LEADING ARTICLE

SLEEP AND BREATHING: THE PATHOPHYSIOLOGY OF SLEEP APNOEA

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We spend about a third of our lives asleep, yet the physiologic purpose of sleep still eludes us. The refreshing feeling we have after a good night's sleep is vaguely ascribed to the restorative function of sleep. Exactly what needs restoring and what is restored is unknown. Despite these uncertainties, breathing during sleep has been increasingly studied in the past 20 years, and a distinct syndrome of nocturnal recurrent apnoeas and daytime hypersomnolence (the sleep apnoea syndrome) is now widely recognised. The syndrome is defined, on the basis of polysomnography, as the presence of more than thirty apnoeas in a night's sleep. An apnoea is defined as cessation of breathing for at least t0 seconds.

The sleep apnoea syndrome may be classified as obstructive or central (there is a third type, called the mixed sleep apnoea syndrome, where the individual apnoeic spell has an initial central phase followed by an obstructive phase). In the obstructive syndrome, the commonest type, the apnoeas (not uncommonly several hundred episodes per night's sleep) occur despite continuing efforts to breathe due to periodic occlusion of the upper airway. As described previously (1), the patient makes increasing inspiratory efforts against a progressively narrowing upper airway (the preapnoeic snoring phase). When complete occlusion occurs, great inspiratory diaphragmatic activity, failing to draw air into the chest draws in the rib cage instead, resulting in paradoxical chest wall movements. The apnoea is terminated by electroencephalographic arousal which restores upper airway patency (2). The sudden upper airway opening in the face of enormous inspiratory efforts result in the characteristic loud inspiratory snort that marks the end of an apnoeic episode which may last for as long as one minute. During such an episode, the oxygen saturation falls (to as low as 50%), the pulmonary and systemic artery pressures rise (3) and various cardiac arrythmias may occur (4). Intuitively, we would assume that the daytime hypersomnolence in these patients is due to sleep deprivation (because sleep is interrupted several hundred times a night) but this is not certain (5). Also it would seem easy to understand why some patients have daytime carbon dioxide (CO2) retention and cor pulmonale (because of the often profound blood gas and pulmonary pressure derangements at night). Indeed the reversal of daytime abnormalities (eg cor pulmonale) by correction of the nocturnal events alone (eg by nocturnal nasal continuous positive airway pressure, NCPAP) (6) lends support to the notion that nocturnal events can upset daytime physiology. However, only a minority of patients have either CO2 retention or cor pulmonale (7) (= 12%). Bradley and coworkers (7) found that "sustained hypoxia and/or hypercapnia over a 24-hour period is a necessary prerequisite for the development of right heart failure in patients with obstructive sleep apnoea". They also found that mild diffuse airways obstruction predisposed to CO2 retention in these patients (8). This suggests that while neither nocturnal events nor mild airways obstruction results in CO2 retention, the combination of the two way.

Why does the upper airway occlude in obstructive sleep apnoea (OSA)? Occlusion may be active. Weitzman and coworkers (9) documented concentric narrowing (implying active muscle contraction) of the upper airway under direct fibreoptic bronchoscopic vision. This may plausibly result from swallowing activity during REM (rapid eye movement) sleep. But this mechanism is probably operative in the minority. Passive occlusion depends on airway transmural pressure and collapsibility of the upper airway. If the airway is already narrowed, greater inspiratory efforts are needed to maintain airflow. But these greater efforts themselves predispose to dynamic airway collapse (10). Thus OSA has been described in patients with anatomically compromised upper airways, eg tonsillar enlargement (1, 11), adenoidal hypertrophy (12), nasal obstruction (13, 14) macroglossia (15), and retrognathia (16). Even in the absence of upper airway pathology, patients with so-called idiopathic OSA have been found to have narrower upper airways than controls using special techniques (17, 18, t9).

The upper airway muscles are respiratory muscles and respond to chemical stimuli (hypercapnia (20) and hypoxia (21)) in a similar way that the diaphragm does. Thus the upper airway muscles contract phasically, during inspiration, stabilising the airway against inspiratory negative pressures generated by the diaphragm. It is conceivable therefore that if there is delayed or reduced activation of upper airway muscles relative to that of the diaphragm, the upper airway becomes vulnerable to col-

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lapse. Alcohol causes selective depression of genioglossal activation in humans (22). Alcohol has been known to convert a nonapnoeic snorer into an OSA snorer (23). Sedative drugs probably have a similar effect (24). There is evidence that the upper airway in patients with OSA are more collapsible than controls (25, 26). Thus upper airway anatomy, muscle function and collapsibility are factors to be considered in the pathogenesis of airway occlusion.

The usual explanation for the relative rarity of OSA in this region has been underrecongnition due to lack of awareness. The paper (in this issue of the journal) from Hong Kong expresses that view. If the prevalence of sleep apnoea is similar to that in the West, there would be at least several thousand patients (1-4% of 700,000 males > 20 years, 7000-28,000) in Singapore. Yet we (unpublished data) have detected only 10 cases in 2 years. Undoubtedly, increased awareness will increase the pickup rate of the disease. However, the other explanation, that sleep apnoea is indeed less common here than in the West, merits consideration. We speculated that the lower incidence of obesity locally may account for the relatively high rate of ENT (Ear nose throat) pathology in our patients. Implied is that locally, obesity, a common cause of the syndrome in the West, is not common, therefore sleep apnoea is not common. The less common causes of sleep apnoea viz ENT disease, then become prominent. An even more interesting speculation is that the functioning and reflexes of the upper airway muscles may be fundamentally different between Orientals and Caucasions. Upper airway muscles, which are used in phonation as well as in breathing, may be differently trained from childhood due to language differences. Since upper airway muscles play a crucial role in the pathogenesis of OSA, Oriental upper airway muscles may be in some way protect against airway collapse.

Central sleep apnoea (CSA) is uncommon. The apnoeas occur in the absence of detectable respiratory efforts. The pathophysiology is less well understood. Cherniack (27) proposed that this was an extreme form of periodic breathing due to shift of breathing control from CO2 drive to hypoxic drive. During slow wave sleep (SWS) the CO2 drive to ventilation is reduced. If this reduction is great, breathing becomes more influenced by the hypoxic drive. But the hypoxia-ventilation relationship is hyperbolic and therefore is prone to instability particularly at the bend of the curve. Further, while a stable arterial carbon dioxide tension (PCO2) is easier to maintain as the body is able to absorb transient fluctuations of CO2 production or elimination because of a large storge capacity, a stable PO2 is much harder to maintain, if hypoxia were the main controller of ventilation, because of small oxygen stores. Thus the damping effect on fluctuations is lost during hypoxic control. If this were the explanation, administering oxygen should abolish the periodic breathing that occurs in normal subjects. This was not the case. Phillipson (28) proposed that periodic breathing was due to different CO2 drives during wakefulness and light sleep. As sleep at onset alternates between light sleep and wakefulness (before SWS sleep is established), so the ventilatory drive fluctuates between that of light sleep and wakefulness resulting in cyclical breathing. Normal subjects break out of this oscillating sleep onset phase in 10 to 60 minutes and enter SWS. It has been suggested that patients with sleep apnoea are unable to break out of this phase and therefore apend the whole night at "sleep onset". Another explanation is delayed chemical feedback to the central chemoreceptors due to slow circulation time (27). This may cause the central apnoea that occurs in congestive cardiac failure (29).

The foregoing disscussion assumes the problem in CSA is central. But recent findings suggest that the cessation of central drive may be due to reflex inhibition from stimuli originating from a peripheral source. White DP and coworkers (30) found that upper airway anaesthesia caused central and obstructive apnoeic events during sleep. Issa and Sullivan successfully used NCPAP in patients with CSA (31). A study on sleeping dogs (32, 33) showed that laryngeal irritation during SWS caused reflex central apnoea. They speculated that this could be a cause of the sudden infant death syndrome,SIDS, (the ultimate apnoea!) as it is well known that gastro-oesophageal reflux occurs during sleep in infants. These findings suggest that breathing (at least during sleep) may be influenced by input from upper airway receptors, and that sleep induced quantitive or qualitative changes in these reflexes may be pathogenetically linked to apnoea.

We have discussed OSA and CSA as though they were separate entities. It has been argued that the two conditions may not be so disparate. Some have suggested that the difference between OSA and CSA is only in the degree of the upper airway versus the inspiratory muscle activation, ie in CSA upper airway and inspiratory muscle drives are both reduced whereas in OSA upper airway activation is selectively reduced (34). The finding by Sullivan that NCPAP is effective in treating both OSA (35) and CSA (31) implies a common underlying pathogenesis. He was able to convert central episodes to obstructive ones, obstructive episodes to snoring, and snoring to normal breathing in a particular patient depending on the level of NCPAP used (31). Also many patients have both obstructive and central apnoeic episodes within a night's sleep*. Finally, a patient with OSA may sometimes convert to CSA after tracheostomy (36). Thus, the pathophysiology of OSA and especially CSA is not fully understood yet, but with the amount of ongoing research in sleep, the picture should become clearer in the coming years.

Footnote:

*Each apnoeic spell is designated obstructive, central or mixed but each patient may have more than one type of apnoea in a single night's sleep. The patient is then labelled OSA, CA or mixed apnoea according to the predominant type.

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