Last year we promised to develop a "special edition" of ResMedica focusing on the treatment of Cheyne-Stokes respiration (CSR) and central sleep apnea (CSA) in patients with congestive heart failure (CHF) using adaptive servo-ventilation (ASV). This special edition complements our second issue of ResMedica, which focused on CHF.

You will find that this issue of ResMedica moves away from our usual generic information to concentrate on specific product therapy for the treatment of CSR in CHF patients. This issue has been developed to assist in promoting awareness of this syndrome and the new form of treatment—ASV.

One of the major stories in this issue is from Dr Gernot Vogt-Ladner. In this article he compares the effectiveness of ASV with that of nocturnal oxygen therapy for long term treatment of patients with CHF and pure CSR. I am sure you will find the results very interesting.

We are also pleased to publish an article from Dr Winfried Randerath. He compares the effectiveness of ASV with that of standard continuous positive airway pressure (CPAP) therapy in patients with CSR due to heart failure. This article raised several questions that have been of immense value to ResMed in the development of our newly launched AutoSet CS™2 machine, which is used in the treatment of CSR. We discuss these issues in an article that describes how this, and other feedback, has contributed to the evolution of the ASV device to its latest form—AutoSet CS2.

Our special issue also includes background information on CHF and CSR, their consequences and treatment; an update on the DGK cardiology symposium held in Germany in April; and a list of suggested reading articles on the topic of CSR.

We've also included two "new technology" stories. The first deals with the launch of ResMed's new ASV machine. The second describes the innovative simulator software developed by our researchers. This improves efficacy and validation testing, and is also to be used as a vital tool in training and education for the AutoSet CS2.

We received some very complimentary feedback on our last issue of ResMedica on non-invasive ventilation, and trust that you find this "special edition" equally informative and useful. Please be sure to send us your feedback via email clinicalnews@resmed.com.au. Look out for our next regular ResMedica issue later this year, which will focus on the cardiovascular consequences of sleep-disordered breathing.
CHF in review—
Summary of an interview with Dr Ian Wilcox

The Congestive Heart Failure issue of ResMedica elicited much interest in an interview with Associate Professor Ian Wilcox. In this interview he reviewed the causes, treatment and current thinking on CHF. He also discussed the relationship between CHF and sleep disordered breathing (SDB).

Prof. Wilcox described CHF as a serious and life shortening syndrome, usually caused by coronary artery disease, high blood pressure or diseases of the heart’s valves or muscle. As a result, the weakened heart muscle is unable to supply the oxygen rich blood the body needs during exercise and at rest. The body compensates by building up fluid in the lungs and vascular space which, over time, causes congestive heart failure.

Symptoms of CHF include tiredness, breathlessness, muscle fatigue and edema (including pulmonary edema) which may present as paroxysmal nocturnal dyspnea (PND), which causes patients to wake up gasping for breath interrupting sleep.

The prognosis for patients is generally poor, similar to other serious illnesses such as cancer. Patients move through stages ranging from Class I, where there are no limitations to daily life, to Class IV, where they have symptoms at rest and cannot carry out any physical activity without breathlessness. These patients may have a 50% mortality rate within 12 months.

US research indicates:
• the incidence of CHF is 1% after the age of 65
• CHF patients have a five-year mortality of around 50%
• 80% of male and 70% of female CHF sufferers, under the age of 65, will die within 8 years
• the cost of care for CHF patients in 1993 was estimated at US $17.8 billion
• between 1979 and 1999, CHF deaths increased by 145%.

Prof. Wilcox said that although research is being conducted into gene therapy and implant devices, currently the only ‘cure’ for CHF is a heart transplant. Treatment of CHF is determined by the cause of the condition, and aims to improve symptoms, quality of life and survival.

Sleep-disordered breathing is so common in CHF patients that Prof. Wilcox noted “a case can be made for performing an SDB screening study on all patients with CHF”.

He said, "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".

CHF patients commonly develop CSR, which increases the already difficult job of breathing. Prof. Wilcox suggests that increased difficulty of breathing may worsen heart failure, as respiratory muscles require greater blood flow, while cardiac output is reduced at the same time.

The sudden arousals that occur (and several hundreds may occur in a single night) are associated with increased output of adrenalin, which also places stress on the heart.

Prof. Wilcox noted, "fragmented sleep also affects daytime symptoms and quality of life in CHF. Clinically, this is particularly relevant since improving quality of life is a major goal of the medical management of patients with CHF.”

He concluded with the opinion that CPAP benefits the heart both in reducing left ventricle ejection fraction (LVEF), and in reducing the degree of mitral regurgitation in patients with CHF.
ResMed has launched a new device for CHF patients with Cheyne-Stokes respiration (CSR), a common disorder in heart failure patients.

The AutoSet CS2 has evolved from Positive Airway Pressure (PAP) ventilators. Controlled trials of medically treated patients with heart failure and obstructive sleep apnea have shown that after one month of PAP therapy, daytime systolic blood pressure is reduced and left ventricle function is improved.

The ResMed AutoSet CS2 uses a unique set of adaptive servo-ventilation algorithms to provide ventilatory support to rapidly normalise CSR. These are called ASV–CS algorithms; CS stands for Cheyne-Stokes.

**How the algorithms work**

By ventilating the patient appropriately during periods of apnea and hypopnea, and reducing support during periods of hyperventilation and normal breathing, ASV–CS algorithms rapidly stabilise breathing patterns and arterial blood gases. AutoSet CS2 therapy reduces sympathetic nervous system activity and the stress on the failing heart.

To determine the degree of pressure support needed, the ASV–CS algorithm continuously calculates a target ventilation. Based on respiratory rate and tidal volume, the target is 90% of the patient’s recent average ventilation. This means that ventilation can vary gradually and naturally over the course of the night.

The algorithm uses three factors to achieve synchronization between pressure support and the patient’s breathing:

1. the patient’s own recent average respiratory rate, including the ratio of inspiration to expiration and the length of any expiratory pause
2. the instantaneous direction, magnitude and rate of change of the patient’s airflow, which are measured at a series of set points during each breath
3. a backup respiratory rate of 15 breaths per minute.

Delivered ventilation is matched to patient respiration via a series of set points identified in each breath. To ensure ventilatory support is synchronized to the patient’s effort, the AutoSet CS2 relies on the first two factors. When a central apnea/hypopnea occurs, support initially continues to reflect the patient’s recent breathing pattern. However, as the apnea/hypopnea persists, the device increasingly uses the backup respiratory rate.

As long as ventilation is at or above the target:

- the magnitude of the pressure support remains minimal
- the underlying or end expiration pressure (EEP) is adjustable and helps reduce dyspnea, excessive preload and pulmonary congestion, while preventing obstructive apneas.

As breathing resumes and total ventilation exceeds the target, pressure support is rapidly reduced. This reduces the likelihood of over-ventilation and hypocapnia, which can lead to vocal chord closure and further apneas.

The ASV–CS2 algorithm provides therapy designed for CHF patients with CSR. Many CHF patients periodically have upper airway obstruction during sleep as well. AutoSet CS2 can easily be adjusted to treat obstructive sleep apnea (OSA) while resolving CSR.

AutoSet CS2 is currently undergoing clinical trials in the USA prior to FDA clearance. It is currently available outside the USA.

* AutoSet CS2 is not for respiratory failure patients

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**Further reading on SDB in CHF**

Cheyne-Stokes respiration—
The inside story

What is CSR?
Cheyne-Stokes respiration occurs when periods of hyperventilation with waxing/waning tidal volume alternate with periods of central hypopnea/apnea.

Figure 1. CSR: crescendo and decrescendo pattern of hyperventilation alternates with apnea/hypopnea

Among congestive heart failure patients, CSR may be diagnosed when respiratory monitoring demonstrates:

• at least three consecutive cycles of a cyclical crescendo and decrescendo change in breathing amplitude
• one or both of the following:
  • five or more central sleep apneas or hypopneas per hour of sleep
  • at least 10 consecutive minutes of the cyclic crescendo and decrescendo change in breathing amplitude.

Consequences of CSR
In the heart failure population, nocturnal CSR is known to be an independent risk factor for mortality or cardiac transplantation.

CSR is expected to accelerate the progression of heart failure by causing:

• repetitive hypoxia
• increased afterload
• increased sympathetic activity
• oscillations in heart rate and blood pressure.

The sleep fragmentation resulting from CSR also diminishes quality of life by causing fatigue and daytime sleepiness.

Figure 2. Survival of CHF patients with or without CSR

Proposed mechanisms underlying CSR
Although its causes are not fully understood, the following sequence has been proposed to explain the periodic breathing pattern of CSR.

• Pulmonary edema stimulates lung vagal receptors. As a result of increased central and peripheral chemoreceptor sensitivity, chronic hyperventilation and hypocapnia ensue.
• Within this setting, CSR is often triggered by a spontaneous arousal with a large breath. This causes PaCO$_2$ to plunge below the level required by the autonomic system to maintain ventilation (the apneic threshold).
• A central apnea occurs: airflow stops, oxyhemoglobin saturation drops and PaCO$_2$ starts to rise.
• When PaCO$_2$ exceeds the apneic threshold, breathing resumes and is often accompanied by an arousal at the peak of hyperventilation.
• Hyperventilation once again drives PaCO$_2$ below the apneic threshold.

The length of the CSR cycle typically varies from 40 to 60 seconds. In patients with reduced cardiac output, the hyperventilation phase tends to last longer. This is because poor circulation increases the time it takes for changes in alveolar blood gas pressure to be detected by the chemoreceptors.
Adaptive servo-ventilation—an effective way to treat CSR

Various methods have been used to treat CSR. These include oxygen therapy, continuous positive airway pressure (CPAP), bi-level ventilatory support and, most recently, adaptive servo-ventilation (ASV-CS).

A study, comparing the effects of each of these therapies over one night, demonstrated superior results with ASV-CS technology.

Several studies have shown the long-term advantages of ASV-CS technology in treating patients with stable CHF:

- fewer respiratory events
  - AHI reduced from a pre-treatment mean value of 49 to 6 events/hour at three months in one study and from 26.9 to 4.3 at four months in another study.
  - Central RDI reduced from a pre-treatment mean value of 37.3 to 0.9 at three months.
  - RDI reduced from a pre-treatment mean value of 49 to 9 at two years.
- improved sleep quality—arousals reduced from a pre-treatment mean value of 275 to 40 at three months and from 275 to 53 at two years.
- higher than average left ventricular ejection fraction (LVEF) (increased from a mean value of 36.4% at baseline to 45.8% at three months).
- increased exercise capacity (6 minute walk distance (MWD) and VO₂ max increased by about 20%).

Fact file

Congestive heart failure (CHF) is a syndrome that affects millions worldwide.

In the USA
- 4,900,00 people are estimated to have CHF in 2003.
- There are almost equal numbers of males and females with CHF.
- There are 550,000 new cases diagnosed per year.
- These new diagnoses approach 10 per 1000 population above the age of 65.

In Europe
- Heart failure prevalence was estimated at 6,500,00 in 1997.
- There are 580,00 new cases per year.
- Consolidated data for western countries indicate that new diagnoses of CHF each year are 1–4 per 1000 population.
- Approximately 50% of CHF patients experience sleep-disordered breathing with either Cheyne-Stokes respiration (CSR) or obstructive sleep apnea (OSA) predominating. However both are often present.
- CSR is believed to be the most prevalent form of SDB in patients with severe left ventricular dysfunction.
- Nocturnal CSR is associated with increased mortality in CHF patients and is also an independent risk factor for cardiac transplant.

3 Bradley TD, Floras JS. Sleep apnea and heart failure Part II: Central sleep apnea. Circulation 2003; 107; 1822
Adaptive servo-ventilation in patients with periodic breathing during sleep

Introduction:

Dr. Winfried Randerath (University Reader) is a specialist in internal medicine, pneumology, immunology and environmental medicine. From 1996, he was Chief Consultant (Deputy Director) at the Ambrock Clinic in Hagen (Germany). The Clinic, headed by Prof. Karl-Heinz Rühle, specializes in pneumology, immunology and sleep disorders, and houses one of Europe's largest sleep laboratories, treating over 4400 patients for sleep disorders each year. Dr Randerath wrote his qualifying thesis to become a university lecturer in 2000 on impedance-controlled, self-adjusting CPAP therapy (APAPFOT) for sleep apnea patients.

Winfried Randerath is a member of the editorial advisory board of the journal Somnologie, the Cochrane Airways Group, and is a consultant to the journal Chest. He has also published widely in international journals. He has recently conducted a study in the sleep laboratory, comparing the effectiveness of adaptive servo-ventilation (AutoSet CS, ResMed Ltd.) with that of standard CPAP therapy in patients with Cheyne-Stokes respiration due to heart failure.

In addition to its use in this study, AutoSet CS has for some time been the treatment of choice in the Ambrock Clinic in Hagen for treating patients with periodic breathing. Here Dr. Randerath describes his experience with the adaptive servo-ventilator therapeutic method.

The study: Performed with the first AutoSet CS Device

In the treatment of obstructive sleep apnea syndrome (OSAS), the efficacy of treatment with continuous positive airway pressure (CPAP), bilevel pressure, and automatic CPAP is widely recognised. Although approximately 20-30% of patients reject this therapy, there are few types of medical treatment that achieve such high levels of efficacy and acceptance. Despite the range of therapeutic options, approximately 5-10% of patients in the sleep clinic cannot be adequately treated. Some of these are patients suffering from central respiratory regulation disorders, or periodic breathing patterns during sleep.

A special form of periodic breathing is Cheyne-Stokes respiration (CSR), which typically occurs in patients with heart failure. Even though CPAP often has little effect on the clinical picture of respiratory disorders in CSR patients, the use of pressures up to 10cmH₂O has been shown to result in improved cardiac performance and decreased mortality. Factors such as the influence of increased left ventricular transmural pressure are believed to be primarily responsible for the improvement in cardiac performance.

A new method proposed for the treatment of Cheyne-Stokes respiration is adaptive servo-ventilation (AutoSet CS). This form of treatment is based on the principle of administering pressures which vary from one breath to the next. The objective is to support respiration so as to attain a target minute ventilation. An inspiratory swing (pressure support), which can vary from 3 to 10cmH₂O, is superimposed on an individually determined CPAP pressure, which for most patients is initially 5cmH₂O. If spontaneous breathing remains below 90% of the target value, a higher pressure is applied (maximum: CPAP 5cmH₂O + swing 10cmH₂O = IPAP 15cmH₂O). During hyperventilation phases, a minimum pressure support of 8 cmH₂O during inspiration is applied (CPAP 5cmH₂O + swing 3cmH₂O). The maximum swing of 10 cmH₂O can be attained in 12 seconds.

The question is how adaptive servo-ventilation compares to CPAP therapy in congestive heart failure, particularly with respect to cardiac performance parameters. This problem has been investigated in a randomised prospective study of heart failure patients with Left Ventricular Ejection Fraction (LVEF) 20-40%. When adaptive servo-ventilation was first used for patients with Cheyne-Stokes respiration, it was observed that, in most of the patients, normalisation of periodic breathing could be attained within a few days. This finding was surprising, in that these were generally patients who were not successfully treated using established positive pressure methods. On the basis of these observations, the clinical use of the adaptive servo-ventilation method was progressively extended. The therapy was also used for patients with periodic breathing who had an underlying cardiac disorder, but with no decrease in the LVEF as demonstrable by echocardiogram. Subsequently, the treatment group was extended to include patients who had no history or clinical condition of cardiac disorders. This form of therapy is not yet widely recognised, and hence is currently prescribed only following complex, resource-intensive procedures. Once the diagnosis has been confirmed using polysomnography, treatment is first attempted...
with CPAP bilevel and auto-CPAP supplemented in some cases by nocturnal supply of O₂. Only when such options had failed was adaptive servo-ventilation initiated. The process required a significantly longer stay in the sleep laboratory than is required, for example, with OSAS.

At the time of writing this article, this form of treatment has been used with 52 patients (49 men, 3 women), with an age range of 63.1 ±8.2 years and BMI of 29 ±3.8kg/m². The diagnosis of sleep apnea syndrome with periodic breathing had been made between 1 and 108 months previously (mean 13.1 ±25.3 months). Initial AHI was 54 ±19.3/h, and initial minimum O₂ was 76.7 ±12.2%. 45.6% of the patients suffered from arterial hypertension, 25.6% from coronary heart disease, 4.7% from valvular heart disease and 2.3% from cardiomyopathy. Arrhythmias were present in 34.9% of the patients, and heart failure was present in 25.6%. LVEF was not lower than 40% (patients with more severe heart failure were included in another study). In addition to cardiac disorders, 16.3% of the patients also suffered from cerebral ischaemia. In 16.3% of the patients, no underlying disorder related to periodic breathing could be established either in the patients’ prior history or clinically (idiopathic period breathing). Patients were treated with adaptive servo-ventilation over periods of 1 to 21 months, with a mean of 7.5 ±6.1 months. Normalisation of periodic breathing with AHI <10/h occurred in 77.1% of the patients, and a substantial improvement (AHI 10-20/h) was achieved in 14.3%. The treatment outcome was unsatisfactory in only 8.6% of the patients. This method thus represents an effective form of therapy for patients for whom there has been no viable treatment up to now.

Although the results were favourable, a number of problems were observed in the introductory phase of the treatment, and with long-term use. For example, it was found that some patients repeatedly interrupted treatment during the night. Particularly those who have dyspnea or frequent nocturia, tended to have some problems using the AutoSet CS. The software for the device requires therapy phases lasting 3 minutes in order to acquire sufficient data for optimal pressure adjustment between one breath and the next. So frequent removal of the mask during the night impairs effectiveness of adaptive servo-ventilation. As a result, this form of therapy requires the patient to have a better understanding of the treatment than is the case with CPAP therapy, for example. Another disadvantage with protracted use is that the complex algorithm used for the device is intolerant of large leaks and so most patients are ideally treated with Mirage Full Face masks. These are only available in three sizes, and in some some instances, we were unable to find appropriate tight-fitting masks. In such cases, the only options are either to tolerate a significant leak or to refrain from using this form of therapy.

The introductory phase required considerable time input from the staff providing medical care. In addition to the important factor of mask optimization, patients needed to be trained in the operating principle of adaptive servo-ventilation, so that they would not find the varying level of pressure support annoying. During the initial phase of the therapy, close attention was paid to the possibility of sudden falls in arterial blood pressure, particularly in patients treated with diuretics, but no clinically relevant cases of hypotension were observed in this group of patients. There were also no adverse cardiovascular side effects from the therapy in the above group.

Our findings can be summarised as follows. Adaptive servo-ventilation provides a new form of therapy for periodic breathing in cases where all other therapeutic treatment has failed. After an introductory phase, which places demands on staff resources, it provides adequate ongoing treatment for this difficult patient category. This spares the patients the stress of protracted, and generally unsuccessful, experiments with different systems, and saves needless expenditure generated by ineffective forms of therapy.

Note: This article was submitted by Dr Randerath in October 2002.

References
The evolution of a better device—
AutoSet CS2

‘There’s always room for improvement.’ This old adage, fundamental to the concept of continuous improvement, underlies the evolution of machines such as ResMed’s new AutoSet CS2.

Feedback from physicians, clinicians and patients is highly important and suggestions, such as what Dr Randerath described in the previous article, aids in the improvement in devices, masks, and ultimately the therapy for the patient.

Over the two-year development phase, the ResMed team set out to resolve problems clinicians had noted with the existing technology. We combined these solutions with the best of the existing AutoSet technology to produce the superior new generation AutoSet CS2.

The key challenges were the need for a better fitting full face mask and an increased range of nasal mask compatibilities. There was also some difficulty in setting up the equipment and patients who repeatedly interrupted treatment during the night.

1. Masks

Over the past two years, several new and very advanced masks have been developed.

ResMed recommends the use of the new Ultra Mirage full face mask with AutoSet CS2. This new mask has been developed to help solve the problem of mask leak. It offers six cushion sizes (compared with three sizes in older versions), standard and shallow profiles for different facial shapes, and an adjustable forehead support to help resolve leaks.

The AutoSet CS2 also has a Mask Fit Assessment feature. This rating system gives clinicians and patients an indication of how well the mask fitted during the therapy session and helps them to make appropriate adjustments.

AutoSet CS2 is also compatible with existing Mirage full face and nasal masks, including the newest and most advanced Mirage Vista and Mirage Activa nasal masks.

2. Difficulty in setting up

Feedback from the development process has helped ResMed create a smaller, lighter, more compact, and much quieter machine.

It is easier to set up. Previously the set up involved using a PC; now adjustments are made directly on the flow generator via the LCD screen.

This screen also displays live data, giving clinicians instantaneous feedback about the effectiveness of the therapy. It also contains stored data.

AutoSet CS2 uses a sensitive SmartStart feature, which automatically detects patient breathing and begins the therapy.

The air circuit is simplified and the optional humidifier is integrated into the device, to reduce the bulkiness of the equipment.

An optional ResLink™ module with SmartMedia card stores large volumes of information about the therapy, supplementing the AutoSet CS2 data. This card can be transferred to the clinician to give a superior picture of patient status.

ResLink can also include an oximeter—given that desaturation during sleep is a major issue of sleep apnea, oximetry is a useful means of assessing how well therapy is working.

3. Interrupted treatment during the night

Interrupted sleep can become a repetitive cycle. Improved mask fit reduces leak and discomfort, which in turn decreases disturbance during the night and increases the effectiveness of therapy.
Dr. Gernot Vogt-Ladner is an internist and Somnologist (DGSM) who, until recently, worked at the Klinikum Fuerth Medical Sleep lab in Germany, as a fellow of cardiologist Professor Heinrich Worth.

Dr. Vogt-Ladner has been working with the AutoSet CS for three years. In the following article he describes a trial he conducted at the Klinikum Fuerth where he compared ASV—CS (AutoSet CS) with nocturnal oxygen as long-term treatments in patients with CHF and pure Cheyne-Stokes respiration.

The exclusion criteria (obstructive or mixed respiratory events during sleep) meant that the recruitment phase was lengthy. Patients were monitored for the period of the trial as well as for a three-month follow-on period. Data from the total period of 24 months is now available, although it has not yet been published.

**Introduction**

Patients in an advanced stage of left heart insufficiency frequently have central disturbances of respiratory regulation during sleep. Larger studies have shown a coincidence between CHF and Central Sleep Apnea Syndrome (CSAS) of about 45-66%. Inclusion criteria for this study have LVEF = 40% in NYHA class II—IV. All patients received optimal medication.

Obviously the severity of CSA (mainly CSR) increases with decreasing left ventricular function. Patients up to NYHA class III mainly show disturbances in central breathing regulation during light sleep stages (Non-REM stages 1 and 2) and rarely during REM sleep. With the progression of left heart insufficiency (NYHA IV), central apnea may occur while awake as well. The deeper sleep stages Non-REM 3 and 4 seem to be less affected by unstable breathing.

The prognosis of CHF patients clearly deteriorates if an additional disturbance of central breathing regulation occurs. Ventricular extra-systoles, ventricular tachycardia and sudden cardiac death—can be seen more often in patients who have CHF accompanied by CSR. Apart from the prognostic importance, CSR during sleep also causes worse sleep quality, with consecutive daytime sleepiness and limited physical performance.

**Definitions**

Central sleep apnea (CSA) includes the complete cessation of airflow for at least 10 seconds or longer. Unlike obstructive sleep apnea, no complete atony of the pharyngeal muscles and closure of the upper airway occur. In CSA, the cessation of signals to the respiratory muscles from the respiratory regulation centre in the brainstem causes the apnea.

Central hypopneas can occur as a pathological breathing pattern as well. Hypopneas are defined as a reduction in tidal volume (Vt) of 50 % or more with respect to the averaged Vt while awake but without complete airflow cessation. Disturbances of ventilation during sleep, are quantified by an Apnea-Hypopnea Index (AHI, synonym: Respiratory Disturbance Index, RDI). AHI stands for the number of Apneas and Hypopneas per hour sleep. An AHI > 15/hr is classified as pathologic.

Typically in CHF patients with CSA, apneas and hypopneas are embedded in a waning and waxing tidal volume. Cycles with slowly increasing Vt up to hyperventilation and consecutive hypopnea or apnea are called CSR.

**Mechanism of action of ASV-CS**

AutoSet CS is a pressure support servo-ventilator, specially designed for nasal ventilation in CSR due to CHF. The system consists of a flow generator with variable turbine, a tube system, a full-face mask and a microprocessor, which regulates the technique via algorithms, ‘fuzzy logic.’

**Clinical results with AutoSet CS**

Healthy probands have been ventilated with ASV-CS mode for several nights and cardio respiratory monitored. No negative effects (e.g. hyper—or hypoventilation, tachycardia, etc.) or malfunction of the device have been seen. In CHF, NYHA III, significant improvements of respiration during sleep have been shown. In our study, the effects of three months of treatment with AutoSet®CS in ASV-CS mode have been significantly better than supplemental nasal O₂ (2L/min). Patients preferred the new ventilation mode compared to nCPAP and nBilevel.

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The development of ResMed’s unique new second generation device for Cheyne-Stokes therapy, the AutoSet CS2, presented particular challenges.

As with any complex product development, extensive verification and validation is required. Once the product is launched to market, effective education and training are critical.

While the AutoSet CS2 clinical results speak for themselves, the product does not fit within an established sector. To help explain the algorithm, the ResMed Product Development team developed a "simulated bench patient." This has delivered product quality, shorter and safer clinical trials, and will assist in education and training.

The simulator is a personal computer application that provides a basic understanding of:

- the condition of Cheyne-Stokes Respiration
- the principle of the AutoSet CS2 therapy and
- how to use the AutoSet CS2.

The simulator is a complementary tool to assist education of clinicians regarding CSR and training in therapy using the AutoSet CS2. This application is particularly important for the AutoSet CS2 product, where ResMed is showing the merit of applying a respiratory therapy to improve cardiac function in this group of patients.

Study:  
The following are numbers in detail: A randomised, controlled study was conducted to investigate the effects of ASV-CS (AutoSet CS) and nocturnal supplemental oxygen on sleep quality, cardiac function and performance, and quality of life (QOL) in severe CHF with CSR. Twenty patients with severe CHF and NYHA classification III were enrolled and randomised into two groups.

Method:  
Analysis of sleep quality polysomnography (PSG), QOL, Epworth Sleepiness Scale (ESS), heart function (Echo, ECG, LT-ECG), and physical performance (6 MWD, Spirometry) took place prior to and at 4 and 12 weeks after initialisation of the nocturnal therapy.

Result:  
With elimination of CSR and arousals in the ASV–CS (AutoSet CS) arm, an increase in LV function and significant improvements in physical performance and QOL has been shown. In the oxygen group improvements in QOL and LV function have been shown, but not in physical performance. Sleep architecture was disturbed by frequent arousals. These were improved but there was still existing CSR in PSG. Nocturnal haemoglobin saturation was balanced.

Conclusion:  
Due to improvements of heart function and physical performance, the treatment with ASV–CS (AutoSet CS) in severe CHF with CSR is preferable to nocturnal oxygen therapy, if patients comply with the elaborate treatment.

Comment:  
To reduce nocturnal apneas and hypopneas and improve saturation, the modulation of chemoreception via pharmacological methods on the one hand, and the symptomatic treatment via the modern and well tolerable, non-invasive ventilation method ASV–CS (AutoSet CS) on the other hand, is promising.

Whether successful treatment of nocturnal CSR influences high mortality and transplant rates in patients with left heart insufficiency, will need to be investigated in further studies with bigger collectives.

The follow-up data of patients in the study showed a more stable LV function in the AutoSet CS than in the O₂–group. It also showed less than 50% of the hospitalisation days in total over a 24 month period.

Note: The publication of this data is in process.
The AutoSet CS2 model

The simulator replicates both the therapy and the user interface. The AutoSet CS2 user interface emulates the controls on the real device, in that therapy can be activated and configured on-screen using the mouse to exercise the keypad buttons. The menu strings can be displayed in different languages. The CS2 therapy pressure waveform can be seen on screen, allowing the user to understand the interaction between therapy and patient.

The Cheyne-Stokes patient model

This complex cardio-respiratory model was originally devised and developed as a verification/validation tool for the AutoSet CS2 development program. It acted as a 'bench patient' eliciting realistic CSR and responding realistically to therapy. Such a tool was essential given the particular challenges an adaptive servo-ventilator poses for device testing, with other benefits including shorter development timelines and improved product quality. A poster describing this 'bench patient' was presented at the World Congress on Sleep Apnea 2003 (a copy of this presentation is available on request via email clinicalnews@resmed.com.au).

Note that the 'patient' is not a ResMed-conceived model conveniently designed to respond to a ResMed-conceived therapy. Rather, it is based on a published respiratory model (Khoo 1982, 1991), modified to possess phasic breathing instead of continuous ventilation. Using a published model ensures a high level of objectivity and independence, of particular importance to its original role as a validation tool.

The model can be generally applied, but in this case the parameters were adjusted to elicit Cheyne-Stokes respiration. The resulting respiration of the "bench patient" compared favourably to real patients, both with and without treatment.

Figure 2. Comparison of CS patient response to cessation of Autoset CS therapy. The verticle dotted line indicates the instant at which therapy was discontinued and resumption of CSR occurs.

Panel A—Actual CS patient therapy, showing pulse oximetry (top trace), respiratory flow (nasal cannulae - middle trace), and the Autoset CS therapy pressure waveform (bottom trace).

Panel B—'Bench CS patient', showing arterial oxygen saturation (top trace) and respiratory flow (bottom trace).
German cardiology meeting—an update

Each spring, the German city of Mannheim hosts one of the biggest conferences of the year—the annual Society of Cardiology (DGK) meeting. More than 5,000 participants attend the meeting to discuss the newest scientific and technical developments relating to diagnosis and treatment.

ResMed GmbH & Co. KG has attended the meeting for the past three years, initially as a small exhibitor; but more recently taking a higher profile. Last year ResMed organised and sponsored a symposium entitled ‘Cardiovascular diseases and sleep-disordered breathing’.

Building on the success of this first symposium, ResMed organised a second symposium this year; ‘the importance of sleep-disordered breathing in cardiovascular diseases—cardiorespiratory interactions’.

The organisers were overwhelmed by the response. In fact, the event was so popular that there was standing room only—and even then some people had to stand outside!

The organisers attributed much of the success to the high quality of the speakers, who made some outstanding presentations. Prof. Helmut Teschler (Ruhrlandklinik, Essen) and Prof. Raimund Erbel (University of Essen, Cardiologist) chaired the symposium, putting a lot of effort into handling the discussions and questions after each presentation.

It is evident from the response to the symposium that interest in SDB in CVD is increasing as cardiologists become more aware of the relationship between sleep and heart disorders and the opportunities for diagnosis and treatment. The ResMed team is more determined than ever to ‘wake people up to sleep’!

Here is the agenda for the meeting indicating the panel of distinguished speakers and the range of topics were presented and discussed:

**Agenda**

The importance of sleep-disordered breathing in cardiovascular diseases—cardiorespiratory interactions

Chaired by Prof. R. Erbel (Head of Cardiology, University Hospital Essen) and Prof. H. Teschler (Head of Pulmology, Sleeplab, Ruhrlandklinik: Essen)

Topics and speakers:

1. Heart-insufficiency and sleep-disordered breathing  
   Dr. T. Welte (Cardiology Department, University Hospital Magdeburg)

2. Hypertension and sleep-disordered breathing  
   Dr. H. Becker (Pulmology Department, Head of Sleeplab, University Hospital Marburg)

3. Pathophysiology of Cheyne-Stokes respiration  
   Dr. V. Töpfer (Pulmology Department, Head of Sleeplab, University Hospital Ulm)

4. Screening and diagnostic of sleep-disordered breathing in a cardiology centre  
   Dr. B. Lamp (Cardiologist, Cardiology Centre Bad Oeynhausen)

5. The role of noninvasive respiration in cardiology  
   Dr. H. Wöhrle (Pulmologist, Cardiac Centre, University Hospital Ulm)

6. Therapy of obstructive and central sleep apne in patients with heart insufficiency  
   Dr. G. Vogt-Ladner (Department of Cardiology and Pulmology, Krankenhaus Furt)

**Waking people up to sleep**