these peripheral receptors and control the pattern of breathing. This metabolic system keeps ventilation rhythmic and ensures that the quantity of ventilation occurring at any time is well matched to the metabolic needs of the body. It is useful to consider the respiratory control system to be composed of two subsystems, one for the regulation of  $PCO_2$  and the other for  $PO_2$ , that differ in their control characteristics.

### *Respiratory Control: $CO_2$ Subsystem*

The important role for  $PCO_2$  in the maintenance of normal rhythmic ventilation during sleep has been outlined by Cherniack [13,14]. In the normal state, the relationship between increasing  $PCO_2$  and ventilation is linear, and it requires only a small change from the resting  $PCO_2$  level to increase ventilation. The relative linearity of the ventilatory carbon dioxide response curve tends to keep respiration stable when hypercapnia is the major respiratory drive. In unconscious subjects, there is a threshold level of  $PCO_2$  at which a type of breathing begins that is not often seen in fully alert subjects. This threshold for the carbon dioxide effect in breathing produces an alinearity in the carbon dioxide role and thus acts as a potential source of instability. Aside from this threshold phenomenon, however, the slope of the ventilatory carbon dioxide response curve is constant over a wide range of carbon dioxide tensions.

This arrangement yields a stable ventilatory control system for a number of reasons. First, hypercapnia is the major respiratory stimulus during sleep, and, as stated, the relationship between  $PCO_2$  and ventilation is linear. In addition, there are relatively large stores of carbon dioxide in the body, such that large increases in ventilation are necessary to produce changes in  $PCO_2$  (a damped system), especially in the central nervous system where such changes are detected. Figure 2 shows the ventilatory control system and its components. When there is a change in carbon dioxide tension level in the blood and tissues, the feedback communication channel (in this case, the circulation) transports the blood to the carotid, aortic, and medullary chemoreceptors. These receptors detect the difference between the current values and the normal values of blood gas tension and relay this information electrically to the respiratory neurons in the brainstem (the controller). The normally operating carbon dioxide controller (a proportional controller) increases ventilation by two to four liters per minute for each millimeter rise in arterial carbon dioxide tension. This linear relation persists over a wide range of carbon dioxide tensions, indicating a constant controller gain (see Fig. 2). Impulses are sent via intercostal and phrenic nerves (neural output) to respiratory muscles that adjust the

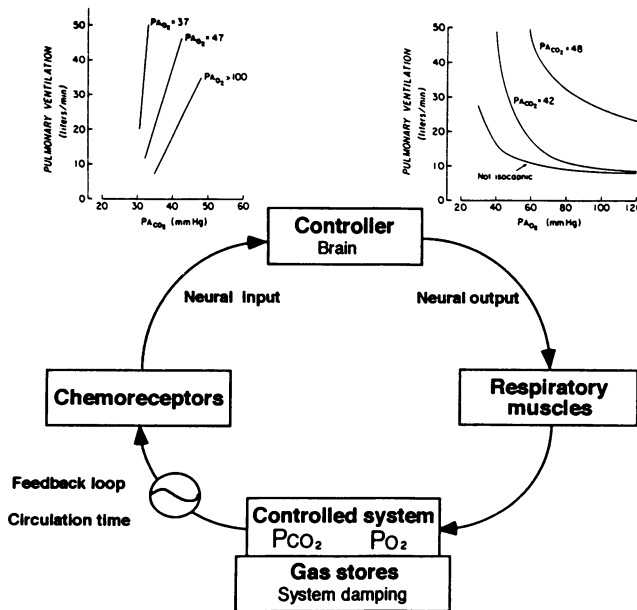


FIG. 2. Respiratory control system. The blood gas tension levels (controlled system) are sensed by the chemoreceptors, where electrical information is sent to the brainstem (controller) for regulation of the respiratory output. The neural output to the respiratory muscles is governed by the gain of the controller: i.e., the slopes of  $PA_{CO_2}$  and  $PA_{O_2}$  ventilation curves. The fluctuation of blood gases is not only dependent on the minute-by-minute variation in pulmonary ventilation, but it is also affected by the amount of gas stores in the body (system damping).

ventilation so as to minimize changes in body gas content and blood gas tensions. The cycle continues until a steady state is reached.

### Respiratory Control: $O_2$ Subsystem

In contrast to the carbon dioxide control system, the hypoxic response is neither linear nor damped. Changes in  $PO_2$  in the normal range have little influence on ventilation (Fig. 2). Since the relationship between hypoxia and ventilation is nearly hyperbolic, however, increases in controller gain (the slope of  $PO_2$  ventilation curve) for  $PO_2$  occur continuously and at an increasingly greater rate as hypoxia becomes more severe. This process tends to destabilize breathing when hypoxia becomes the major respiratory drive and could yield apnea or periodic breathing [10,15,16].

The ratio of the volume of gas (oxygen) stored in the body to change in gas (oxygen) tension (e.g.,  $PO_2$ ) is a measure of the distensibility of the system; the more gas stored for a given change in gas tension, the more the distensibility and, therefore, the greater the damping. The body oxygen stores (lung gas and blood oxygen content) are minute compared with the carbon dioxide stores. This fact results in underdamping or decrease in the distensibility of oxygen stores, hence greater fluctuation of  $PO_2$  around the normal range. The combination of a nonlinear controller gain and an underdamped system could lead to an unstable control system, where  $PO_2$  and  $PCO_2$  fluctuate widely around the mean values [17]. This condition results in the development of apnea and hyperpnea in the form of periodic breathing.

### CONTROL OF VENTILATION DURING SLEEP

More recent studies have confirmed a prominent role played by  $PCO_2$  in the maintenance of rhythmic breathing during sleep. Skatrud and Dempsey [18] showed that, with passive positive-pressure hyperventilation of sleeping subjects, apnea could be produced by a reduction in  $PCO_2$  of only 3–6 torr below the sleeping value;

the actual  $\text{PCO}_2$  level associated with apnea might only be 1–2 torr below the awake values. Each individual seemed to have an “apnea threshold”  $\text{PCO}_2$  level, below which apnea was commonly seen. Therefore, the waking  $\text{PCO}_2$  level was at or near this apnea threshold, so that the waking  $\text{PCO}_2$  level may be inadequate to stimulate ventilation during sleep. It was also demonstrated that periodic breathing during sleep, which is frequently seen during prolonged hypoxia, could be abolished by elevating the  $\text{PCO}_2$  above the predetermined apnea threshold. This finding suggests that hypopnea induced by hypoxia, not hypoxia itself, is the pivotal element in such periodic breathing. These studies suggest that ventilation is remarkably dependent on the metabolic control system during sleep, and that the primary stimulus to respiration during sleep may be arterial  $\text{PCO}_2$ . If the  $\text{PCO}_2$  drops below a certain level (“apnea threshold”), breathing is likely to become dysrhythmic whether hypoxia is present or not. This drop may partly explain the dysrhythmic breathing frequently seen at sleep onset. As an individual changes from wakefulness to stage 1 or 2 sleep, the  $\text{PCO}_2$  level that was adequate to stimulate ventilation during wakefulness may be inadequate to do so during sleep when an apnea occurs [16]. This apnea may arouse an individual, and the process may repeat itself. Once a stable sleep stage is reached, ventilation should become rhythmic under metabolic control. Any disease process that adversely affects this metabolic ventilatory control system could, however, lead to unstable or periodic breathing during sleep. An individual with such a problem may breathe adequately during wakefulness when the behavioral influences on respiration are playing an important role.

#### ALTERED RESPIRATORY CONTROL SYSTEM AND CHEYNE-STOKES RESPIRATION

CSR is an instability in the ventilatory control system in which circulation time, controller gain, and the damping characteristics of the oxygen and carbon dioxide stores play an important part [15,17,19]. In the respiratory system, circulation time corresponds to delays in information transfer, and the controller gain corresponds to the slopes of the curves relating ventilation to  $\text{PCO}_2$  and  $\text{PO}_2$ . Damping is affected by the dynamic characteristics of the body’s gas stores (oxygen and carbon dioxide in the lung, dissolved in body fluids, and in chemical combination).

Four major theories have been advanced to explain periodic breathing: (1) That CSR can occur in a normal person when circumstances increase the influence of oxygen control on ventilation and decrease that of carbon dioxide by producing hypoxia and hypocapnia simultaneously, such as occurs at high altitude and in persons with cerebrovascular disease causing depression of carbon dioxide responsiveness. (2) That CSR is due to removal of inhibiting cortical influences by disease or medications, which may increase the gain of the carbon dioxide receptors, increasing the propensity for instability; this state could occur in the setting of cerebrovascular disease, anesthesia, use of sedatives, and use of morphine. (3) That CSR is due to underdamping of the system, as in pulmonary congestion, where lung volumes are decreased and the ability to store carbon dioxide and oxygen in the functional residual capacity is diminished. (4) That CSR is due to prolonged circulation time with delay in feedback loop; this theory explains why alveolar and arterial gas tensions are out of phase during CSR. Arterial carbon dioxide tends to be highest and oxygen lowest during hyperpnea, whereas the reverse is true of alveolar gas levels. Prolonging the circulation time or delay in the feedback loop may be one

of the explanations for CSR occurring in patients with congestive heart failure. This idea was first postulated by Pembrey in 1908 [20] and later demonstrated by Guyton et al. in anesthetized dogs with prolonged circulation time [21]. It is thought that, with delayed circulation, the receptors (carotid body and medullary chemoreceptors) would not be exposed to fluctuations in blood gas levels until hypoxemia has already occurred. Because of this delayed response, the abnormalities in blood gas levels may be amplified. Because of this amplified input, the response is increased and, because of the increased circulation time, the normal end point will not be reached and an overcorrection will be achieved. This process promotes a cycle which results in hypercapnia on one end of the spectrum and hypocapnia on the other. Guyton et al. [21] artificially prolonged the circulation time in dogs and achieved CSR; they prolonged the circulation time by two to five minutes and bypassed the normal circulation to the brain. There was no data on the neurologic function of these dogs and whether this condition also may have played a role in the CSR. The circulation time in congestive heart failure is usually prolonged, but not to this degree. Brown and Plum investigated 28 patients, five of whom were free of cardiac disease [7]. They measured circulation time by an ear oximeter adjusted to respond to methylene blue. These investigators found that the circulation time was prolonged in patients with CSR, compared to a control group. They also found that circulation time was prolonged in patients with congestive heart failure but without CSR. In some of the patients with CSR, they demonstrated a normal circulation time. These studies suggest that a delay in the circulation time may play a role, along with other factors, in promoting CSR, but that is not in and of itself the pathogenetic mechanism.

Increase in oxygen controller gain (increasing the hypoxic ventilatory response) was demonstrated to yield periodic breathing by Chapman et al. [16] in a group of normal subjects when they were exposed to various levels of hypoxia. This increase in controller gain of the system magnifies the effects of chemical responses on the minute ventilation, yielding a lower  $PCO_2$ , which may lead to apnea. Hypoxemia, which is commonly present in pulmonary edema and congestive heart failure, tends to increase sensitivity to hypoxia and carbon dioxide levels.

Another possible mechanism, which works in conjunction with the hypoxic response as well as the delayed feedback loop, is a shift in the  $CO_2$  ventilatory response curve to the right. This rightward shift theoretically can increase the  $CO_2$  threshold before a respiratory response is initiated. Cooling the ventral surface of the medulla in cats caused blunting of the  $CO_2$  response curve, which resulted in periodic breathing [17]. In man, metabolic alkalosis or sleep tends to shift the  $CO_2$  response curve to the right.

In summary, there are several mechanisms responsible for the generation of CSR. The pathophysiology lies in a combination of mechanisms, some of which have been described above. In patients with congestive heart failure, there is an instability in respiratory drive due to underdamping of the system (decreased functional residual capacity is often seen in patients with congestive heart failure), delayed feedback loop (prolonged circulation time), and increased controller gain due to hypoxia and hypocapnea.

#### CLINICAL FEATURES ASSOCIATED WITH CHEYNE-STOKES RESPIRATION

The clinical features associated with CSR have been categorized according to the phase of respiration, hyperpnea or apnea (refer to Table 2). Arrhythmias are

TABLE 2  
Physiological Changes During Cheyne-Stokes Respiration

| Physiologic Parameters | Hyperpnea       | Apnea                |
|------------------------|-----------------|----------------------|
| PO <sub>2</sub>        | ↓               | ↑                    |
| PCO <sub>2</sub>       | ↑               | ↓                    |
| Heart rate             | ↓ ; Heart block | ↑                    |
| Cardiac output         | ↑               | ↓                    |
| Cerebral blood flow    | ↑               | ↓                    |
| Reflexes               | ↑               | ↓                    |
| Sensorium              | Awake, agitated | Somnolent, stuporous |

commonly observed during the apneic phase of CSR. Cardiac arrhythmias have been described in as many as 20 percent of patients with CSR and include sinus bradycardia, heart blocks, atrioventricular dissociation, ventricular ectopic beats, ventricular tachycardia, and ventricular asystole with Stokes-Adams attacks. It is believed that perhaps increased vagal discharge during the apneic phase may be important in the pathogenesis of these arrhythmias. Other contributing factors to the increased incidence of arrhythmias include the presence of underlying cardiac disease and heart failure, use of digoxin, and electrolyte disturbances and hypoxia. During the apneic phase, the cerebral blood flow is increased. This increase is in response to an elevation in the PCO<sub>2</sub>, resulting in cerebral vasodilation. The sensory reflexes are depressed during apnea when the arterial oxygen saturation is high and the arterial CO<sub>2</sub> tension and cerebral blood flow are low. In contrast, the hyperpneic phase is often accompanied by restlessness, agitation, muscle twitching, and hyperreflexia with occasional arousals and awakenings.

The association of CSR with congestive heart failure was first noted by Cheyne and Stokes [1,2] and then later by Harrison et al. [22]. The incidence of CSR appears to be quite high in patients with decompensated left ventricular function, being present in 40–100 percent of patients (refer to Table 3). Findley et al. [11] studied 15 patients with left ventricular heart failure without known breathing disorders. All the patients were dyspneic at rest and rated New York Heart Association (NYHA) functional class III or IV (dyspnea at rest or with minimal exertion). On polysomnography, six of the 15 patients (40 percent) exhibited CSR with five or more central apneas per hour of sleep. The authors also examined the relationship between CSR and short-term mortality in this group of patients. Remarkably, 100 percent of the

TABLE 3  
Prevalence of Cheyne-Stokes Respiration (CSR) in Patients with Congestive Heart Failure

| Study                       | No. of Patient | NYHA <sup>a</sup> Class | Patients with CSR (%) |
|-----------------------------|----------------|-------------------------|-----------------------|
| Findley et al.<br>1985 [11] | 15             | III–IV                  | 6/15 (40)             |
| Dark et al.<br>1987 [23]    | 6              | N/A                     | 5/6 (83)              |
| Hanley et al.<br>1989 [25]  | 10             | III–IV                  | 10/10 (100)           |

<sup>a</sup>NYHA, New York Heart Association functional class of congestive heart failure

In these studies, Cheyne-Stokes respiration was documented by polysomnographic method in patients with decompensated left heart failure.

TABLE 4  
Cheyne-Stokes Respiration in Congestive Heart Failure Pre- and Post-Medical Therapy

| Patient | Age<br>(years) | Central Apnea    |                  | Hypopnea |      | SaO <sub>2</sub> <sup>c</sup> < 85% (minute) |                  |
|---------|----------------|------------------|------------------|----------|------|--|------------------|
|         |                | Pre              | Post             | Pre      | Post | Pre  | Post             |
| 1       | 62             | 230 <sup>a</sup> | 42 <sup>a</sup>  | 19       | 9    | 139  | 1                |
| 2       | 73             | 7 <sup>a</sup>   | 2 <sup>a</sup>   | 109      | 0    | 52   | 0                |
| 3       | 46             | 50               | 0                | 48       | 0    | 0  | 0                |
| 4       | 59             | 17 <sup>a</sup>  | 0                | 82       | 14   | 7  | 0                |
| 5       | 76             | 54 <sup>a</sup>  | 84               | 6        | 2    | 12   | N/A <sup>b</sup> |
| 6       | 44             | 241 <sup>a</sup> | 229 <sup>a</sup> | 26       | 33   | 46   | 60               |

<sup>a</sup>Denotes Cheyne-Stokes respiration

<sup>b</sup>Not available

<sup>c</sup>SaO<sub>2</sub>, arterial oxygen saturation

Adapted from [23]

patients with CSR died within the following six months, whereas only 33 percent of the remaining patients without CSR died within the same period. Dark and colleagues [23] performed polysomnography within the first 48 hours of admission of six patients with decompensated left ventricular failure. A second study was performed after medical treatment prior to their discharge. None of these patients was known to have breathing abnormalities prior to their admissions. They found that all patients during the initial sleep study had abnormal breathing patterns. The respiratory disturbances were predominantly central apneas, followed by hypopneas and, less frequently, by obstructive and mixed apneas. Five of the six patients (83 percent) exhibited CSR. Three of these five patients had severe and prolonged arterial oxygen desaturations. Following medical therapy, which included inotropic agents, diuretics, and oxygen, and once judged clinically compensated, all patients underwent repeated polysomnography without supplemental oxygen. The researchers found a significant decrease in the number of sleep disturbances as well as improvement in oxygenation following medical therapy (refer to Table 4). One patient who continued to do poorly despite vigorous treatment underwent cardiac transplantation. A repeat polysomnography performed one month after transplantation showed no evidence of breathing abnormalities, and previously noted severe desaturation was no longer present.

Hanly et al. evaluated ten patients with stable and "maximally" treated congestive heart failure for respiratory disturbances during sleep [24]. All of these patients were NYHA III or IV and were not known to have abnormal breathing during sleep prior to enrollment in this study. On polysomnography, CSR was found in all patients and occurred predominantly during stage 1 and 2 non-REM (rapid eye movement) sleep. Arterial oxygenation was normal during wakefulness; however, significant hypoxemia developed during sleep as a consequence of CSR. Sleep was disrupted in all patients secondary to frequent arousals, which occurred during the hyperpneic phase. The predominance of CSR occurring during non-REM sleep reflects the difference in respiratory control between non-REM and REM sleep. The ventilatory responses to hypoxia and hypercapnia are less during REM sleep, and hence there is more stability in the control system. This study further illustrated that, in this group of high-risk patients, awake oxygen saturation did not correlate with oxygen satura-



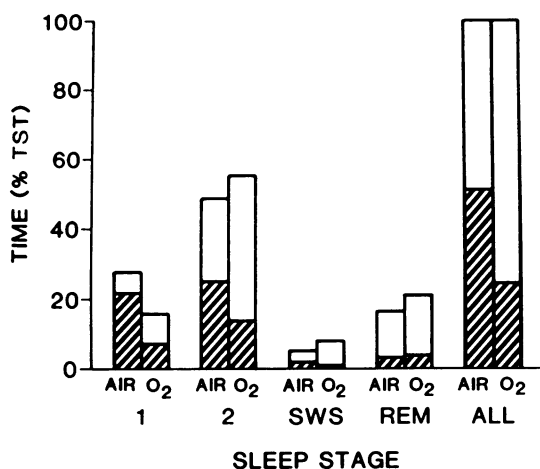


FIG. 3. Prevalence and distribution of Cheyne-Stokes respiration (*hatched bars*) and non-Cheyne-Stokes respiration (*open bars*) during sleep in patients with congestive heart failure while they are breathing air or oxygen (O<sub>2</sub>). There was a significant reduction in the duration of Cheyne-Stokes respiration (expressed as percentage of total sleep time, % TST) while breathing oxygen for all sleep stages, including REM sleep. SWS, slow-wave sleep; REM, rapid eye movement sleep; ALL, all sleep stages. Reproduced with permission from [25].

tion during sleep. Severe hypoxemia can adversely affect an already compromised cardiovascular system and may contribute to increased mortality of these patients. Moreover, the neuropsychiatric consequence of impaired sleep needs to be considered in the rehabilitation of these patients.

### TREATMENT

The treatment of CSR in congestive heart failure, much like its incidence and pathogenesis, remains to be clarified. In addition to standard medical treatment of congestive heart failure with inotropic agents, diuretics, and preload and afterload reducing agents, however, other modalities such as oxygen, positive-pressure breathing, and theophylline may prove effective as adjunct treatment modalities.

#### *Oxygen*

As described, Dark et al. found a significant improvement in the number of respiratory disturbances as well as in oxygenation following aggressive medical therapy [23]. They did not comment on improvement in functional class or survival, however. Hanly et al. [25] investigated the effects of oxygen therapy versus compressed air in patients with CSR and congestive heart failure. They found a significant reduction in the amount of CSR as a percentage of total sleep time in the oxygen-treated groups versus the compressed air-treated groups, while no change was made in medical therapy in either group. They also found that oxygen corrected nocturnal hypoxemia and improved sleep (see Fig. 3). Again, improvement in clinical status and survival were not evaluated.

#### *Nasal Continuous Positive Airway Pressure (Nasal CPAP)*

The efficacy of nasal continuous positive airway pressure (CPAP) in central apnea has been previously documented [26]. Takasaki et al. [27] evaluated the effects of nasal CPAP in patients with chronic stable congestive heart failure who demonstrated CSR during sleep. They evaluated five patients who were NYHA class III or IV. All patients treated with nasal CPAP showed marked improvements in apnea index, as well as improved nocturnal oxygenation (refer to Table 5). The cardiac status improved in all patients while on nasal CPAP for seven to 23 months of

TABLE 5  
Cheyne-Stokes Respiration in Congestive Heart Failure: Effect of Nasal CPAP<sup>a</sup>

| Variable                      | Condition | Group Data | <i>p</i> Value |
|-------------------------------|-----------|------------|----------------|
| Apneas                        | Control   | 60 ± 12    |                |
| No./hours of sleep            | CPAP      | 9 ± 7      | <0.01          |
| Apnea time                    | Control   | 44 ± 8     |                |
| % of TST <sup>b</sup>         | CPAP      | 5 ± 4      | <0.01          |
| Apneas plus hypopneas         | Control   | 69 ± 9     |                |
| No./hours of sleep            | CPAP      | 15 ± 7     | <0.005         |
| Mean low nocturnal            | Control   | 84 ± 3     |                |
| SaO <sub>2</sub> <sup>c</sup> | CPAP      | 91 ± 5     | <0.025         |

<sup>a</sup>CPAP, continuous positive airway pressure

<sup>b</sup>TST, total sleep time

<sup>c</sup>SaO<sub>2</sub>, arterial oxygen saturation

Data are expressed as the mean ± SE. Statistical analyses are by paired *t* tests.

Adapted from [27]

follow-up. All patients showed marked improvement in exercise tolerance as well as improvement in their functional class, from NYHA class III or IV to class II, while no change was made in their cardiac medications during this time.

Patients with congestive heart failure have a reduction in their functional residual capacity as well as oxygen and carbon dioxide stores. Nasal CPAP increases the lung volume by recruiting alveoli and increasing the lung oxygen store. Another mechanism by which nasal CPAP may help these patients is its effect on left ventricular function [28]. Positive intrathoracic pressure causes a reduction in the preload, as well as a reduction in afterload, by decreasing left ventricular transmural pressure. As a result, left ventricular ejection fraction may increase with concomitant decrease in circulation time. In a recent study, nasal CPAP at a level of 5 cmH<sub>2</sub>O pressure in a group of patients with congestive heart failure and elevated pulmonary capillary wedge pressure (PCWP) of 19 ± 3 mmHg resulted in a 17 percent increase in cardiac index and a 10 percent decrease in PCWP [29]. Nasal CPAP had no effect on cardiac hemodynamics in patients with normal PCWP.

Taken together, these data suggest that nasal CPAP and oxygen might prove efficacious in the treatment of patients with symptomatic congestive heart failure and CSR.

### *Theophylline*

Aminophylline has been reported to be effective in the treatment of CSR [30–32] and central apneas [33,34]. In a more recent study on five patients with CSR (two of whom had congestive heart failure, NYHA class III), theophylline significantly decreased the CSR, while it produced no change in non-CSR breathing disorder [35]. The drawback of theophylline in the treatment of CSR is that it might increase arousals and cause sleep fragmentation. In the aforementioned [35] study, however, theophylline actually decreased the sleep disruption and fragmentation because the majority of disordered-breathing events were responsive to theophylline.

The mechanism by which theophylline ameliorates CSR is unknown at present. Two possible mechanisms have been proposed [35]: (1) Theophylline has a car-

diotonic effect and may increase cardiac output and decrease circulation time in patients with heart disease. (2) Reversal of hypoxic ventilatory depression is mediated through inhibition of adenosine receptors [36,37]. Further studies are needed, however, to determine if these mechanisms of action of theophylline are therapeutically important in the treatment of CSR.

In conclusion, although CSR in patients with congestive heart failure is a well-described entity, this breathing abnormality and its clinical consequences often go unrecognized. The true incidence of CSR in patients with severe congestive heart failure is unknown, although, from the studies described, it appears to be common and the clinical implications undesirable. Patients with stable NYHA class III or IV heart failure or patients who are repeatedly admitted for decompensated heart failure, despite maximal medical therapy, may benefit from sleep investigation. Nocturnal oximetry may identify patients with a significant cyclical pattern of oxygen desaturations. This subgroup of patients should undergo polysomnography to define better the sleep architecture, sleep efficiency, and to characterize the respiratory disturbances. Patients who exhibit CSR with severe oxygen desaturation may benefit from treatment. If medical management of their underlying heart failure is not already maximized, then this action would be the first step of therapy. Nocturnal oxygen, at least in the small studies discussed, has been shown to be of benefit in this patient population. Nasal CPAP, as described, may benefit these patients by increasing left ventricular ejection fraction and improving their functional class.

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