“Each night, when I go to sleep, I die. And the next morning, when I wake up, I am reborn.”
— Mahatma Gandhi

Humans spend approximately one third of their lives asleep. Although generally considered to be a peaceful, stable period for the body and mind to rest and heal, sleep in fact represents a complex, dynamic process involving dramatic changes in physiological state. Sleep-related cardiac arrhythmias are very common and often diagnosed incidentally on Holter monitor; the vast majority are benign but, nevertheless, up to 15% of sudden arrhythmic deaths occur during sleep and therefore an understanding of normal and abnormal findings is essential.

**Normal Cardiovascular Physiology during Sleep**

Sleep is conventionally divided into rapid eye movement (REM) and non-rapid eye movement (non-REM) stages, each of which is associated with characteristic patterns of autonomic control of the heart.

Non-REM stages account for approximately 80% of sleep\(^1\). During this time there is a profound reduction in sympathetic neuronal firing rate to around 50% of waking levels, causing vasomotor relaxation and hypotension. Increased dominance of vagal nerve influence results in the characteristic sinusoidal heart rate profile of sinus arrhythmia, in which bradycardia alternates with a few seconds of relative tachycardia to compensate for increased venous return during inspiration.

REM sleep episodes occur approximately every 90 minutes and are associated with the majority of dream activity. Increased brain excitability disrupts the stable autonomic state of non-REM sleep, triggering short bursts of sympathetic neuronal activity that can exceed that of the waking state. This results in irregular periods of dramatic hypertension and tachycardia, often associated with disruption of the regular breathing pattern of non-REM sleep.

**‘Benign’ Bradycardia during Sleep**

Many studies have demonstrated a high prevalence of bradyarrhythmias during non-REM sleep in young, healthy individuals. In a cohort of 50 male medical students\(^2\), a quarter had episodes of bradycardia (<40 bpm), while 68% had sinus pauses of >1.5s and a significant proportion had evidence of AV node conduction delay (see table). In asymptomatic individuals, these findings are of no prognostic significance and warrant no further investigation; the management consists largely of reassuring the patient (and referring physician).
Healthy individuals demonstrate an age-related increase in resting heart rate with relative loss of the normal respiratory sinus arrhythmia. In healthy individuals over the age of 60, sinus pauses and nocturnal Wenckebach are uncommon and should precipitate a thorough search for intrinsic conduction system disease. Current guidelines for pacemaker implantation should apply for advanced AV node disease (3rd degree, or infra-His type 2b) or symptomatic sinus node dysfunction. Correlation with symptoms can be particularly difficult with pauses during sleep; where there is a suspicion of syncopal episodes, empirical pacemaker implantation may be appropriate in the presence of prolonged sinus pauses (>6 seconds) even where correlation has not been demonstrated.

Table 1: Frequency of bradyarrhythmias in healthy individuals, from Adlakha and Shepard (1998)

<table>
<thead>
<tr>
<th>Study</th>
<th>Brodsky et al</th>
<th>Sabotka et al</th>
<th>Fleg and Kennedy</th>
<th>Kantelip et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>50</td>
<td>50</td>
<td>98</td>
<td>50</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>23 - 27</td>
<td>22 - 28</td>
<td>60 – 85</td>
<td>80 – 100</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>50:0</td>
<td>0:50</td>
<td>69:29</td>
<td>6:44</td>
</tr>
<tr>
<td>Bradycardia &lt;40bpm</td>
<td>24%</td>
<td>8%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Sinus pauses &gt; 1.5s</td>
<td>68%</td>
<td>36%</td>
<td>2%</td>
<td>12%</td>
</tr>
<tr>
<td>1st Degree AV block</td>
<td>8%</td>
<td>12%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wenckebach AV block</td>
<td>6%</td>
<td>4%</td>
<td>1%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Profound bradycardic episodes and impressive pauses can occur, albeit less commonly, as a result of intense bursts of vagal nerve activity. These typically occur during REM sleep, and can result in prolonged (>6 seconds) sinus node arrest, or episodes of apparent high degree atrioventricular block (often preceded by sinus rate slowing and/or AV prolongation). These phenomena may occur in athletically-trained individuals with slow resting heart rates, in whom invasive EP studies typically demonstrate normal SA node and AV node function. It has also been suggested that some individuals may exhibit abnormal autonomic balance during REM sleep, with sudden episodic withdrawal of sympathetic activity resulting in bradycardia exclusively during these stages. Although current ESC guidelines do not recommend pacemaker implantation for either sinus pauses or vagally-mediated AV block in the absence of symptoms, some authors advocate consideration of pacemaker implantation where AV pseudoblock is associated with very long pauses to reduce the risk of associated ventricular arrhythmias, particularly where there are concurrent repolarisation abnormalities due to drug-induced or genetic long QT syndromes.
**Ventricular Arrhythmias**

The shift towards a parasympathetic-dominant control during non-REM sleep appears to have a protective effect against ventricular arrhythmias; typically there is suppression of premature ventricular ectopic beats in healthy individuals\(^1\). However, approximately 15% of sudden arrhythmic deaths occur during sleep, and studies of ICD discharges demonstrate a non-uniform nocturnal distribution with peaks in the early hours corresponding with increasing sympathetic activity\(^2\). Conditions including heart failure, ischaemia and hypertensive heart disease are associated with impairment of the normal sympathetic withdrawal during sleep; this may manifest as an increase in nocturnal ventricular ectopic beats, coinciding with catecholaminergic surges that may reach 250% of waking levels. Furthermore, vagally-induced hypotension can exacerbate ischaemia across critical stenotic lesions, which combined with episodic hypoxaemia due to apnoeic breathing (see below) may provide a rich pro-arrhythmic substrate.

Nocturnal changes in vagal nerve tone have also been suggested as a likely mechanism for the striking pattern of sudden nocturnal death seen in Brugada syndrome. Current guidelines recommend ICD implantation either where there is a documented ventricular arrhythmia, or previous syncope with a spontaneous Type I ECG.

**Obstructive Sleep Apnoea**

Obstructive Sleep Apnoea (OSA) may be associated with multiple arrhythmias including sinus arrest, high degree AV block, and non-sustained VT (table 2). Although there does not appear to be a significant association with sustained VT or ICD discharges, there is a sharp peak in nocturnal sudden death and myocardial infarction amongst patients with the condition\(^3\), coinciding with a characteristic pattern of Cyclical Variation in Heart Rate (CVHR). Hypoxaemia during apnoeic episodes causes progressive bradycardia, followed by tachycardic surges as breathing resumes with partial awakening and withdrawal of vagal tone. Analogous to repetitive episodes of ischaemia/reperfusion, this occurs at a far slower cycle length than normal sinus arrhythmia (minutes rather than seconds) and where observed should precipitate close questioning for symptoms including drowsiness, morning headaches and snoring.

Table 2: Frequency of arrhythmias in 400 patients with OSA (from Guilleminault et al, 1983\(^4\))

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Bradycardia &lt;30 bpm</td>
<td>11%</td>
</tr>
<tr>
<td>Sinus pauses (2 – 13 seconds)</td>
<td>11%</td>
</tr>
<tr>
<td>Wenckebach AV block</td>
<td>8%</td>
</tr>
<tr>
<td>Frequent ventricular ectopy</td>
<td>20%</td>
</tr>
<tr>
<td>VT</td>
<td>3%</td>
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</table>

The gold standard investigation for OSA remains overnight sleep study, including continuous
monitoring of ECG, EEG and oxygen saturations. Although 24 hour Holter monitoring has been suggested as a screening tool, as yet attempts to develop criteria with adequate sensitivity and specificity have been disappointing. Interestingly, the minute ventilation sensors incorporated within certain standard DDDR pacemakers are capable of outputting a thoracic impedance signal which mirrors very closely the findings of formal sleep studies\textsuperscript{15}. Recently Sorin have released a model which alerts the physician to abnormal overnight breathing patterns\textsuperscript{16}, although at present there are no large-scale studies to support this strategy in the conventional pacemaker population.

In addition to improving daytime sleepiness, treatment with continuous positive airway pressure ventilation (CPAP) has been demonstrated to reduce the risk of arrhythmias and substantially reduce the need for cardiac pacing\textsuperscript{17}. Initially promising results in studies of high rate atrial pacing\textsuperscript{18} have not been confirmed in a meta-analysis which showed minimal benefit in reducing sleep apnoea symptoms\textsuperscript{19}.

Heart Failure

Approximately 20\% of heart failure-related deaths occur at night, and around 50\% of patients with heart failure have some form of sleep-related breathing disorders\textsuperscript{20}. Although OSA is prevalent (reaching around 30\% in some studies\textsuperscript{21}), heart failure is also associated with a characteristic pattern of central sleep apnoea (CSA) known as Cheyne Stokes Breathing. This takes the form of a crescendo-decrescendo ventilation pattern, in which breathing progressively speeds then slows to complete cessation over the course of a few minutes. Associated with sometimes dramatic changes in blood PO2 and PCO2 levels, this can precipitate significant bradyarrhythmias and tachyarrhythmias and has been identified as a very strong adverse prognostic marker in otherwise stable heart failure patients\textsuperscript{22}. In contrast with OSA, heart failure-related CSA does not respond to conventional CPAP\textsuperscript{23}; however, adaptive servoventilation (ASV) is a novel ventilatory therapy that provides support only during apnoea. This appears to be very effective in reducing the frequency of apnoeic episodes\textsuperscript{24}, and a recent large registry study\textsuperscript{25} demonstrated a significant reduction in associated ICD discharge rates, possibly by stabilising the neurohumoral dysregulation that occurs during these episodes. In addition, small pilot studies suggest that biventricular pacing does appear to have at least a modest benefit in improving sleepiness symptoms from both CSA\textsuperscript{26} and OSA\textsuperscript{27} in heart failure.

Conclusions

- Arrhythmias during sleep are very common, reflecting complex and dynamic changes in autonomic state.
- Even long pauses during sleep are unlikely to cause symptoms, and guidelines at present do not generally recommend pacemaker implantation.
- The prevalence of benign nocturnal bradycardias declines with age. Nocturnal pauses in the elderly are more likely to be due to intrinsic conduction system disease and standard pacemaker guidelines should apply.
- Ventricular ectopy is normally suppressed at night. Comorbidities including heart failure, hypertension and ischaemia may manifest as an increase in nocturnal ventricular ectopy.
- Obstructive Sleep Apnoea (OSA) is commonly associated with bradycardia and, to a lesser extent, VT. There should be a high index of suspicion in obese patients or those with daytime sleepiness as appropriate CPAP treatment may prevent the need for pacing.
- Sleep disturbances are common with heart failure and are associated arrhythmic risk and poor prognosis, although optimal therapy remains to be established.

3 Adiakha A, Shepard JW “Cardiac arrhythmias during normal sleep and in obstructive sleep apnea syndrome” Sleep Medicine Reviews 1998; 2, 45-60
7 Siebermair J, Pohl T, et al. “22-year-old athlete with sinus arrest and pauses to 7 seconds” Der Internist 2012, 53.2; 218-222 (German)
9 Serafinia A, Dolsoa P "REM sleep brady-arrhythmias: An indication to pacemaker implantation?" Sleep Medicine 13.6: 759–762
10 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Developed in collaboration with the European Heart Rhythm Association (EHRA). doi:10.1093/eurheartj/eht150
16 Evaluation of the Performances of the Sleep Disordered Breathing Monitoring Function in Pacemaker (DREAM); study registered by Sorin Group Feb 2012. ClinicalTrials.gov Identifier: NCT01537718
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26 Sinha AM, Skobel EC “Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure” J Am Coll Cardiol 2004, 44; 68–71