Sleep and heart failure

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"For several days his breathing was irregular; it would entirely cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again: this revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration" CHEYNE, 1818 [1].

Despite the over 150 yrs since its description in a patient with heart failure, Cheyne-Stokes respiration (CSR) remains something of a physiological and medical enigma. Although there have been hundreds of articles written about Cheyne-Stokes respiration, including many models of respiratory control, it is probably fair to state that we currently do not understand precisely what mechanisms initiate Cheyne-Stokes respiration, what mechanisms perpetuate the oscillation in the breathing pattern or what mechanisms terminate the oscillation. In addition, there is surprisingly little known about whether the breathing pattern itself may have an impact on the patient with congestive heart failure. In contrast to the large quantity of literature about the effect of obstructive apnoea on sleep structure and cardiorespiratory physiology, there is a paucity of information about the effect of CSR on these variables in the sleeping heart failure patient. For example, the most widely cited article on Cheyne-Stokes respiration with 186 references does not even mention sleep [2].

Two features are known by every student of medicine to be classic in heart failure; Cheyne-Stokes respiration, and paroxysmal nocturnal dyspnoea. However, very little has been written linking the two. HARRISON et al. [3] in 1934, in a classic work, reported that periodic breathing was present in all congestive hear failure (CHF) patients with dyspnoea on sleep onset. They also reported that the breathing pattern could be normal when the patient was awake and became abnormal "at the moment of sleep". After Cheyne-Stokes respiration started "following a long period of apnoea the subject would awaken as breathing set in"; some of the awakenings seemed to occur during the hyperpnoeic phase of CSR. HARRISON et al. [3] pointed out that such patients "may live for days and never sleep more than a few minutes or seconds at a time" and, not surprisingly, were described as being exhausted. All this was published three years before the first use of the electroencephalograph (EEG) to classify sleep [4].

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REES and CLARK [5] reported data in four patients with heart failure. They found that two of them had CSR awake and asleep, while in two, CSR developed only with sleep onset. An extremely important observation was that it was the phase of hyperventilation which disturbed sleep. The conventional wisdom from the sleep apnoea literature would have predicted that arousals terminated the apnoeic phase and not that the hyperpnoeic phase caused the arousals. These authors also suggested, as did HARRISON et al. [3] that there was a clear-cut link between CSR and dyspnoea; the latter occurring on awakening during the hyperpnoeic phase. The main problem with this work was that sleep was not monitored neurophysiologically.

FINDLEY et al. [6] reported polysomnographic data in seven heart failure patients, three of whom had CSR. It was found that the CSR patients had markedly disrupted sleep with reduced total sleep time, many episodes of apnoea, oxygen desaturation and arousals. The temporal relationship between arousals and apnoea was not reported.

HANLY et al. [7] reported detailed sleep studies in ten CHF patients all of whom had CSR. All the patients were out-patients on optimal therapy and were stable in spite of a low left ventricular ejection fraction. None had pulmonary oedema, and, in fact they were clinically "dry". CSR did not occur uniformly throughout the night but was linked to specific sleep stages. It was found that the CSR was most common in sleep Stages 1 and 2 and uncommon in rapid eye movement (REM) sleep. These findings are similar to what has been reported about the periodic breathing after ascent to high altitude [8]. Severe sleep oxygen desaturation occurred in spite of normal awake arterial oxygen saturation (Sao_2). Mean systemic blood pressure also oscillated markedly in the one patient in whom it was measured. The most interesting findings related to sleep quality which was extremely poor. There was a marked reduction in total sleep time, frequent arousals, and increased Stage 1 sleep. Most of the arousals were not synchronous with the resumption of ventilation post-apnoea, but were delayed just as described by HARRISON et al. [3] and REES and CLARK [5]. Thus, the arousals do not serve a useful purpose as they do in obstructive apnoea (to re-establish ventilation) but simply disrupt sleep. Thus, CSR is not simply a curiosity. This breathing pattern causes morbidity and in turn possibly may even further worsen the heart failure due to its effect on oxygenation and blood pressure.

Not surprisingly, some recent work has focused on reducing CSR in heart failure. HANLY *et al.* [9] found that in nine CHF patients, oxygen by nasal cannulae reduced the amount of CSR by about half and there was improvement in sleep quality; total sleep time increased, Stage 1 was reduced, and the arousal frequency was markedly reduced with the reduction being mainly in the delayed arousals during hyperpnoea. There are several mechanisms which may explain the improvement with oxygen. It is believed that CSR is maintained by the peripheral chemoreceptors [10] and perhaps hyperoxia, by reducing baseline carotid body output, may shift chemical control from the carotid body to the central chemoreceptor which would tend to stabilize the breathing pattern [11]. Oxygen breathing may also result in an increase in arterial carbon dioxide tension ($Paco_2$) which may stabilize the breathing pattern as has been shown for the hypocapnia-related CSR at high altitude [10].

In a series of five CHF patients, two of whom were markedly obese, nasal continuous positive airway pressure (CPAP) was shown to abolish apnoeic episodes and to improve sleep quality [12], and also improve some measures of cardiac performance. It is unclear why nasal CPAP would be effective in central apnoea. It is possible that upper airway collapse, by an as yet unknown mechanism, could lead to central apnoeas, and abolition of the obstruction would alleviate the CSR. It is also possible that the CPAP-induced changes in lung volume or cardiac output would stabilize the breathing pattern. It is possible that the pressure may stimulate breathing by some yet unknown reflex. All five patients reported by TAKASAKI *et al.* [12] were habitual snores, and thus they may represent an overlap between classic obstructive apnoea and heart failure.

When confronted with a treated heart failure patient, the clinician should consider whether the clinical features normally used to decide that the heart failure is under control are adequate. CSR may represent a marker that control is not optimal. The assessment of such a patient should thus include questioning about insomnia, nocturnal dyspnoea, disrupted sleep, and excessive daytime sleepiness. If a patient has any of these features, then CSR is likely.

If CSR is present, is it clinically important? We know that CSR is associated with hypoxaemia and changes in blood pressure and these can theoretically worsen myocardial function and thus in turn worsen CSR - a vicious circle. We do not know whether preventing CSR will prevent further myocardial compromise. We do know that sleep structure is very abnormal in these patients, and the patients do complain of severe sleep problems. It is likely that these symptoms will improve with treatment of the CSR.

Now that it is apparent that CSR itself may cause morbidity, systematic evaluation of methods to abolish CSR is warranted. It is likely that many strategies may be employed in reducing CSR, including reducing arousability as has been done in idiopathic central apnoea [13], reducing chemical drives to breathe as well as the methods mentioned above. The end-points to be examined should not simply be variables measured during sleep, but daytime performance (sleepiness, cognitive testing) and effect on mortality. Such clinical trials will answer the question about whether CSR is clinically important and more important, whether its treatment will improve patient outcome.

References

1.   Cheyne J. – A case of apoplexy, in which the fleshy part of the heart was converted into fat. *Dublin Hospital Reports*, 1818, 12, 216–222.
2.   Dowell AR, Buckley E III, Cohen R, Whalen RE, Sieker HO, Durham NC. – Cheyne-Stokes respiration. *Arch Intern Med*, 1971, 127, 712–726.
3.   Harrison TR, King CE, Calhoun JA, Harrison WG. – Congestive heart failure. Cheyne-Stokes respiration as the cause of paroxysmal dyspnoea at the onset of sleep. *Arch Intern Med*, 1934, 53, 891–910.
4.   Loomis AL, Harvey EN, Hobart GA. – Cerebral states during sleep as studied by human brain potentials. *J Exp Psychol*, 1937, 21, 127–144.
5.   Rees PJ, Clark TJH. – Paroxysmal nocturnal dyspnoea and periodic respiration. *Lancet*, 1979, Dec 22/29, 1315–1317.
6.   Findley LJ, Zwillich CW, Ancoli-Israel S, Kripke D, Tisi G, Moser KM. – Cheyne-Stokes breathing during sleep in patients with left ventricular heart failure. *South Med J*, 1985, 78 (1), 11–15.
7.   Hanly PJ, Millar TW, Steljes DG, Baert R, Frais MA, Kryger MH. – Respiration and abnormal sleep in patients with congestive heart failure. *Chest*, 1989, 96, 480–488.
8.   Reite M, Jackson D, Cahoon RL, Weil JV. – Sleep physiology at high altitude. *Electroencephal Clin Neurophysiol*, 1975, 38, 463–471.
9.   Hanly PJ, Millar TW, Steljes DG, Baert R, Frais MA, Kryger MH. – The effect of oxygen on respiration and sleep in patients with congestive heart failure. *Ann Intern Med*, 1989, 111, 777–782.
10.   Berssenbrugge A, Dempsey J, Iber C, Skatrud J, Wilson P. – Mechanisms of hypoxia-induced periodic breathing during sleep in humans. *J Physiol*, 1983, 343, 507–524.
11.   Younes M. – The physiologic basis of central apnea and periodic breathing. *Curr Pulmonol*, 1989, 10, 265–326.
12.   Takasaki Y, Orr D, Popkin J, Rutherford R, Liu P, Bradley TD. – Effect of nasal continuous positive airway pressure on sleep apnea in congestive heart failure. *Am Rev Respir Dis*, 1989, 140, 1578–1584.
13.   Bonnet MH, Dexter JR, Arand DL. – The effect of triazolam on arousal and respiration in central sleep apnea patients. *Sleep*, 1990, 13 (1), 31–41.