OBSTRUCTIVE SLEEP APNOEA (OSA)

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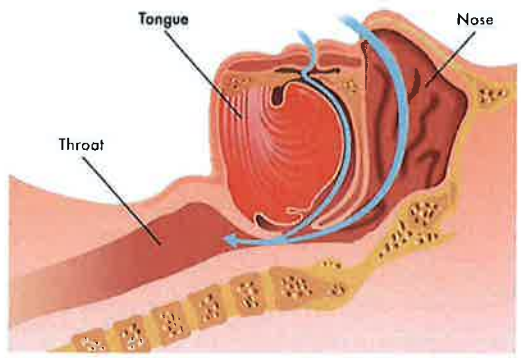
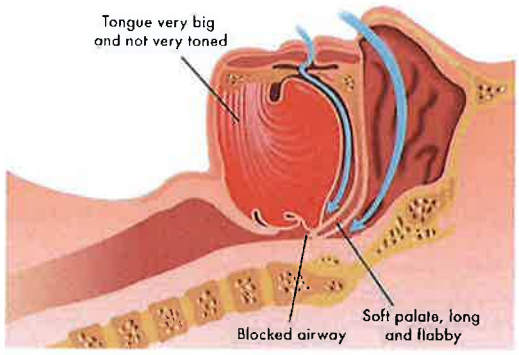


Normal breathing during sleep



Obstructive sleep apnea

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OSA is one of three types of sleep apnoea that is characterised by partial or complete blockage of the airway during sleep as the tongue and other soft tissues of the throat obstruct airflow. This cause's altered brain activity and complete or partial awakening with gasping, choking or snorting as the body tries to overcome the obstruction. Once a breath occurs the brain typically returns to sleep.

Causes of OSA can include:

- Physiological factors such as age (over 65), narrowed airways, short neck, hypertension, chronic nasal congestion, diabetes, asthma, a family history of OSA and gender. Men are two to three times as likely as women to have OSA
- Lifestyle factors such as alcohol, obesity and smoking.

OSA produces disrupted sleep patterns where the individual can rapidly cycle through stages 3 and 4 producing repeated occurrences of hypoxic (low blood oxygen), hypercapnic (high levels of blood CO2), and transient hypertensive episodes. This pattern makes normal restorative sleep impossible. Diagnosis of OSA is done with your medical practitioner who may refer you to an Ear, Nose and Throat specialist and/or a sleep specialist. It will include a thorough physical assessment and possibly an overnight sleep study (Polysomnogram). The Polysomnogram monitors heart, lung and brain activity, breathing patterns, arm and leg movements, and blood oxygen levels while you sleep.

The episodic OSA sleep pattern can produce changes in:

- Cerebral Pathophysiology and Cognitive functioning

Grey matter loss in multiple sites of the brain, including the frontal and parletal cortex, temporal lobe, anterior cingulate, hippocampus, and cerebellum. This occurs within sites involved in motor regulation of the upper airway as well as in areas contributing to cognitive function. This can suggest the early onset of physiological neural deficits and changes in short to long term memory processing.

OSA can produce severe daytime fatigue and drowsiness impeding concentration and the likelihood of falling asleep at work, watching TV or while driving.

- Cardiovascular

Sudden drops in blood oxygen levels produce increased cardiovascular effort which can lead to PAH, hypertension and is associated with an increased risk of coronary artery disease, arrhythmias, heart failure and stroke. If there is underlying cardiac disease these repeated hypoxic states can lead to cardiac arrest.

- Mental Health and Relationships

Depression, irritability and mood swings often characterise individuals with OSA. Children and young adults with OSA may do poorly in school and can exhibit attention and behavioural problems.

OSA's impact on relationships cannot be understated. The disruption the OSA patient's partner's sleep pattern often leads to them experiencing sleep deprivation and/or physically relocating to another room to sleep.

- Medications and Surgery

Medications such as sedatives, narcotics and those used in General Anaesthesia that relax the upper airway can worsen OSA and may increase the likelihood of complications after major surgery.

(Mayo Foundation for Medical Education and Research, 2018) (Eckhart, 2008, February 15) (Macey, et al., 2002)

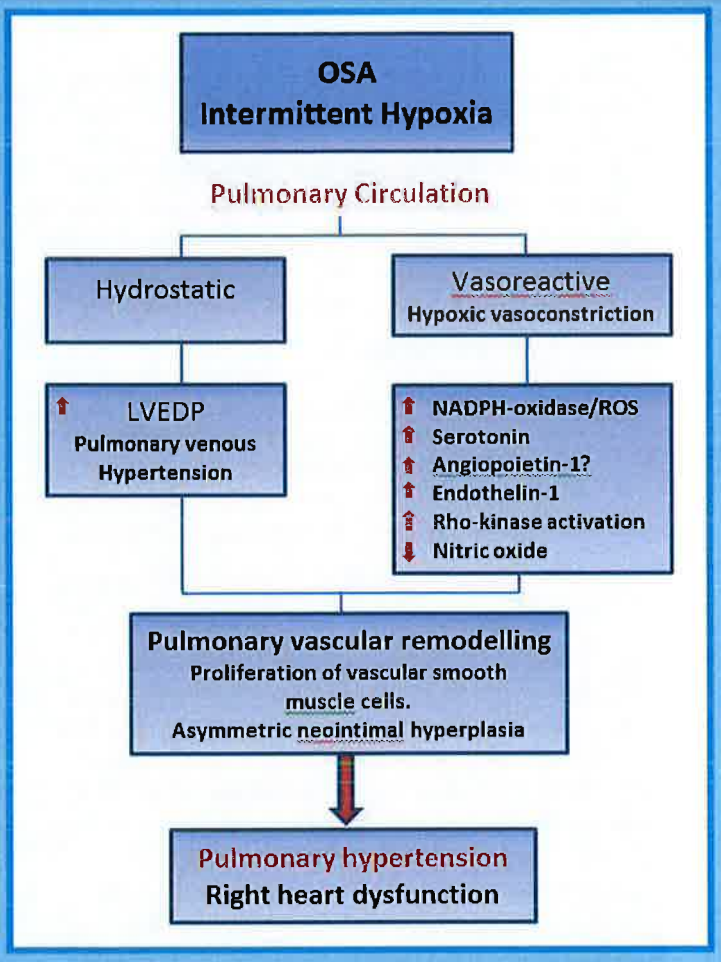

Figure 1: 'Obstructive sleep apnea (OSA) causes pulmonary hypertension through hypoxia pathways with activation of vasoactive factors and hydrostatic mechanism due to increase in left atrial pressure leading to pulmonary venous hypertension. Both pathways eventually cause vascular remodeling, pulmonary arterial hypertension, and right heart dysfunction. (LVEDP: left ventricular end-diastolic pressure; NADPH: nicotinamide adenine dinucleotide phosphate; ROS: reactive oxygen species).' (Kholdani, et al., 2015)

TWO SIDES OF THE COIN:

OSA with pulmonary hypertension and pulmonary hypertension with OSA

In normal sleep there is minimal impact between the sleep cycle and pulmonary haemodynamics but this relationship is dramatically altered during episodes of apnoea.

OSA with pulmonary hypertension.

Several studies have described significant increases in Pulmonary Arterial Pressure (PAP) from the middle of the OSA episode to the end. This reaches a maximum during the first few breaths once the obstruction is relieved (post apnoeic hyperventilation). These changes are more pronounced during rapid eye movement (REM) sleep than in non-REM sleep, and are felt to be related to acute changes in intrathoracic pressure, hypoxia, and reflex mechanisms. Repeated OSA episodes with attendant hypoxia can produce a sustained augmentation of the pressor response of the pulmonary arterial system, which escalates progressively during the night. It is possible that the marked oxygen desaturation in REM sleep augments progressive increases in PAP without time to recover to the baseline in the consecutive prolonged OSA episodes and with shortened inter OSA intervals. This produces pulmonary vascular changes and hypoxic vasoconstriction. (See Figure 1.)

There are many factors that may contribute to the development of PH subsequent to OSA and it is commonly associated with left ventricular dysfunction. Pulmonary vascular changes leading to PH are due to both hypoxic vasoconstriction and vascular remodeling. The research literature suggests that the more severe the PH is the better the response to treatment by continuous positive airway pressure (CPAP) treatment. In this scenario PH tends to improve but may not totally resolve with the treatment of the OSA. (Sajkov, 2009) (Khalid, et al., 2015) (Chua, 2009) (Kholdani, et al., 2015)

PULMONARY HYPERTENSION WITH OSA

The other side of the coin! Whilst there is good evidence linking OSA leading or contributing to Pulmonary Hypertension (PH) the reverse is not so clear cut nor well documented.

Currently, the treatment paradigm for newly diagnosed PAH patients often includes evaluation for OSA with a Polysomnogram (overnight sleep study). A Clinical Trial in the USA looked for a link between PAH's associated fluid retention and OSA. The investigators proposed that untreated or sub-optimally managed PAH patients have significant fluid retention which redistributes to the upper body during sleep and exacerbates or even mimics OSA. The investigators hypothesized that treatment of PAH patients with vasodilators and diuretics to optimize fluid balance would attenuate or even resolve OSA prior to the initiation of specific therapy for OSA (CPAP). Unfortunately the trial was terminated early

due to insufficient participant recruitment so there was no conclusive outcome. (NIH US National Library of Medicine, 2014)

The American College of Chest Physicians (2004) reported that 17% to 53% of people with OSA had pulmonary hypertension, whilst a review by John Hopkins Medicine (2015) found that 82% of PAH patients had an underlying sleep disorder. From the literature whether PAH leads to OSA; contributes to it or exacerbates it has yet to be conclusively proved.

What does stand out is that PAH physiological changes lead to alterations in sleep patterns and this may lead to, or exacerbate sleep disorders such as OSA. Depending on your Functional Class the level of physical and respiratory symptoms and accompanying sleep alterations will vary. It is worthwhile familiarising yourself with the WHO Functional Classes (4 different classes Refer back to Directors report) so you are more fully informed when talking to your physicians and therapists about your treatment regime and options.

Assigning a functional class helps the PH healthcare team to understand how the patient is affected by their condition. A goal of PH treatment is to make everyday living easier, so it is very important to have an accurate picture of how PH is affecting a patient's daily life including their sleep patterns.

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