Ian Wilcox, MD, PhD, FRACP, FCCP, is a Clinical Associate Professor in the Department of Medicine at the University of Sydney Australia, and a Senior Research Associate at the Woolcock Institute. He currently works as a Cardiologist at Royal Prince Alfred Hospital, Sydney and is Chairman of the Department of Medicine at Strathfield Private Hospital.

In this interview he discusses the relationship between congestive heart failure (CHF) and sleep-disordered breathing (SDB).

1. What is CHF?
CHF is a syndrome, not a single disease, and has many causes. It occurs when heart disease leads to a generalized weakening of heart muscle, which leads to reduced blood flow to the organs and tissues of the body. The inadequate blood flow results in a series of neurohormonal and physiological compensatory responses that cause fluid build-up (edema) in tissues throughout the body. This fluid build-up, or congestion, led to the term congestive heart failure (CHF).

CHF is a serious and life-shortening condition, with a wide variety of symptoms. These include tiredness, worsening effort tolerance associated with increased breathlessness (dyspnea), muscle fatigue, and peripheral edema. Patients also commonly experience breathlessness when lying flat in bed (orthopnea) or interrupted and fragmented sleep, paroxysmal nocturnal dyspnea (PND), a form of central sleep apnea, from which they awake gasping for breath.

2. What causes CHF?
Heart failure is usually the result of coronary artery disease, high blood pressure, or diseases of the heart's valves or muscle (cardiomyopathy). Heart failure occurs when compensatory mechanisms can no longer maintain adequate blood flow to all tissues and organ systems in all circumstances.

3. Are there different types of CHF?
CHF can be broken into two broad types - systolic heart failure (reduced contraction of the heart) and diastolic heart failure (reduced relaxation of the heart). Diseases that damage the myocardium affect systolic and diastolic function differently. For example, in hypertension, diastolic function becomes abnormal early on, but later in the course, systolic dysfunction also develops.

4. What is the prognosis of CHF sufferers?
The rate of disease progression varies. While the disorder generally deteriorates relentlessly, in 10-20% of patients, particularly younger patients and those with a more acute onset, it can improve spontaneously. Even with improved medical therapy the overall prognosis is poor and similar to other serious illnesses such as cancer. The New York Heart Association (NYHA) classification is a well accepted grading of CHF. It is based on symptoms of breathlessness, varying from class I, when there are no limitations during daily life, through to class IV, when patients have symptoms at rest and are not able to exert themselves without being breathless. Patients with class IV heart failure may have 50% mortality in 12 months.

5. What are some of the current methods of treatment and how effective are they?
The first principle of treatment is to diagnose the cause of CHF, as this will guide treatment. For example, coronary heart disease and valvular heart disease are well-known, potentially correctable causes of CHF. The aim of treatment is to improve symptoms, quality of life, and survival. The two main causes of death in patients with CHF are progressive heart failure and sudden death—the latter usually due to ventricular tachycardia or fibrillation (overly rapid heart rate).
We had an overwhelming response to the first issue of ResMedica, our clinical newsletter, which many of you found informative and useful. Thank you for your enthusiasm, positive feedback, and general suggestions.

We have received numerous stories from around the world and unfortunately we could not publish all of them in this edition. We have therefore decided to release a “special” edition of ResMedica in the new year, concentrating on the treatment of Cheyne-Stokes respiration (CSR) and central sleep apnea in patients with congestive heart failure (CHF) using adaptive servo-ventilation. We have plans to release the latest data which shows the effectiveness of this new form of treatment in CHF sufferers. Naturally we will do our best to bring you an interview with a prominent physician on the subject.

Special thanks to Dr. Winfried Randerath from Germany, for submitting a very interesting article comparing the effectiveness of adaptive servo-ventilation with that of standard continuous positive airway pressure (CPAP) therapy in patients with CSR due to heart failure. This article will be published in the special edition of ResMedica, so watch this space!

If you would like to send us a story, case study, interesting article, or further suggestions on this subject for our “special issue,” I encourage you to do so.

This issue of ResMedica concentrates on the diagnosis of CHF and CSR.

We are delighted to bring you an interview with Dr. Ian Wilcox, who has worked widely in this field.

We’ve included an interesting case study from the US, which describes a patient’s significant improvement in all measured cardiac outcomes, following eight months of CPAP treatment.

There are also some useful facts and figures about CHF as well as our regular updates on upcoming events, interesting websites, and pertinent abstracts.

We hope you find this second issue of ResMedica valuable. ResMedica is published twice a year, so keep watch for our regular editions, where we will turn the spotlight on Non-invasive Positive Pressure Ventilation (NPPV) and women and SDB.

Please be sure to send us your feedback or suggestions via our email address clinicalnews@resmed.com.au

Lisa MacKenzie
International Clinical Application Specialist
Editor
Congestive heart failure (CHF) is a clinical condition in which the heart is unable to supply the body with enough oxygen-rich blood to accommodate the body’s needs during exercise and at rest. As a result of the decreased cardiac function, body fluids may accumulate in the lungs and peripheral vascular space. The most common cause of CHF is ischemic heart disease. Other causes of CHF include hypertension, myocarditis, valvular disease, and idiopathic etiologies. Patients with CHF typically have cardiomegaly (enlarged heart). Symptoms of CHF include dyspnea, shortness of breath, orthopnea, rales, and peripheral and pulmonary edema.

Natriuretic peptides are a family of hormones that function to regulate blood pressure, electrolyte balance, and fluid volume. B-type (B = brain) natriuretic peptide (BNP) is a 32 amino acid hormone that is synthesized in the ventricles. This is released in patients with hypertension, volume overload and hyponatremia.

High concentrations of BNP in the blood produce sodium retention and vasodilation by suppressing renin and aldosterone release, which reverses the effects of hypotension.

BNP is stable in whole blood and a portable 15 minute assay has been developed for measuring BNP in blood samples. BNP levels are elevated in patients with CHF.

BNP is used as a marker for diagnosis and staging of the disease. Quantitative measurement of BNP in blood provides an objective indicator of CHF disease severity. The New York Heart Association (NYHA) classification index helps to classify the disease into 4 stages.

Within a NYHA stage, the mean and median concentrations progressively increase from stage I to IV. In a multi-centre trial BNP concentrations pg/ml were:

Stage I = 71
Stage II = 204
Stage III = 349
Stage IV = 1022

BNP helps to determine the success of treatment. The level of BNP should be significantly reduced as an indication that the treatment is progressing successfully.

Excerpts from Wu A. H. B-Type natriuretic peptide and its clinical utility in patients with heart failure.

New York Heart Association classification of congestive heart failure:¹

<table>
<thead>
<tr>
<th>Class</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Cardiac disease, but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.</td>
</tr>
<tr>
<td>II</td>
<td>Cardiac disease resulting in slight limitation of physical activity. The patient is comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain.</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity. The patient is comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.</td>
</tr>
<tr>
<td>IV</td>
<td>Cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart disease or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.</td>
</tr>
</tbody>
</table>

Pathophysiology of the reninangiotensin-aldosterone axis and the natriuretic peptide axis.⁴

High Arterial Blood Pressure

- ANP/BNP release
- Vasoconstriction

Sodium/water loss
- Sodium/water retention

Vasodilation
- Renin/aldosterone release

Low arterial blood pressure

References:
fact and figures

The American Heart Association statistics for 2002 report: Based on the 44 year follow-up of the National Heart, Lung and Blood Institute’s (NHLBI) Framingham Heart Study:

- In the US, it is estimated that there are 550,000 new cases of CHF per annum with around 4,800,000 Americans (2,360,000 males and 2,440,000 females) currently diagnosed as having congestive heart failure (CHF).
- The incidence of CHF approaches ten per 1,000 population (1%) after age 65 (2002 Heart & Stroke Statistical Update, American Heart Association) and is the most common diagnosis in hospital patients aged over 65 years (National Heart, Lung & Blood Institute CHF Fact Sheet, 1996).
- CHF patients are believed to have a 5-year mortality of around 50% (National Heart, Lung & Blood Institute CHF Fact Sheet, 1996) with roughly 20% dying in the first year (2002 Heart & Stroke Statistical Update, American Heart Association).
- 75% of CHF cases have antecedent hypertension.
- Myocardial infarction will disable 22% males and 46% females within 6 years.
- 80% of men and 70% of women under the age of 65 with CHF will die within 8 years.
- After CHF is diagnosed, survival is poorer in men than in women, but fewer than 15% of women survive more than 8-12 years. Their one-year mortality rate is higher with one in five dying.
- In people diagnosed with CHF, sudden cardiac death occurs at six-nine times the rate of the general population.
- In 1993 the cost of care for CHF patients was estimated at 17.8 Billion dollars US (National Heart, Lung & Blood Institute CHF Fact Sheet, 1996).
- From 1979 to 1999, CHF deaths increased by 145%.

French statistics furnished from the Programme Médicalisé des Systemmes d’information and Service des études et des sytèmes d’information du Ministère de la Santé.

- In France it is estimated that there are > 500,000 people with CHF and 120,000 new cases per year (population 60,000,000).
- The incidence of CHF is estimated to be 1% for people 50-60 years old and up to 10% >80 years old.
- Hospital costs per year for heart failure are estimated to be between 700-900 million Euros/year.

It is important to start treatment with simple general measures such as avoiding alcohol and reducing salt intake. Regular isometric exercise is also encouraged, as it is invaluable in improving exercise capacity in these patients.

Hypertension is a common cause of both diastolic and systolic heart failure. Therefore, lowering blood pressure is critically important in all patients with CHF and forms one of the key modes of treatment. This helps to reduce the afterload (resistance) against which the heart ejects blood.

Drugs that block production of angiotensin (angiotensin converting enzyme or ACE inhibitors) or drugs that block angiotensin receptors have major benefits in delaying the progression of CHF and improving symptoms. These drugs increase afterload. The use of Beta Blockers has been a major advance in heart failure treatment with proven benefits in improving left ventricular (LV) function and quality of life for patients with CHF.

Drugs such as diuretics, digoxin and nitrates are mainly used to treat symptoms of heart failure and do not improve LV function or prognosis.

Devices such as pacemakers designed to resynchronize the heart’s contraction sequence and automatic cardioverters/defibrillators (AICDs) are of benefit in improving symptoms and survival in CHF. However the indications for these expensive devices are still being defined in the general population with CHF.

Currently the only ‘cure’ for CHF is a heart transplant with a lifetime of anti-rejection drugs. However, research is being conducted into gene therapies and implantable mechanical devices such as Left Ventricular Assist Devices (LVAD) and these may provide alternatives in the future.

The benefits of continuous positive airway pressure (CPAP) in CHF have been known since the 1930s. CPAP has been proved to be effective in the treatment of acute pulmonary edema. It improves oxygenation by improving gas exchange and reducing the work of breathing. It is also known to improve cardiac output. The use of CPAP and other similar devices in chronic CHF is still being defined. Patients with a combination of OSA and CHF clearly need CPAP treatment.

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Treating patients with predominantly central sleep apnea (CSA) in CHF is possible with CPAP, low flow oxygen without sedation.

Cheyn Sorensen syndrome with n positive CSA has a major impact on the patient's quality of life. The patient with CSA may have daytime somnolence, Orthostatic Hypotension, and OSA with CSA is associated with a reduced exercise capacity in these patients.

When the patient is on the ventilator, treatments for CSA become more effective. Pneumonia and central hyperventilation syndrome improve with CPAP treatment. The patient's sleep quality improves with CPAP treatment. This helps the patient to maintain a regular sleep pattern. The use of CPAP and other similar devices in chronic CHF is still being defined. Patients with a combination of OSA and CHF clearly need CPAP treatment.

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6. What is Cheyne-Stokes Respiration?

Cheyne-Stokes Respiration (CSR) is a cyclical breathing pattern, involving waxing and waning or crescendo and decrescendo breathing amplitude with relatively stable respiratory rate. This may or may not be associated with central apneas during which no respiratory effort occurs. CSR occurs first during sleep but, in its severest form, it occurs in awake patients and is well known to be an indicator of a poorer prognosis.

7. What is the prevalence of SDB in CHF patients?

The prevalence and type of SDB in CHF depends on the patient population. CSR is common in CHF patients. Traditional teaching has been that CSR and CSA occur in end-stage patients with CHF but we now know this is not the case. At least half of all patients with medically stabilized heart failure have SDB and, according to most published studies, the majority of these will have CSA rather than OSA. When you look at unstable or acutely ill patients, the proportion will increase to about 70%.

Current thinking suggests that OSA predominates in NYHA class I & II (see page 7 New York Association classification of CHF) patients with CSR being exhibited in the sicker patients of NYHA classes III & IV. In heart failure patients, the type of sleep apnea is often mixed, with a predominance of one type. Pure examples of OSA and CSR are less common. In our own studies, we have used a simple pragmatic 75% cut off to define apnea type, so I think of predominant OSA and predominant CSA in CHF.

It seems likely that the proportion of CHF patients with OSA has been significantly underestimated in previous studies because of the way patients were selected. Certainly, the prevalence of SDB in CHF means that a case can be made for performing some form of SDB screening study on all patients with CHF.

8. What is the mechanism by which CHF patients might develop CSR?

The precise mechanism by which a CHF patient might develop CSR is still unknown. We have developed a better understanding of factors which influence this from studies at different altitude of people with and without CHF.

In order to control breathing accurately, the respiratory control centers in the brainstem need to be able to promptly sense, and respond to, changes in arterial carbon dioxide and oxygen levels. In heart failure, reduced circulation time causes a delay between the changes in blood gases, (which occur with changes in breathing amplitude) and the chemoreceptors in the brainstem in particular. Clearly not all patients with CHF will develop CSA and not all patients with CSR have severely prolonged circulation time. Therefore other factors are involved.

Carbon dioxide CO\textsubscript{2} levels are critically important in the control of breathing. Hypocapnea (low CO\textsubscript{2}) inhibits breathing to the extent of causing apnea at a threshold value ("apnea threshold") in some patients during sleep. Thus, hypocapnea promotes central apnea. In the setting of CHF, changes in CO\textsubscript{2} in the blood take longer to reach the brainstem, making control of breathing more unstable. While in amplitude waxes and wanes CSR breathing, average minute ventilation is increased and therefore average CO\textsubscript{2} levels fall. Factors promoting hyperventilation include an individual's natural level of chemoreceptor responsiveness, well known to vary substantially between individuals, and pulmonary congestion causing hyperventilation by stimulating J receptors in the lungs, increasing minute ventilation. It is well recognized that lung water is increased in patients with CHF even when they are apparently optimally treated with drug therapy.

9. Is CSR found exclusively in patients with CHF?

No, CSR is found in patients with stroke too. The patient described in Cheyne's original report had a history of CHF and a prior stroke.

Continued on page 6
10. What physiological impact does CSR have on the patient?

In CHF the work of breathing is increased because of lung congestion. This increased work may worsen heart failure, as respiratory muscles require greater blood flow while cardiac output is reduced at the same time. Patients with CSA/CSR are also hyperventilating, even at rest, so the work of breathing is increased further.

Sleepiness occurs because there are numerous arousals. The arousals from sleep occur towards the peak of post-apneic hyperventilation. These arousals are associated with increased output of adrenaline, which places stress on the myocardium and results in arrhythmias and increased afterload.

In severe cases, several hundred of these episodes may occur in a single night with each episode causing stress to the heart at a time when it is receiving the smallest amount of oxygen. Fragmented sleep also affects daytime symptoms and quality of life in CHF. This is particularly relevant clinically since improving quality of life is a major goal of the medical management of patients with CHF.

CSA/CSR identifies a group of patients with CHF who tend to have worse left ventricular function, poorer functional status and poorer survival. The changes in blood gases with hypocapnea and hypoxia are probably important also and may, for example, promote cardiac arrhythmias, such as atrial fibrillation and high-grade ventricular arrhythmias.

11. Is SDB being treated in CHF patient groups and if so, how is it treated?

SDB in patients with CHF is still largely unrecognized as the symptoms of fatigue, tiredness and sleepiness may overlap with those of CHF or its treatment, leaving many of these patients with undiagnosed SDB.

A cardinal symptom of CSA/CSR in CHF is paroxysmal nocturnal dyspnea. This differs from post-apneic arousals in OSA patients without heart failure, in that the patient will classically describe the need to sit up or actually get out of bed when it occurs. Although this symptom indicates the patient has CSA/CSR, its absence does not exclude the possibility of SDB in a patient with CHF.

Identifying and treating SDB in patients with CHF has not become part of standard medical practice despite the accumulated evidence base. However, that situation is highly likely to change given increasing patient and physician awareness of these breathing disorders and the availability of methods to diagnose and treat them.

Fixed or variable CPAP devices are being increasingly used by cardiologists. Emergency Room physicians are treating acute pulmonary edema with positive airway pressure (PAP) devices. So the changing paradigm of CHF treatment increasingly includes this type of therapy.

Low oxygen levels (hypoxia) appear to act as an amplifier rather than being of primary importance. When supplemental O₂ is given to patients with CSA/CSR it improves by approximately 50% but does not eliminate it. Adding CO₂ to supplemental O₂ improves CSA/CSR substantially but at the expense of increased sympathetic stimulation and is likely to affect patients with CHF adversely.

12. How does CPAP benefit the heart?

CPAP appears to benefit the heart in several ways. Positive airway pressure increases intrathoracic pressure and, in doing so, reduces the work the heart has to do to eject blood, i.e. it reduces left ventricular (LV) transmural pressure and therefore LV afterload. In heart failure the left ventricle dilates; this may cause mitral regurgitation, which further worsens heart function. The use of CPAP has been shown to reduce the degree of mitral regurgitation in patients with CHF.

New, exciting data on adaptive servo-ventilation is proving to be very effective in treating CHF sufferers.
What is Adaptive Servo-Ventilation?

The device has a unique ventilation algorithm specifically designed for congestive heart failure (CHF) patients. AutoSet CS sets a target ventilation equal to 90% of the patients recent average ventilation (time constant of three minutes). This continuously updated target is the "adaptive" part of "adaptive servo-ventilation".

The AutoSet CS is capable of delivering varying amounts of ventilatory support on a breath-by-breath basis. In the steady state (once CSR/CSA has been brought under control) the AutoSet CS delivers 3cmH₂O pressure support, using a smooth and comfortable waveform, superimposed on 5cmH₂O positive pressure. The small amount of positive pressure support helps reduce dyspnea, excessive preload, and pulmonary congestion/edema.

If the patient starts to enter a central apnea or hypopnea, the degree of support is very rapidly increased, over a few breaths, until the breathing is stabilized (or up to a default maximum of 10cmH₂O). If the patient enters another hyperpnea or resumes normal breathing, the degree of support is reduced over 3-4 breaths, further helping to stabilize breathing. This is the "servo-ventilation" part of adaptive servo-ventilation.

Once breathing is stabilized, AutoSet CS very gradually reduces the degree of support back towards the comfortable minimum support of 3cmH₂O, reducing the likelihood of over-ventilation. This is important, as over-ventilation and hypocapnea lead to vocal cord closure and further apneas.

Watch out for our "Special Edition" of ResMedica, devoted to adaptive servo-ventilation.

Adaptive servo-ventilation at work

AutoSet CS at work

Upper trace shows patient breathing. Middle trace shows AutoSet CS pressure delivery. When AutoSet CS therapy ceases, patient returns to CSR or periodic breathing.
At the meeting of the American Thoracic Society in May, thirteen studies were presented that examined congestive heart failure (CHF) with sleep-disordered breathing (SDB). Four of the presentations examined SDB in relation to CHF and nine evaluated the effect of different treatment modalities on SDB in CHF.

**SDB with CHF**

There was a mini-symposium on the treatment of SDB in heart failure. A study by Jobin et al examined the patency of the upper airway during Cheyne-Stokes Respiration (CSR) using the forced oscillation technique. They found that marked increases indicative of significant airway narrowing were common during central CSR apneas and hypopneas. These increases occurred most often in the middle or toward the end of events. Their findings indicate that upper airway narrowing is common during CSR events. This seems likely to contribute to the interaction between obstructive sleep apnea (OSA) and CSR in CHF patients.

The other study of interest presented at the mini-symposium examined whether central sleep apnea (CSA) in patients with CHF can be alleviated either by optimizing medical therapy or by heart transplant (Mansfield et al). Left ventricular ejection fraction, overnight norephedrine, and respiratory pattern during sleep were monitored in a group of 13 patients with CSA and CHF before, and six months beyond, heart transplant. After transplant, three patients continued to have CSA and four had developed OSA. This led to the conclusion that heart transplant does not abolish CSA in all patients and may lead to the development of OSA.

Two poster presentations examined the effect of sleep apnea, both central and obstructive, on 21-month mortality in patients with CHF (Roebuck et al) and the relationship of OSA to interventricular septal hypertrophy in patients with dilated cardiomyopathy (Usui et al).

The Roebuck study involved 78 patients who had been referred for heart transplant assessment. Medical therapy was optimized and patients with an apnea/hypopnea index $>15/hr$ were commenced on CPAP or oxygen therapy if they were symptomatic. The patients were divided into three groups: those with CHF and an AHI $<5/hr$ ($n=23$), those with CHF and OSA with an AHI $>5/hr$ of which $<85\%$ were central events ($n=21$) and those with CHF and CSA as defined by an AHI $>5/hr$ with $>85\%$ central events ($n=32$). At the end of the study period, 17\%, 29\%, and 34\% of patients respectively had undergone transplant while 22\%, 33\%, and 31\% had died. The study reported that the prevalence of CSA and CSA with OSA was similar in the group that survived to those that did not, with left ventricular ejection fraction being a predictor of mortality; however, at 21 months, mortality was increased for the group that had OSA with CSA.

In the Usui study, it was hypothesized that patients with OSA and dilated cardiomyopathy would have a greater prevalence of left ventricular hypertrophy than the patients with dilated cardiomyopathy alone. Of the 41 patients involved in the study, among those with OSA (AHI $>10$ $n=17$), eight had left ventricular hypertrophy while in the non OSA group ($n=24$), four had left ventricular hypertrophy. Interventricular septal thickness was highly correlated to AHI ($p<0.001$). The conclusion was that a unique form of dilated cardiomyopathy is associated with OSA, characterized by left ventricular hypertrophy affecting the interventricular septum.

**The effect of different treatment modalities on SDB in CHF**

Nine studies were presented that examined the efficacy of four interventions on correcting SDB breathing in patients with CHF. They were adaptive servo ventilation (ASV), nocturnal oxygen therapy (NOT), continuous positive airway pressure (CPAP), and non-invasive bilevel ventilation.

**Websites of Interest**

- [www.sleepnet.com](http://www.sleepnet.com)  
  The interesting, informative popular site for SDB patients.
- [www.heartcenteronline.com](http://www.heartcenteronline.com)  
  All you need to know about CHF.
who plant sized index of left and right main stem bronchus had gone died. All evidence of nocturnal sleep in patients with CHF and OSA. Both groups found that the patients receiving CPAP therapy had an improvement in cardiac function when compared to controls (p<0.05 Mansfield et al).

In a similar study, Kohnlein et al compared the effect of CPAP and bilevel ventilation on sleep in a group of 18 patients with stable CHF. They found that both modalities significantly improved sleep quality, daytime fatigue, NYHA functional class, and circulation time, although there was no difference in efficacy between the modalities.

There was one study that examined the effect of nocturnal oxygen on sleep quality and left ventricular function. N seguint al all reported that nocturnal oxygen decreased central AHI although there was no improvement in left ventricular function.

Finally, five studies reported on the results of treatment with adaptive servo-ventilation (ASV) (ResMed AutoSet CS™). Four studies examined the effect of ASV on sleep quality (Pepperell et al), cardiac function and sleep quality (Schaedlich et al), anaerobic threshold (Topfer et al), and quality of life (El-Sebai et al). The fifth compared ASV to nocturnal oxygen (Vogt-Ladner et al).

The first four studies examined the effect of ASV on sleep quality, cardiac function, and quality of life over a period of between four weeks and three months. At four weeks, Pepperell et al found that objectively measured sleepiness improved and Cheyne-Stokes breathing was controlled with ASV when compared to a non-therapeutic control delivering <3cm H₂O. At six weeks El-Sebai et al found that ASV improved cardiac-specific quality of life (daytime naps, nocturia, Minnesota Living with Heart Failure questionnaire, and Epworth Sleepiness Score) and Topfer et al reported that anaerobic threshold improved leading to an improvement in exercise capacity. At three months, Schaedlich et al found that ASV suppressed Cheyne-Stokes breathing from the first night and was related to an improvement in cardiac function. However, this group did not find a significant improvement in sleep quality or scores on the Minnesota Living with Heart Failure questionnaire and Epworth Sleepiness Score when compared to pre-treatment values.

Finally, Vogt-Ladner et al compared the effect of ASV with nocturnal oxygen therapy (NOT). They found that, at three months, ASV provides a greater improvement in sleep, nocturnal breathing, exercise capacity, and left ventricular function than two liters a minute of OT in patients with CSR associated with CHF.

Conclusion

There is increasing evidence that SDB in patients with CHF compromises cardiac function, disrupts sleep, and may have an impact on a patient’s quality of life. Both OSA and CSR are common forms of SDB in this patient population. It is clear that OSA should be treated with CPAP therapy and will benefit cardiovascular effects. There is also growing evidence that overnight noninvasive ventilation has a beneficial effect on cardiac performance, sleep quality, and quality of life in patients with CSR associated with CHF. Both CPAP and bilevel ventilation have been used. However, ASV has been introduced in order to provide a method of delivering noninvasive ventilation that is acceptable to this patient group and gives maximum benefits to cardiac function and overall patient quality of life. Although the sample sizes were small and the power calculations not given, it has been suggested in these studies performed over up to three months that ASV is able to give these benefits.

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8. Pepperell C J T, et al. Prospective Randomized Controlled Trial Of Adaptive Proportional Assist Ventilation Vs Sub-Therapeutic Control In Chronic Heart Failure With Cheyne-Stokes Respiration (CSR).
11. V. Topfer, et al. Six Weeks Adaptive Servo-Ventilation Improves Anaerobic Threshold in Central Sleep Apnoea Due To Heart Failure.
A Case Study: CHF and AutoSet T

The case at a glance:
- **Patient**: 69 year-old American male.
- **Cardiovascular Outcomes**: Improvement after obstructive sleep apnea treated with AutoSet T for 8 months.

Clinical factors | Outcome
---|---
BNP | reduced by >60%
6 minute walk | increased by >35%
LVEF | marginally increased by 5%
Cardiac Output | marginally increased by 5%
ESS | marginally decreased by 3 points

A brief background of the patient
Mr. M is a 69-year-old congestive heart failure (CHF) patient with obstructive sleep apnea (OSA). After his treatment with AutoSet T during the SAHFE study*, Mr. M has found distinctly favorable changes in his lifestyle. These are reflected in the measured clinical outcomes.

Married for 38 years, Mr. M lost his wife when he was 61 years of age. He himself was diagnosed with CHF during the period when he was running his ill wife and mother around from physician to physician. However, he had never been screened for, nor diagnosed with, OSA, until his involvement in the SAHFE study despite his family history of cardiac problems and the fact that he had many typical OSA symptoms: snoring, excessive daytime sleepiness, and witnessed episodes of apnea. In fact, he had a known history of snoring for over 20 years.

This case study highlights the details of his treatment, mask fit issues, cardiac, and lifestyle outcomes.

**Mr. M’s introduction to the SAHFE trial**
Prior to treatment for OSA, Mr. M was frequently short of breath. He describes the severity of this condition: “On my visits to the heart failure clinic, I would have to take a break walking the short distance from the parking lot to the hospital. Once inside the hospital, I would have to take another break before taking the elevator to the CHF clinic.” He was taking 16 pharmacological medications to manage his heart failure. The principal investigator running the study invited him to participate in the SAHFE trial using Embletta PDS and the AutoSet T. Mr. M accepted. On his overnight sleep study, Mr. M had an AHI of 26 events per hour with a nadir oxygen concentration of 81%.

Mr. M was introduced to AutoSet T treatment by the CPAP clinic at the hospital. A case manager followed up on Mr. M’s progress with regular phone calls and AutoSet T downloads, including compliance and efficacy data. This follow-up was very important: mask problems had to be addressed at two subsequent visits, prompted primarily by the AutoSet T measurement of mask leak.

**Mask fit issues**
At his six-week check-up visit, Mr. M complained that the gel-based mask he had been provided with was too tight and was causing irritation around his nose. The study case manager chose to re-fit Mr. M with ResMed’s Mirage Full-Face Mask. At the 3-month follow-up Mr. M claimed that the mask was now far more comfortable. However, the AutoSet T download showed that there was significant mask leak. Mr. M was then fitted with the just-released medium shallow Mirage Full Face Mask Series II. He found this to be the most comfortable of all three masks. The subsequent download showed good compliance and elimination of the previous mask leak. The study showed a strong correlation of mask fit issues with two cardiac outcomes measures: b-type natriuretic peptide (BNP) [Fig. A] and the more traditional six-minute walk test [Fig. B]. At t=8 months, after five months on the AutoSet T with the Mirage Full Face Series II, cardiac parameters had improved significantly. He continues to maintain compliance with this mask.

**Cardiac outcomes improvement**
After the mask problems had been resolved, and after eight months on positive airway pressure treatment, all measured cardiac outcomes showed significant improvement. Mr. M’s BNP levels decreased by greater than 60% to the target range for heart failure patients of less than 100 pg/ml [Fig. A]. His six-minute walk test showed an increase in distance walked of greater than 35% [Fig. B]. Additionally, left ventricle ejection fraction (LVEF) marginally increased by 5 percent. Cardiac output marginally increased by 5 percent. Six-minute walk increased by >35% [Fig. B]. Additionally, left ventricle ejection fraction (LVEF) marginally increased by 5 percent. Six-minute walk increased by >35% [Fig. B].
ventricular ejection fraction improved by approximately 5%, while cardiac output also improved by 5%. The measured Epworth Sleepiness Scale decreased by 3 points.

Traveling with heart failure... and the AutoSet T
Mr. M travels at least once a year accompanied by his daughter and granddaughter. When asked about traveling with AutoSet T, Mr. M said "I wouldn’t travel without my AutoSet T system...I carry it on the plane with no problems."

His most recent trip was to the Bahamas, on a cruise last March. Once aboard the cruise-ship, he let the room steward know of his needs and arrangements were made to use the flow generator in his room.

Quality of life improvements
Treatment for OSA has allowed Mr. M to enjoy normal activities of daily living, without feeling exhausted. Currently his physicians have decreased his dosage of Lasix from twice a day to once a day. His Aldactone dosage has also been reduced. This has helped reduce nocturia symptoms from five-six events per night to one-two events. This has meant fewer awakenings through the night and consequently improved sleep quality. His physician attributed the reduction in CHF medications to the improvements associated with positive airway pressure treatment. The aim is to reduce other medications gradually.

For a gentleman who previously had barely enough energy to walk across the hospital car park, Mr. M is now able to walk more than 16 blocks before he is tired. Today he leads a very active social life. His hobbies include photography and travel. Mr. M is very much involved with his church as an elected Elder; he is also a volunteer alcohol and chemical addiction counselor. Mr. M personally attributes all his quality-of-life improvements during the last eight months to his use of the AutoSet T system.

*AHAF E=Sleep Apnea and Heart Failure with an Emblettta Study

Figure A: SAHFE OSA, CHF BNP timeline data - patient: 69 year-old, male

Figure B: SAHFE OSA, CHF Six Minute Walk timeline data - patient: 69 year-old, male

The Sleep Apnea and Heart Failure with Emblettta study ("SAHFE") is being conducted at a leading hospital in San Diego, California, USA. The objective of the trial is to screen, diagnose and treat OSA in patients with CHF. Positively diagnosed OSA/CHF patients are treated with ResMed’s AutoSet T for 12 months and key cardiac disease outcomes measured, including 6 minute walk, left ventricular ejection fraction, cardiac output, b-type natriuretic peptide.
At the recent meeting of the European Respiratory Society in Stockholm, four studies were presented investigating the effect of adaptive servo ventilation (ASV) (AutoSet CS™) on Cheyne Stoke Respiration (CSR) associated with congestive heart failure (CHF).

Three of the studies involved patients suffering from CHF, and one was a bench study using a computer-controlled breathing waveform generator.

In the studies with patients as the study group, all the patients were reported to have stable CHF. Sample size ranged from eight to 22 patients. The efficacy of ASV was compared to deadspace (Szollosi et al 2), a placebo (Topfer et al 3), and nocturnal oxygen therapy (NOT) (Worth et al 4).

The study by Szollosi et al 2 investigated the effect on sleep of two interventions—500mls of deadspace and ASV—in a group of patients with CSR associated with CHF. They found that sleep quality improved with ASV, while with deadspace, polysomnography showed an increase in arousals and decrease of total sleep time and sleep efficiency.

In the study by Topfer et al 3, 14 patients with CHF and sleep apnea (AHI>15/hr) were randomized to ASV or a placebo (Breathe-Right® nasal strips). Quality of life and anaerobic threshold were measured at six weeks. The study concluded that ASV improves quality of life and anaerobic threshold in patients with central sleep apnea and CHF although the results were not highly significant.

In the study by Worth et al 4, a randomized control trial was performed over two years on 22 patients to investigate the effects of ASV and NOT on sleep quality and cardiac performance as measured by left ventricular ejection fraction and six-minute walking distance with ASV, as compared to NOT.

Finally, Montserrat et al used a bench model to test the responsiveness of the ResMed AutoSet CS to CSR and obstructive events. They found that in the presence of central apneas, AutoSet CS increased tidal volume to a level slightly below usual normal breaths. In the presence of obstructive apneas, inspiratory pressure increased, but expiratory pressure did not.

Although these studies were all performed on small sample sizes, with no power calculation given, they demonstrated that the AutoSet CS improves tidal volume in the presence of apneas. This improves sleep quality, cardiac performance, and quality of life when compared to studies with NOT, deadspace, and a placebo.

Compiled by Fenella Connell

References
**Cheyne-Stokes Breathing Syndrome (CSBS) - Scoring**

**Essential features**
CSBS (also known as Cheyne-Stokes Respiration - CSR) is characterized by a cyclical fluctuation in breathing with periods of central apneas or hypopneas alternating with periods of hyperpnea in a gradual waxing and waning fashion. It occurs in patients with cardiac dysfunction usually in association with severe congestive heart failure (CHF) or neurologic disease/dysfunction, usually cerebrovascular. CSR is present during sleep and, in more severe cases, may also be observed during wakefulness.

**Diagnostic criteria**
- Presence of CHF or cerebral neurologic disease, and
- Respiratory monitoring demonstrates:
  - At least three consecutive cycles of a cyclical crescendo and decrescendo change in breathing amplitude. Cycle length is most commonly in the range of 60 seconds, although the length may vary.
  - One or both of the following:
    - a) Five or more central sleep apneas or hypopneas per hour of sleep.
    - b) The cyclic crescendo and decrescendo change in breathing amplitude has a duration of at least 10 consecutive minutes.

**Severity criteria**
The extent of CSR can be documented as the number of events per hour of sleep or the proportion of total sleep time spent with patient having CSR. At this time it is recommended that the severity of this syndrome not be rated.

From:

ResMed’s AutoSet CS is not available for sale in the US, but currently undergoing FDA trial.
Recent Research Articles


Population-based epidemiological studies have uncovered the high prevalence and wide severity spectrum of undiagnosed obstructive sleep apnea (OSA), and have consistently found that even mild OSA is associated with significant morbidity. Evidence from methodologically strong cohort studies indicates that undiagnosed OSA, with or without symptoms, is independently associated with increased likelihood of hypertension, cardiovascular disease, stroke, daytime sleepiness, motor vehicle accidents, and diminished quality of life. Strategies to decrease the high prevalence and associated morbidity of OSA are critically needed. The reduction or elimination of risk factors through public health initiatives with clinical support holds promise. Potentially modifiable risk factors considered in this review include overweight and obesity, alcohol, smoking, nasal congestion, and estrogen depletion in menopause. Data suggest that OSA is associated with all these factors, but at present the only intervention strategy supported with adequate evidence is weight loss. A focus on weight control is especially important given the expanding epidemic of overweight and obesity in the United States. Primary care providers will be central to clinical approaches for addressing the burden and the development of cost-effective case-finding strategies, and feasible treatment for mild OSA warrants high priority.

2. Sleep-disordered breathing and pregnancy. Edwards N; Middleton P G; Blyton D M; Sullivan C E David Read Laboratory, Department of Medicine, U of Sydney,Australia. Thorax Jun 2002, 57(6) p555-8

Many changes in the respiratory system occur during pregnancy, particularly during the third trimester, which can alter respiratory function during sleep, increasing the incidence and severity of sleep-disordered breathing (SDB). These changes include increased ventilatory drive and metabolic rate, reduced functional residual capacity and residual volume, increased alveolar-arterial oxygen gradients, and changes in upper airway patency. The clinical importance of these changes is indicated by the increased incidence of snoring during pregnancy, which is likely also to reflect an increased incidence of obstructive sleep apnea/hypopnoea syndrome. For the respiratory physician asked to review a pregnant patient, the possibility of SDB should always be considered. This review first examines the normal physiological changes of pregnancy and their relationship to SDB, and then summarizes the current knowledge of SDB in pregnancy.

3. Obstructive sleep apnea is independently associated with insulin resistance. Ip Mary S M; Lam Bing Ng Matthew M T; Lam Wah Kt; Tsang Kenneth W T; Lam Karen S L Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong S.A.R., PR China. Am J Respir Crit Care Med. Mar 1 2002, 165 (5) p 670-6

Comment in Am J Respir Crit Care Med. 2002 Mar 1;165(5) 562-3

Epidemiological studies have implicated OSA as an independent co-morbidity factor in cardiovascular and cerebrovascular diseases. It is postulated that recurrent episodes of occlusion of upper airways during sleep result in pathophysiologic changes that may predispose to vascular diseases. Insulin resistance is a known risk factor for atherosclerosis, and we postulate that OSA represents a stress that promotes insulin resistance, hence atherogenesis. This study investigated the relationship between SDB and insulin resistance, indicated by fasting serum insulin level and insulin resistance index based on the homeostasis model assessment method (HOMA-IR). A total of 270 consecutive subjects (197 male) who were referred for polysomnography and who did not have known diabetes mellitus were included, and 185 were documented to have OSA defined as an apnea-hypopnea index (AHI) > or =5. OSA subjects were more insulin resistant, as indicated by higher levels of fasting insulin (p = 0.001) and HOMA-IR (p < 0.001); they were also older and more obese. Stepwise multiple linear regression analysis showed that obesity was the major determinant of insulin resistance but SDB parameters (AHI and minimum oxygen saturation) were also independent determinants of insulin resistance (fasting insulin: AHI, p = 0.02, minimum O(2), p = 0.041; HOMA-IR: AHI, p = 0.044, minimum O(2), p = 0.022); this association between OSA and insulin resistance was seen in both obese and non-obese subjects. Each additional apnea or hypopnea per sleep hour increased the fasting insulin level and HOMA-IR by about 0.5%. Further analysis of the relationship of insulin resistance and hypertension confirmed that insulin resistance was a significant factor for hypertension in this cohort. Our findings suggest that OSA is independently associated with insulin resistance, and its role in the atherogenic potential of SDB is worthy of further exploration.
What is Ejection Fraction and why is it an important measure in patients with CHF?

An ejection fraction (EF) is a measurement used to assess how well the heart is "pumping". The left ventricle is a powerful pump, which propels or "ejects" blood throughout the body. "Ejection" refers to the amount of blood pumped out by the chamber during each heartbeat. There is always a "fraction" of blood that remains in the chamber after each contraction (even in a healthy heart).

Therefore an EF is a percentage of the blood within the chamber that is pumped out with every heartbeat. An EF of 55 to 75% is considered normal. An EF of 40% or less, indicates the heart is weakened and may lead to a diagnosis of HF or some types of cardiomyopathy. The heart, therefore, is no longer pumping efficiently and may have difficulty delivering an adequate blood supply to vital organs. A low EF is also a short-term risk factor of sudden cardiac death, or myocardial infarction. An EF between 40 to 55% indicates damage to the heart muscle has occurred.

EF is usually measured using an echocardiogram, a test that uses high-frequency sound waves to create a detailed moving picture of the heart.

It is important to understand that low EF caused by conditions such as congestive heart failure (CHF) is rarely cured. Treatment is focused on reducing symptoms and preventing the worsening of the disease.

While EF is a tool to diagnose CHF, it is possible for a person with heart failure to have a normal EF.

There are two phases to the heart's pumping function. Diastole is the filling phase of the chamber with blood, while systole is the pumping action or emptying of the chamber. EF is the measurement of this emptying stage. Heart failure may be caused by disease of the diastole, systole or a combination of both phases. A person suffering from diastolic heart failure can therefore have a normal EF.

In summary, EF is an important, simple, and painless test, which assists in the diagnosis and monitoring of patients being treated for CHF.

What is the 6 minute walk test (6MWT)?

The 6MWT is a practical simple test that requires a long, 100 ft (30m) in-door hallway with indicators of distance every 10ft (3m) and the turn around point clearly marked. The area must be flat, hard, non-slippery surface, devoid of other traffic.

The patient is required to walk along the hallway (back and forth) at their own pace. The goal for the patient is to cover as much distance as possible in the set time of 6 minutes.

The self-paced 6MWT assesses the submaximal level of exercise capacity and assists to predict survival in patients with heart failure. Most patients do not achieve maximal exercise capacity during the 6MWT, instead they choose their own intensity of exercise and are allowed to stop and rest during the test. Most activities of daily living are performed at submaximal levels of exertion, therefore the distance may reflect the functional exercise level for daily physical activities in this patient group. As walking is an activity performed daily by all but the most severely impaired CHF patient, the 6MWT is therefore considered similar to usual daily activities.

This test is a useful indication for monitoring and tracking progress with medical treatments in patients with moderate to severe heart disease. No exercise equipment is required, however an oximeter is very useful to record the patient's heart rate and oxygen saturation.

The Borg scale is a descriptive marker of subjective physical exertion and is also used to rate the patient’s level of dyspnea after the 6MWT. The patient is asked to rate their baseline level of dyspnea and overall fatigue before and after physical exertion. The rating is from 0, equating to no dyspnea at all, to 10, which equates to very, very severe (maximal) dyspnea.
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### 2002-2003 calendar of events

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<td>Atlanta, GA, USA</td>
<td>Medtrade 2002</td>
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<tr>
<td>November 2-7, 2002</td>
<td>San Diego, CA, USA</td>
<td>CHEST 2002</td>
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<tr>
<td>November 7-9, 2002</td>
<td>Porto, Portugal</td>
<td>17th Mediterranean Meeting of Non-Invasive Ventilation</td>
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<td>November 17-20, 2002</td>
<td>Chicago, IL, USA</td>
<td>AHA Scientific Sessions 2002 (American Heart Association)</td>
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<tr>
<td>March 30-April 2, 2003</td>
<td>Chicago, IL, USA</td>
<td>ACC 2003 (American College of Cardiology)</td>
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<td>May 7-8, 2003</td>
<td>Las Vegas, NV, USA</td>
<td>Medtrade Spring</td>
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<td>May 21-24, 2003</td>
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<tr>
<td>June, 2003</td>
<td>Chicago, IL, USA</td>
<td>APSS 17th Annual Meeting (Associated Professional Sleep Societies)</td>
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<td>June 30 - July 3, 2003</td>
<td>Helsinki, Finland</td>
<td>7th World Congress on Sleep Apnea</td>
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<td>August 30 - Sept 3, 2003</td>
<td>Vienna, Austria</td>
<td>European Society of Cardiology Congress 2003</td>
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<tr>
<td>October 5-9, 2003</td>
<td>Prague, Czech Republic</td>
<td>17th Congress of the European Sleep Research Society</td>
</tr>
<tr>
<td>October 7-9, 2003</td>
<td>Atlanta, GA, USA</td>
<td>Medtrade 2003</td>
</tr>
<tr>
<td>November 9-11, 2003</td>
<td>Orlando, FL, USA</td>
<td>AHA Scientific Sessions 2003 (American Heart Association)</td>
</tr>
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<td>November 21-23, 2003</td>
<td>Zhuhai, China</td>
<td>4th ASRS Congress (Asian Sleep Research Society)</td>
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