



Central Hypoventilation Syndrome

Patient and Carer Information Booklet

1st Edition 2012

This booklet aims to provide patients and carers with basic information on how clinicians diagnose and manage CHS, including its most common form Congenital Central Hypoventilation Syndrome (CCHS). It also provides information on living with CHS. It is available from www.ichsnetwork.eu

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Preface



Central hypoventilation syndrome (CHS) is a rare condition that has been recognised only in the last 40-50 years. The majority of health professionals will never have come across CHS and even clinicians looking after patients affected by CHS will often have only looked after one or two patients. As medicine advances, investigations and management skills become increasingly complex and it is more difficult for these clinicians to keep up to date with the specific issues in rare conditions. Clinical networks have developed, where smaller numbers of clinicians take special interest in larger numbers of these cases.

For CHS, clinicians in France established the first national network and then began to develop links with clinicians in other European countries. The European CHS Network began with a handful of clinicians in 2004 and then in 2009 secured funding for a European development project to develop a CHS Registry, look at services across the EU, develop clinical guidelines, a web site and patient & carer information. This booklet represents one of the first results of this pan-European collaboration and we hope that it serves its purpose. It is important that the clinicians are acknowledged and so they are listed below. Finally, if the patients, families and carers feel this booklet could be improved, please let us know.

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Introduction

Central hypoventilation syndrome (CHS) is a group of disorders involving under-breathing due to a problem in the way the brain processes and sends out signals to the diaphragm and chest wall muscles of breathing. The most common form is congenital central hypoventilation syndrome (CCHS) and presents in the first month of life, often shortly after birth. Milder forms of CHS may present later in childhood or even in adulthood (late-onset CCHS or LO-CCHS). There is also a form of hypoventilation associated with hormonal problems presenting in mid-childhood, known as ROHHAD. All forms involve to some extent problems in other parts of the body's automatic nervous system.

It is unknown how many children there are with CCHS. It has been estimated that the incidence is somewhere between 1 affected baby in every 50,000 – 200,000 live births, making this a very rare condition. In the larger European countries, each probably has between 50 and 100 affected individuals. There is no complete information on where children and adults with CCHS live in most countries, although a pan-European CCHS Registry is being set up, as currently exists in France.

CCHS has been referred to as Ondine's Curse, an unfortunate name which was given to the condition in 1962. This name for the condition comes from a German legend in which the nymph, Ondine, placed a curse on her unfaithful mortal husband, removing all his body's automatic functions and he therefore had to remember to breathe. When he went to sleep, he stopped breathing. However, most individuals with CCHS do not stop breathing altogether, but do not breathe deeply enough.



Understanding Breathing

Why is breathing essential?

Respiration (Breathing) is a vital process by which oxygen is delivered to the blood and carbon dioxide, a waste product of metabolism is eliminated from our body. In the lungs, oxygen from the inspired air is bound to the red blood cells and transported within the blood stream to all cells in the body. Cell function and survival depend on the continuous provision of biochemical energy (“fuel”) through a process called “glycolysis” in which sugar (glucose) and oxygen are consumed (broken down) and carbon dioxide and water are produced. While the body has large reserves of glucose to sustain episodes of fasting there are no stores of oxygen and tissue injury may occur within minutes when breathing stops.

How does breathing work?

Our breathing apparatus consists of the airways (nose, throat, trachea, bronchial tree), the bony rib cage, the breathing muscles (diaphragm and chest wall muscles) and the two lungs. Breathing is driven by the brain which sends regular impulses via the spinal cord and peripheral nerves to the breathing muscles. Muscle activity increases and decreases the volume of the chest, moving air into and out of the lungs. Gas exchange occurs while the lungs are filled and oxygen diffuses from the air space into the blood and carbon dioxide moves the opposite way.

Picture of whole respiratory system

How is ventilation controlled?

Both the concentration of oxygen and the concentration of carbon dioxide in the blood are closely monitored by specific nerve tissue sensors, mainly in the brain. The normal pressure of oxygen in arterial blood (PO_2) is 70-100 mm Hg (9.7-13.3kPa) and the oxygen saturation (SpO_2), which can be measured more easily by pulse oximetry, is 95-100%. The normal pressure of carbon dioxide (PCO_2) is 35-45 mm Hg.

The amount of air that is inhaled with each breath is called Tidal Volume (TV). The Respiratory Rate (RR) and the Tidal Volume determine the Minute Ventilation (MV).

$$TV \text{ (ml)} \times RR \text{ (min}^{-1}\text{)} = MV \text{ (ml} \times \text{min}^{-1}\text{)}$$

When metabolic demands and thus the need for oxygen uptake and carbon dioxide elimination rise, as with exercise or fever, respiratory drive will increase the rate and depth of breathing to adjust Minute Ventilation.

What is Hypoventilation?

In a variety of pathological circumstances respiratory drive may be insufficient to maintain normal gas exchange. These include depressed states of consciousness and central hypoventilation syndromes. Depending on the decrease in Minute Ventilation, arterial oxygen saturation drops and the concentration of carbon dioxide rises. While there are some compensatory mechanisms to maintain tissue oxygen supply in acute states of diseases, even mild degrees of chronic hypoventilation are harmful to the developing brain, the heart and the lungs.

How does breathing change with age?

The young and growing organism has a high demand for energy and oxygen. Minute ventilation is adjusted to these needs mainly through the respiratory rate, ranging between 40 breaths per minute in the newborn period and a rate of 12 - 18 in adulthood. In contrast, tidal volumes (about 7 – 10 ml per kg body weight) remain relatively constant over time.

The Presentation of Hypoventilation

What does hypoventilation mean?

In medicine, *hypo* means *below* and *ventilation* means *breathing*. So hypoventilation means 'under-breathing'. This occurs when breathing is insufficient to bring in enough oxygen to the lungs and breathe out sufficient of the waste gas, carbon dioxide. The oxygen levels in the blood are therefore low (hypoxaemia) and the carbon dioxide levels are raised (hypercapnia or hypercarbia), or there may be dependency on a ventilator.

Hypoventilation can be caused by diseases of the muscles, lungs, upper airways and the brain, particularly in the deep brain structures (so called brainstem).

Picture of sagittal section of brain showing brainstem

What is Central Hypoventilation?

Central hypoventilation means that the hypoventilation is due to a disorder at the base of the brain, the brain stem, which is situated just above the back of the neck.

Picture of sagittal section of brain showing brainstem

If central hypoventilation has either the finding of a specific genetic mutation (PHOX2B) or the absence of any other diagnosed disorder of the brain, nerves, muscles or metabolism and no other genetic syndrome, this is called central hypoventilation syndrome.

What is Congenital Central Hypoventilation Syndrome?

Congenital means that you are born with the condition. Symptoms are either present immediately or soon after birth, or the genetic abnormality is present but may not show itself for many months or years due to a milder version of the condition. If the symptoms appear after the first month of life or later, the disease is sometimes called late-onset CCHS (LO-CCHS).

Are there other types of central hypoventilation syndromes?

Hypoventilation that appears later in childhood and is associated with a rapid weight gain and hormonal disorders is called Rapid-Onset Obesity with Hypothalamic and Autonomic Dysfunction (ROHHAD).

How does CHS present?

Hypoventilation may occur only during deep sleep with normal breathing when awake. In other cases, breathing stops completely during sleep with severe hypoventilation during wakefulness. The ways this presents are as follows:

- needing mechanical (assisted) ventilation from birth
- episodes of turning blue, very pale or grey
- apparent life-threatening events
- severe chest infections
- poor weight gain or growth
- slow development
- heart failure
- seizures (fits or convulsions)

In children, we would also consider CHS if they have one of the above with one of the following:

- rapid onset obesity
- behavioural disorders

- excessive thirst
- hormonal disorders

CHS should also be considered in children and adults who have:

- severe sleep apnoea
- bad reactions to anaesthesia
- severe chest infections needing prolonged ventilation

How is hypoventilation diagnosed?

Hypoventilation is diagnosed by measuring the levels of carbon dioxide in the blood and finding measurements above 50mmHg (millimetres of mercury) or 6.7 kPa (kilopascals). These are pressure measurements and are made by either taking a blood specimen, using a stick-on sensor on the skin (transcutaneous carbon dioxide) or from exhaled breath (end-tidal carbon dioxide).

In hypoventilation, the carbon dioxide is found to rise during sleep, particularly during one stage of sleep known as Quiet Sleep (QS). Taking a blood sample may be inaccurate, as the needle puncture of the skin commonly causes upset, wakes the child and increases breathing effort.

What is the cause of hypoventilation in patients with CHS?

Patients with CHS do not react to changes in oxygen and carbon dioxide in the blood. This is because sensors in blood vessels in the neck and brain do not send messages to the brainstem correctly. The brainstem does not respond with an increase in breathing when needed. The affected individual does not recognise, either consciously or unconsciously, that their breathing is inadequate. He or she then has shallow breathing and does not take in enough oxygen or breathe out enough carbon dioxide.

Do patients with CHS suffer from other symptoms than hypoventilation?

CCHS and LO-CCHS (but not ROHHAD) are genetic disorders caused by mutations in [PHOX2B](#) gene. This [gene](#) is important for the normal development of the [autonomic nervous system](#) which controls many organs and muscles within the body. The [PHOX2B](#) mutations therefore affect many body functions.

About 20% of patients suffer from an absence of nerves in the large intestine (Hirschsprung disease). Others experience feeding difficulty with acid reflux, indigestion and difficulty swallowing solids. Some patients with CHS are at risk of developing cancer in the nerve tissue (neuroblastoma) in the adrenal glands (above the kidneys), neck, chest or spinal cord. Among other symptoms are abnormal reactions of pupils to light, sporadic profuse sweating episodes, thirst and abnormal regulation of blood pressure, heart rhythm and body temperature.

Introduction to CCHS

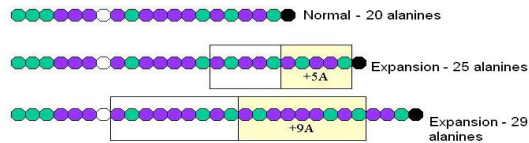
What is CCHS?

Congenital Central Hypoventilation Syndrome (CCHS; Ondine's Curse) is a genetic condition involving the autonomic nervous system, which controls the body's automatic functions, including breathing. It is **congenital** because babies appear to be born with this condition although some may not have problems immediately after birth. It is **central** because it involves the central nervous system, that is the brain. The breathing centres are at the base of the brain (brain stem), just above where the spinal cord enters the skull. **Hypoventilation** means under-breathing, and this is most serious during sleep – it is proven by measuring rises in carbon dioxide (the body's waste gas) and falls in oxygen levels in the blood.

Problems with breathing can occur also during wakefulness, although usually to a milder degree. So the breathing disorder ranges in severity from relatively mild under-breathing during only parts of sleep and normal breathing when awake, through to a complete cessation of breathing during sleep and severe under-breathing during wakefulness – this may particularly show with feeding (particularly in infancy) or concentrating.

What causes CCHS?

In recent years, we have learnt that CCHS is due to a problem with a specific gene that affects the way nervous tissue in the brain develops early in fetal life. This abnormality is thought to arise in most cases spontaneously at the time of the formation of the new embryo, a situation known as a spontaneous mutation. All cells of the affected infant will have the abnormal gene and parents will usually be unaffected. However, we know that in 5-10% of cases, one parent may carry the genetic abnormality. These parents may have this genetic abnormality in all their body's cells or in only some. This explains in part why some parents have been found to have hypoventilation after positive genetic testing, whereas most do not.



Differences in the gene in normal & CCHS

The genetic abnormality affects the control region, called PHOX2B, in one of a pair of genes on chromosome number 4 (there are 23 pairs of chromosomes in each cell of the body). The PHOX2B gene is responsible for development of brain tissue in the early embryo, ie before 8 weeks of pregnancy. At one point of the gene, there is a run of 20 proteins, called alanine, but the affected gene has anywhere between 25 and 33 alanines – this is called a *repeat polyalanine expansion*. This abnormality is not found in non-affected individuals. Thus PHOX2B has been described as a disease-defining gene. Experiments in mice have shown that if both genes are affected, the fetuses do not survive the pregnancy.

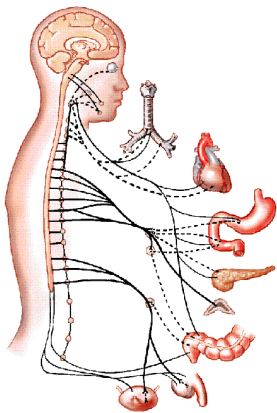
In those children where the PHOX2B gene is not found, there are sometimes other genetic findings in the PHOX2B gene.

If an individual with the PHOX2B mutation has children, they have a 50% chance of passing on the affected gene. If carrying the gene, an individual will be affected to some extent or other, ie there is no silent carrier status. So we are now newly recognising some adults with the condition, in whom it was never suspected earlier in life. If an adult with PHOX2B has a child, detection of the disorder is possible in the affected fetus early in pregnancy.

What is affected in CCHS?

The main problem affects breathing, but any of the parts of the body under automatic control may be affected. This includes the heart, eyes, gut, brain and skin.

Breathing



Affected individuals do not perceive and respond to changes in oxygen and carbon dioxide automatically, as would occur in unaffected individuals. This can lead to poorly inflated lungs, poor growth and development, severe pneumonia, heart strain, fits, brain injury and death.

To treat this, an individual must have their breathing assisted with ventilation. This is known as mechanical ventilation. The condition is life-long and mechanical ventilation will always be needed.

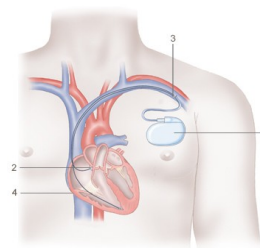
Mechanical ventilation may be given in a number of different ways:

- tracheostomy
- face mask or nasal pillows
- phrenic nerve pacing
- negative pressure ventilation

The choice of which technique(s) are used depends on age, severity of condition and experience of treating physicians. No single method is superior.

Heart

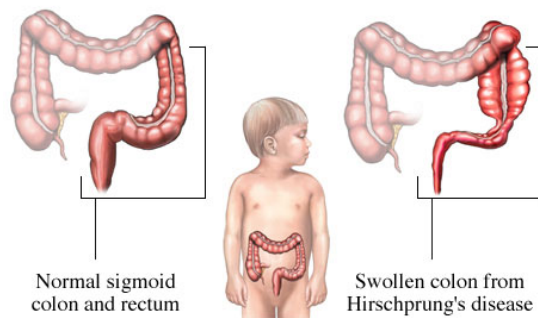
Individuals affected with CCHS may have pauses in heart rhythm (sinus arrest). This may present with episodes of dizziness, collapse or seizures. In some cases a cardiac pacemaker is needed. Mild cases are unlikely to have this complication.



A heart pacemaker

Feeding and bowels

The nerve control to the gullet, stomach and bowels may be affected. If the large bowel is affected, this may present with severe constipation or abdominal distension (known as Hirschsprung's disease) and requires bowel surgery. If the gullet and stomach are affected, this may be associated with indigestion, difficulty swallowing and poor appetite.



Brain and nervous system

Some individuals may show evidence of other problems affecting the brain and development. This may show as learning difficulty, epilepsy, or vision and hearing problems. Also, blue breath holding episodes, triggered by anger, pain or fear, are more common in early life than in unaffected children.

Individuals with more severe forms of CCHS are also at risk of developing abnormal growths of nerve cells (nerve tumours) that are part of the autonomic nervous system. These can be screened for routinely.

Photos of individuals with CCHS



ROHHAD

ROHHAD

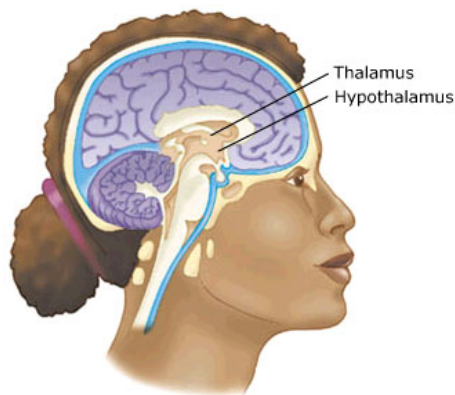
What is ROHHAD?

The name is an abbreviation of: Rapid-onset Obesity, Hypoventilation, Hypothalamic and Autonomic Dysfunction

It is a very rare disease with several associated problems: obesity, hypoventilation, hormonal problems, problems regarding the automatic control of body temperature, sweating, and heart rate and blood pressure changes, . Patients may also have changes in behaviour, such as aggression or showing excessive hunger and thirst. Respiratory symptoms can be severe, even to the point of having respiratory arrest needing resuscitation. Patients may also have eye disorders like strabismus (squint) or differences in pupil sizes. Obesity is a problem of major concern, even being confused as the cause of hypoventilation and missing the diagnosis of ROHHAD

What causes ROHHAD?

The cause of ROHHAD is unknown; since the disease has been reported in two members of the same family, it is thought to have a genetic origin. The disease involves a disorder of the hypothalamus, a part of the brain which controls some important basic functions, such as: hunger, thirst, growth, sexual development, thyroid function, breathing and behaviour.

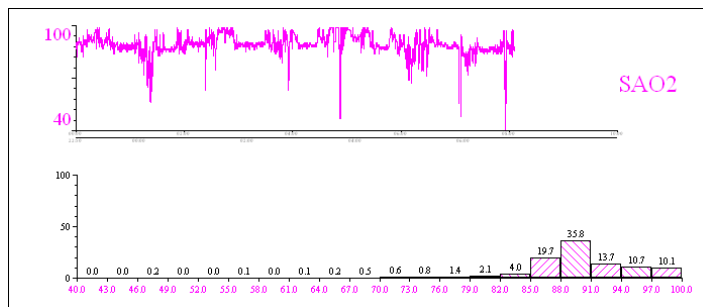


The Hypothalamus

How is hypoventilation diagnosed?

Hypoventilation is more common during sleep and can be diagnosed with different techniques:

Sleep oximetry recording. This will detect falls in levels of oxygen in the blood, but fails to detect less severe problems like breathing pauses (apnoea) without drops in oxygen. As apnoeic pauses can be normal, other types of recording will usually be needed.



Sleep Oximetry

Sleep cardiorespiratory recording. This study will detect apnoeic pauses, but lacks information about the quality of sleep. It may happen that a patient has no apnoeas because they have not slept deeply enough to show the disorder.

Polysomnography: This is the best exam that can be performed since gives all the needed information to evaluate breathing during sleep.

Diurnal (daytime) hypoventilation can be diagnosed by monitoring SpO2 and CO2 levels during the day. Detection of SpO2 < 95% and CO2 > 50 mmHg (6.7 kPa) allows the diagnosis of vigil hypoventilation.

What's wrong with the hormones?

Several hormone disorders occur together in ROHHAD. There may be inadequate production of hormones so that supplements are needed, including from: 1) the thyroid gland in the neck, needing thyroxine, 2) adrenal glands above the kidneys, so that cortisol is needed; and 3) the ovaries or testes, so that sex hormones including oestrogens or testosterone are needed. The regulation of thirst and hunger also depend on some hormonal control and can be faulty in ROHHAD.

What happens in puberty?

Because of the lack of some hormones that are needed during puberty to promote growth and sexual development, puberty may be delayed and extra hormonal therapy should be considered.

What's wrong with the nervous system?

People with ROHHAD have a normal body movements and thinking, and achieve normal intellectual functions like other people. They can have disorders of the autonomic (automatic) nervous system, however, which controls the heart rate, blood pressure, breathing, sweating, body temperature, bowel movements, etc. Affected boys and girls may show changes in the normal workings of these body functions.

Does the condition change over time?

As so few patients have been described up till now, relatively little is known about the disease. One paper about ROHHAD reports that patients commonly show the disease in the first few years of life, the first sign often being obesity. Obesity may be associated with the development of hormonal disorders, like an increase in the prolactin levels (from the pituitary gland in the brain), adrenal and thyroid insufficiency. Hypoventilation may follow after years. The disease does not improve with time.

How does hypoventilation show?

Hypoventilation can happen suddenly, sometimes after anaesthesia, for example, for adeno-tonsillectomy. Hypoventilation may also result in sudden respiratory arrest. This might be prevented by performing a sleep study in children who suddenly become obese, as this sign often occurs before hypoventilation.

Is the hypoventilation managed differently to CCHS?

Hypoventilation may have a range of severity. Some patients may have only nocturnal hypoventilation, others 24 hours a day hypoventilation. Those patients who need mechanical ventilation just during sleep are frequently managed with mask ventilation, while those needing 24 hours a day ventilation have been treated with ventilation through a tracheostomy.

How is the obesity managed?

Obesity can be managed with both hormonal and dietary control. It may aggravate any breathing problems during sleep and needs to be managed so that body weight is reduced.

Are there risks of tumours?

Tumours have been described in ROHHAD patients. They are mainly tumours of the abdomen, deriving from nerve cells. These tumours should be screened for in ROHHAD patients so that there is early diagnosis and removal, if needed.

What more is going to be learnt about ROHHAD disease?

The genetic origin of the disease will soon be defined and allow genetic counselling for parents and relatives.

A European registry of CHS patients, including those with ROHHAD, will help to better define this very rare disease. More data from patients will help our understanding of both the diagnosis and treatment of the condition.

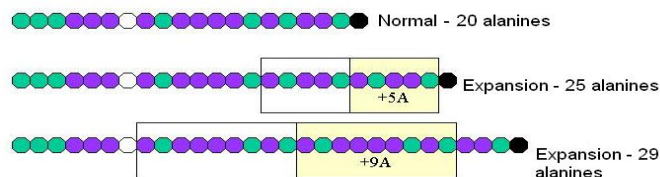
CHS and Genetics

Is a genetic test available?

A genetic test has been available since 2003 for the diagnosis of CCHS. The test finds an abnormality in every cell of the body of affected individuals, and this is never found in non-affected individuals. There are 23 pairs of chromosomes (the genetic material in each cell) and the test finds an abnormality (mutation) in chromosome number 4. The part of the chromosome where the genetic mutation exists is called PHOX2B.

What does the genetic test find?

The most common mutation, found in the 90% of patients, consists of a longer stretch of alanines, one of the amino acids, or building blocks of the DNA spiral. The number of alanines is increased from 20 (normal) up to between 24 and 39 alanines on one of the pair of chromosomes. This is known as a 'polyalanine repeat mutation' (PARM). This produces pairs of chromosomes with 20/24 to 20/39 alanines (the normal being genotype 20/20).



There are other mutations found in under 10% of patients, which are known as missense, nonsense or frame shifts of the gene.

Does the type of mutation predict how the patient will be affected?

There appears to be a relationship between some aspects of the clinical presentation and the type of mutation, including: 1) the risks of nerve cell tumours, like neuroblastoma or ganglio-neuroma; 2) the risks for Hirschsprung's disease; 3) the severity of hypoventilation and the likelihood for needing 24-hour/day mechanical ventilation; and 4) the presence of a disturbance of heart rhythm, a possible cause of sudden death.

For example, patients with a 20/25 genotype are unlikely to need 24 hours/day ventilation, whereas individuals carrying longer mutations have severe hypoventilation even when awake.

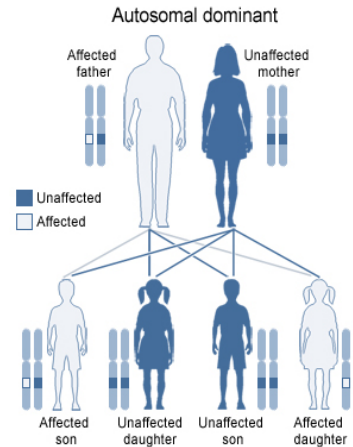
The presence of the other types of mutations (non PARM) can be associated with severe forms of CCHS, with both Hirschsprung's disease (with extensive gut involvement) and tumors of the neural crest more commonly found.

How else does the genetic test help?

Knowledge of the PHOX2B mutation also allows identification of either asymptomatic parents carrying the mutation, who have a higher risk of recurrence in subsequent pregnancies, or adults with mild hypoventilation, which has not been previously observed or diagnosed.

What about diagnosis in pregnancy?

It is possible to perform genetic testing of the fetus during pregnancy to provide prenatal diagnosis. Every affected individual has a 50% risk of transmitting the disorder to each child they have (autosomal dominant inheritance). As a consequence, a single mutation in one of the two



PHOX2B genes is enough to cause the disease.

Do parents carry the genetic mutation?

More than 90% of parents do not carry the genetic mutation. The genetic mutation is thought to occur spontaneously very early in pregnancy when the embryo is first formed. However, 5-10% of parents do carry the gene, so it is recommended that when the genetic mutation is found in an affected individual, the parents are tested.

Most parents carrying the mutation have not been studied to know whether they are affected by the genetic abnormality. Some only carry the abnormality in some cells of the body, a phenomenon known as mosaicism.

Who else needs genetic testing?

At present, only parents of affected or PHOX2B-positive individuals should be tested. Parents and affected young people should have genetic counselling to decide on who should have further PHOX2B testing.

What does the genetic test involve?

To perform the analysis of the PHOX2B gene a sample of blood must be sent to one of the specialized genetic laboratories existing in Europe ([link to the map](#)). Such testing must be done with a referring physician in order that all clinical information is provided.

Can the genetic test identify patients in later childhood or adulthood?

With the introduction of genetic testing, it has been possible to diagnose some adult patients with hypoventilation as a result of CCHS.

Some adults with chronic hypoventilation or late-onset hypoventilation have been found to have a PHOX2B mutation. In addition, some adults with obstructive sleep apnoea or bad reactions to anaesthesia have been found to have PHOX2B mutations. The mutation commonly reported in such patients is the (shorter) expansion of alanines, with a 20/25 genotype. The mild condition associated with this mutation explains why the disease presents in adulthood or remained unrecognised before. Sometimes precipitating events like the use of sedative drugs or acute respiratory distress highlights the onset of hypoventilation.

Is the genetic test always positive?

No genetic test is currently available for diagnosis of ROHHAD syndrome (rapid onset obesity, hypoventilation, hypothalamic and autonomic dysfunction).

In central hypoventilation syndrome with a negative PHOX2B test, the diagnosis is not certain and other explanations need to be looked for.

CHS and Mechanical Ventilation

Why is ventilatory support needed?

Patients with CHS are unable to breathe spontaneously during sleep and sometimes also when awake. CHS does not resolve spontaneously, neither respond to pharmacologic stimulants nor improve with advancing age. Therefore breathing in CHS patients must be supported **by a breathing device**. **The choice of respiratory support varies depending on the age of the patient and severity of symptoms.**

What types of ventilatory support are available?

Four types of ventilatory supports are currently available. They are described in details below

- **Ventilation via a tracheostomy**

The most common method of providing mechanical ventilation, especially in infants and younger children, is via a tracheostomy, that is a surgical opening in the trachea. A tracheal tube is inserted and connected to the ventilator via a special tubing system.

- **Mask ventilation – even called non-invasive ventilation**

Breathing support from a ventilator is delivered via nasal-prongs, nasal- or face-mask. (Fig.x).

- **Diaphragm pacing (DP)**

DP requires a surgical procedure by placing two electrodes into the chest on the phrenic nerves and two radio receivers under the skin. An electric stimulation of the phrenic nerves results in contraction of the largest and most important breathing muscle, the diaphragm. When the external transmitter stops sending the signals, the diaphragm relaxes and passive exhalation starts. (Figure x)

- **Negative pressure ventilation (NPV)**

There are three modes of delivering a negative pressure in order to perform breathing: the chest shell (cuirass Fig x), the Vest (Fig x), A Port-a-lung (Fig x)

For all three types of NPV negative pressure is delivered to the chest and abdomen to cause an inspiration as the negative pressure causes a suction of the air into the lungs.

What are the most common risks with different ventilatory support?

Infection: tracheostomy tube may lead to bacterial and viral infections that can spread to the lungs. As a consequence an increased amount of secretions can plug the airways or results in pneumonia. **Therefore** children with tracheostomy should be under a constant supervision. Infection can also occur with phrenic nerve pacing and NIV.

Leakage: An adequate ventilatory support is crucial to maintain optimal health in children depending on ventilatory support. Therefore, leakage around the mask must be reduced to the minimum by providing patients with well-fitting mask/prongs. Similarly, a well sealed chest shell or wrap is inevitable during negative pressure ventilators.

Malfunction: the respiratory support via DP can be adventured by a faulty (broken) antenna and the wire between the receiver and electrode or by a bad function of the pacer on one side of the chest

Airway occlusion: can occur when breaths are generated by a negative pressure or by phrenic nerve pacing without tracheostomy.

How does it feel on ventilatory support?

The ventilatory support itself does not cause any pain and therefore does not disturb sleep. Optimal settings of the ventilator are important to avoid bad synchrony between patient's breathing rhythm and ventilator settings. A wake person is recommended to be in the room when patient is sleeping to take care of such causes of alarms as disconnection of the tubes or antenna breakdown and leakage.

Will the child be able to speak with a tracheostomy?

During spontaneous breathing a special adapter, called "speaking valve", is placed on the tube to allow speech. Speaking is also possible during mechanical ventilation (Figure x)

Will the family be able to travel with a ventilator?

Most of currently available ventilators are portable and have an internal and external battery.

What is the best ventilatory support for my child?

There is no first choice ventilatory strategy, the mode of ventilation must be decided according to the age, the severity of the illness, the parents preferences and patient's needs in a specialised centre.

Mask (Nasal) Ventilation

What is mask ventilation?

Mask ventilation may use one of a number of different interfaces such as nasal mask, nasal prongs, helmet or facial mask (FIG xx). It involves ventilation without the need for a tracheostomy. This is also sometimes referred to as 'non-invasive ventilation'.

What are the *advantages* of mask ventilation ?

- No surgical procedure needed
- Does not have the potential for affecting speech and language development
- Less frequent respiratory infections

When should mask ventilation be considered for my child?

Some authors recommend ventilation by tracheostomy during the first years of life, while others advocate non-invasive ventilation. If ventilation is needed for 24 hours, tracheostomy is preferred.

If hypoventilation is less severe, non-invasive ventilation with a mask may be an option. The decision will depend, after discussion of the family, on the clinical state and on the experience of your doctor.

In some cases, mask ventilation has been started very early (two weeks of age). Mid-face hypoplasia may be minimized by alternating between nasal and oro-nasal masks every three days. To reduce the risk it is important not to seal the mask too tight. Silicone, customised mask can be helpful. Facial masks are avoided, as long as possible, in children due to the potential risk of aspiration.



Are there different sizes or shapes of mask?

Masks come in different shapes, materials and sizes, although for children there is less variety. The mask that fits best and provides the best ventilation must be chosen carefully.



What are the complications?

- conjunctivitis
- mouth dryness
- gastric distension
- skin sores on the face
- ineffective ventilation due to mask displacement and/or to air leaks (i.e. if the child moves a lot during sleep)
- mid-face hypoplasia is a serious long-term complication related to daily compression from mask on the face (see Fig xx)



CCHS child with nasal mask and three days later with facial mask.

Facial mask may also prevent air leakage through the mouth when it opens during sleep.

How must I care for the interface?

Prongs and mask need to be changed periodically to be sure they are in good condition and the size is adequate.

The mask must be kept clean, washing it every day.

Liaison with the health team will help ensure the best use and care of the mask.

Tracheostomy Ventilation

What is a tracheostomy

An open connection in the front of the neck, which leads directly into the windpipe (trachea) – this is known as a stoma into the trachea, hence tracheostomy. It is created by an Ear Nose and Throat Surgeon under general anaesthetic specifically to allow assisted ventilation long term in CHS; it is also made in other medical conditions where the airway is inadequate in or above the trachea, eg at the larynx (vocal cords) or pharynx (throat).

What are the advantages of tracheostomy ventilation?

Ventilation by tracheostomy provides effective ventilation, especially when the airway above the stoma is prone to collapse or narrowing. In CHS, the brain fails to send sufficient signals to move the muscles of breathing enough, leading to insufficient air entering the lungs. These signals are also sent to the muscles of the throat, which fails to open as fully as a normal individuals. Whilst this may be managed by blowing air down the airway under pressure, as in mask ventilation, this may not always overcome narrowing or collapse of the airway. This is especially the case in young infants, where the airway is smaller.

When is tracheostomy considered for my child?

For most infants with CHS, tracheostomy ventilation will be considered the usual method of supporting breathing. This is especially the case if ventilation is needed the majority of the infants' 24-hour day, eg 12 hours or more, if needed during waking periods and where sleep-wake cycles are not yet established. Older children will also receive tracheostomy ventilation if they need awake ventilation for any period, or where mask ventilation is considered inadequate or unsafe, eg where the upper airway is inadequate to allow effective ventilation.

Is it for life?

At one time, tracheostomy ventilation was considered necessary for life; in some patients, this is still the case - for example, where awake hypoventilation exists. However, a proportion of patients with a tracheostomy are now able to have this removed when other methods of

ventilation have been shown to be effective. The permanent removal of the tracheostomy tube (decannulation) is undertaken when a patient transfers to mask ventilation and in some cases of phrenic nerve pacing.

How do I look after the tracheostomy?

Tracheostomies have a tube placed within them to ensure the stoma remains patent. The tracheostomy tube needs regular cares to be given, including suctioning, cleaning and changing. These procedures are taught to parents, carers and patients and their ability to perform these procedures are checked by skilled nursing / therapy staff. When shown to be competent, the suctioning and changing of the tracheostomy tube is then performed by parents and carers on a regular basis. The tube usually needs changing at intervals dependent on the make of tube, amount and type of secretions and other clinical factors.

What equipment do I need to look after the tracheostomy?

All patients with a tracheostomy need equipment to suction and change the tube. In order to be mobile, a tracheostomy 'kit' is prepared with specific items, including spare tubes of the same and smaller sizes, suction catheters, forceps and suction device.

Does the tracheostomy need extra monitoring?

The patient with CHS needs monitoring of their ventilation whether they have a tracheostomy or other mode of ventilation. The most important monitoring includes pulse oximetry (oxygen saturation monitor), which will alarm if there is a serious problem with the tracheostomy tube or ventilation.

What carers are needed and when?

The patient with CHS needs carers to monitor and respond to changes in needs for ventilation, whether they have a tracheostomy or other mode of ventilation. The duration and type of carers needed varies depending on many factors, including severity of clinical condition, stability, age and availability. There are some families where minimal care is provided or available – this is less usual, as most families have at least overnight carers for some or all nights of the week.

What problems might occur?

Tracheostomy tubes may become blocked and fall out; they can be replaced into the wrong passageway and difficult to suction secretions from. They may increase the likelihood of bacteria entering the trachea or lungs and these can occasionally lead to serious infections such as tracheitis, bronchitis and pneumonia.

Inevitably, tracheostomy tubes effect vocalisation, especially during periods when ventilation is ongoing. It is unclear whether tracheostomy tubes effect the adequacy of lung or airway growth, although this is probably more dependent on the adequacy of ventilation. Tracheostomy tubes are generally associated with an increased risk of sudden death.

How do I deal with these?

Good care can minimise these problems. Care procedures, for example, should be performed as clean procedures; attention may be needed for changes in secretions obtained on suctioning; regular monitoring during sleep with pulse oximetry and use of a speaking valve are all ways to minimise risks.

Is it possible to speak with a tracheostomy?

Nearly all patients with a tracheostomy learn to vocalise and speak, although this may be delayed compared to other children. In these circumstances, some young children learn to use sign language.

Are there any swallowing problems or difficulty eating?

These can be associated problems particularly in infants and young children with CHS and tracheostomy; these are sometimes overcome by use of a gastrostomy – a stoma created into the stomach through the abdominal wall.

What about swimming?

Swimming should not be undertaken in patients with CHS and a tracheostomy; it may be enjoyed by other individuals with CHS, but swimming underwater should be discouraged, as the reduced sensation of asphyxia can lead to dangerously long durations of breath-holding

What ventilators are used with the tracheostomy?

There are a number of different devices used for ventilating by tracheostomy – different countries have medical equipment distributors that provide ventilators from specific companies. It is therefore difficult to be prescriptive about which devices should be used in patients with CHS. It is important the clinician prescribing and managing the ventilator has experience in long term ventilation.

Do leaks occur with the tracheostomy?

Leaks do occur with the tracheostomy, most commonly around the tracheostomy tube and up through the larynx and throat. This may help with developing vocalisations and speech. However, an excessive leak can impair the adequacy of ventilation. Thus a leak can be beneficial or harmful dependent on its severity. The development of an increasing leak over weeks or months may be an indication of a need to increase the tube size.

What does the child feel like with a tracheostomy?

There should not be any pain associated with the tracheostomy. However, most children dislike suctioning, although this is a necessary procedure in caring for a tracheostomy.

What will happen to the tracheostomy with growth?

An increasing leak will develop and need replacement of the tracheostomy tube with a larger size.

What types of tracheostomy tubes (cannulae) are used?

There are different types of plastic tubes used; manufacturers' guidelines should usually be followed for changing and caring the tubes. Tubes that are well tolerated long term are preferred.

Are tracheostomy tubes left open – do I need humidity, speaking valve?

Tracheostomy tubes have a varying need for humidity – sometimes this is provided only during ventilation; electrically heated humidity is most efficient, but there are devices similar to sophisticated filter papers, which trap exhaled (moist) air and moisten inhaled air (humidity moisture exchange, HME devices). Some children need no additional humidity.

Speaking valves are often needed during non-ventilated periods to allow vocalisations.

Phrenic Nerve Pacing

What is Phrenic Nerve Pacing?

Electrical stimulation of the phrenic nerves results in contraction of the diaphragm. Electrodes may also be connected directly with the diaphragm, although this is a new technique with little experience. Phrenic nerve pacing uses the patient's own diaphragm as respiratory pump. This resembles as far as possible the normal mode of breathing, because inspiration is induced by negative pressure within the thorax.

What are the parts of the pacing system?

The phrenic nerve pacing system consists of three external components (a battery-operated transmitter in connection with two antennas, see fig.1) and of four implants: two radio receivers implanted subcutaneously on both sides of the thorax and two electrodes sutured to the phrenic nerves within the thorax (see fig.2). During active pacing the transmitter creates a train of radiofrequency signals which are converted by the receiver into electrical pulses. The electrical stimulation of the phrenic nerves induces diaphragmatic contraction and inspiration. When the transmitter stops generating signals, the diaphragm relaxes and passive expiration starts. In children bilateral synchronous phrenic nerve pacing is recommended to achieve optimal ventilation.

What is necessary to do before implantation?

Before surgical implantation the following diagnostic procedures should be done: chest X-ray, tracheobronchoscopy, transcutaneous stimulation of the phrenic nerve at the neck together with ultrasound of the diaphragm in order to ensure normal function of the diaphragm, and finally careful neuromuscular examination to exclude myopathies. Contraindications to diaphragm pacing are: severe, chronic pulmonary disease, tracheo-bronchial stenosis, diaphragmatic paralysis, and myopathy. A relative contraindication is the age below one year.

What are the benefits of phrenic nerve pacing?

The benefit of phrenic nerve pacing is greatest in patients, who need the ventilatory support 24 hours per day. In these severely affected patients the breathing pacemaker offers freedom from the mechanical ventilator during the day. They use the small and easily portable pacing

system during daytime allowing to be mobile and to participate in all daily activities. Toddlers can carry the transmitter in a little rucksack on their back (fig.3).

During the night they should continue to use a positive pressure ventilator. Pacing more than 12 – 15 hours per day is not recommended because of the risk of neuromuscular fatigue.

Patients who need ventilatory support only during sleep time benefit also from the smaller pacing device, thus facilitating mobility during vacation, camping with school mates, etc.

Is it possible to perform pacing without tracheostomy?

It is possible to remove the tracheal cannula in older children. In young patients – less than six years of age – pacing in combination with a tracheostomy produces a greater stability of tidal volume, oxygen saturation and end tidal pCO₂. Closure of the tracheostomy in this young group might be complicated by a high risk of upper airway collapse during sleep. Between the age of 6 and 12 years successful weaning from the tracheal cannula is more likely, but it should be tried only with careful observation and monitoring in specialized centers.

What are the risks related to the pacing system?

The implantation of the pacing system needs bilateral thoracotomy (opening of the ribcage), general anaesthesia and postoperative treatment, which implies general risks related to these procedures.

Pacer malfunction is possible and is mainly caused by an elevation of the pacing threshold, which can occur during an infection. Very rarely a local infection around the implanted system can occur.

What are the most frequent technical problems?

Within a year the external antenna can break, which can be managed by changing the antenna. A couple of new spare antennas should always be at home.

After ten to fifteen years following implantation a defect of the implants may occur. Most frequently it is a break or an insulation defect of the wire between receiver and electrode. This problem needs a reoperation, which should be performed in a specialized centre.

What should be monitored at home during pacing?

Continuous monitoring of oxygenation (pulse oximetry, SpO₂) is mandatory during sleep. If possible end tidal or transcutaneous pCO₂ should also be monitored, especially during respiratory infection. Both parameters should be kept in the normal range (above 95% SpO₂ and between 30-45 pCO₂ mmHg) with a lower alarm limit for SpO₂ of 90% and the upper alarm limit for pCO₂ of 50 mm Hg.

Even more important than technical monitoring is the presence of a caregiver (that may be a nurse, medical student or a highly trained non-medical person) who can help in an alarm situation.

In patients who use the pacer during daytime a periodical control of SpO₂ in different states of activity should be done.

Does the phrenic pacemaker exclude or interfere with a cardiac pacemaker in the same patient?

Some patients with CCHS may require a cardiac pacemaker in addition to the phrenic pacer. In this situation it is important to implant a bipolar cardiac pacemaker to avoid interference with the monopolar phrenic nerve electrodes.

What is essential for successful phrenic pacing?

Essential for successful pacing is a highly qualified surgical technique during implantation and careful setting of the pacing parameters. Therefore surgery and follow up should be performed only in a centre with experience in phrenic nerve pacing. Annual in-hospital checks and evaluation of the pacing parameters are recommended.

The parents, the caregivers, and the patient himself should be trained how to deal with the pacing system. They can easily vary the respiration rate and the tidal volume according to the actual needs of the patient.

The goal should be to minimize the electrical stimulation stress to the phrenic nerves while providing optimal ventilation.

Follow-up

Transitions in Type of Respiratory Support

When to close the tracheostomy?

Transition from invasive ventilation to another ventilatory support is generally performed not earlier than 6 years of age in children who are ventilated only during sleep. In cases of patients who are dependent on a ventilator for 24 hours / day, such change may be considered later (10-12 years of age) using phrenic nerve stimulation while awake and non invasive ventilation during sleep.

How to switch from invasive to non invasive ventilation?

CHS patients who have their tracheostomy removed invariably start another kind of ventilatory support, usually mask ventilation or phrenic pacing; negative pressure ventilation is now little used.

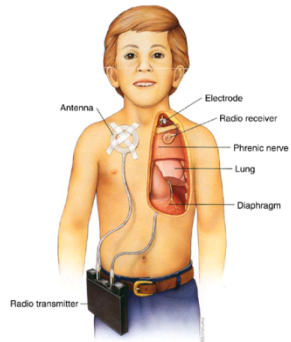


Mask ventilation has been the first choice for the majority of patients. However, some CHS patients who are used to tracheal ventilation find the use of the mask uncomfortable and difficult to begin, and they can be afraid to remove their tracheostomy tube. For this purpose a period of training can be provided, keeping the tracheostomy tube in place and plugged off. Eventually a smaller one can be inserted and plugged, increasing the breathing space around it. Once the patient is assessed during sleep, with both nasal mask ventilation and plugged cannula, they can safely be sent home. When the child becomes used to the mask, and is able to sleep all night with it, a second sleep study is performed. If both breathing and neurological measures are good, the cannula can be removed. Usually the stoma closes spontaneously over a few days to weeks, but sometimes surgery is needed.

How to switch from invasive ventilation to phrenic nerve pacing?

Recently, it has been suggested that patients may switch from tracheostomy ventilation to phrenic nerve pacing. Since phrenic pacing cannot be used 24 hours a day, this is suitable only for patients requiring ventilatory support during sleep. When the patient starts using diaphragmatic pacing, the following steps are essential before the tracheostomy can be removed:

- 1) the tracheostomy tube should be kept during the first months, as previously described for non invasive ventilation;



2) ventilation with diaphragmatic pacing is at first established using an open tracheostomy tube for some months;

3) after the tracheostomy tube is downsized, an overnight sleep study with diaphragmatic pacing and plugged tracheostomy is performed: if the result shows normal level of blood gases, the tracheostomy tube can be removed . In all such cases, patients must learn to use non-invasive ventilation in case the pacer malfunctions, allowing back up ventilatory support until the pacer is replaced.

Home Monitoring

What is monitoring?

Monitoring is the continuous observation of measures of the body's functions, for example breathing and heart rate. Some devices not only monitor, but also record the measurements for later study. In CHS, the usual type of monitoring used is pulse oximetry (also known as oxygen saturation monitoring, SpO₂).

Why monitor the oxygen levels?

Oxygen is critical for the body to function. It is taken in through the lungs from the air we breathe in and circulated around the body in the blood stream. Keeping adequate levels of blood oxygenation (SpO₂), is crucial for survival, adequate growth and learning. In CHS, the breathing is insufficient to keep the oxygen levels normal. Monitoring will inform us what levels are being achieved at any moment in time.

Monitoring is performed using devices that can continuously monitor the levels of oxygen in the blood, but without taking blood samples. Monitoring oxygen tells us about adequacy of ventilation and alerts carers if a life-threatening event occurs. The monitor emits an audible alarm that allows carers to take appropriate steps to restore normal ventilation and oxygen levels.

When do we monitor oxygen?

Monitoring oxygen levels is recommended during ventilation and whenever the child is left alone and likely to fall asleep. Sometimes monitoring is done during wakefulness in the daytime. Your physician will decide this.

How do pulse oximeters work?

Pulse oximeters use the colour of blood to tell us about the amount of oxygen being carried. Blood rich in oxygen is a brighter red colour, while blood depleted in oxygen is dark in colour. The sensor on a pulse oximeter shines red light through the skin and this is variably transmitted to a sensor (probe) depending on the oxygen levels. The measurement is dependent on having a good pulse in the way of the light path and this is usually shown on the front of the oximeter by a bouncing light bar or wave.

What are normal oxygen levels?

These are 95-100%.

When are low oxygen levels dangerous?

Short-lived drops in oxygen may occur in children without CHS when they have short pauses in breathing during sleep. These do not usually cause harm. There is evidence that the more time children spend with lower oxygen levels (<92%), the more likely they are to have effects on their growth and learning. Exact cut-offs cannot be easily defined. Low alarm settings on your pulse oximeter will be decided with your physician.

What may affect the oxygen measurement?

The probe may not detect a pulse if:

- there is a lot of movement
- the foot or hand is too cold
- the probe is too loose or too tight
- there is very bright light
- the probe is too old
- the probe is displaced (the LED is not opposite the sensor)

You need to be taught how to apply the probe correctly and how to obtain and read proper measurements.

What do we do when the monitor sounds an alarm?

Monitors may produce true alarms, when the oxygen level is low, or they may sound false alarms, which identify that the oxygen level is not being measured correctly. It is helpful to learn how to distinguish these, for example, by examining whether there is adequate pulse detection.

If the alarm is due to poor pulse detection, check the probe or re-site it. If the alarm stops and the values shown on the monitor return to normal, it means that this was a false alarm.

If you are not sure, or the individual looks unwell in any way, you should respond as if the oxygen level is truly low. Check whether the chest is moving and whether he/she is responsive. These may indicate either a breathing problem or cardio-respiratory arrest: see Emergencies on page xx.

Are there any risks from the oxygen monitoring?

You need to know how to look after the skin to avoid harm. A too tightly attached probe can affect the blood supply or burn the skin.

What else can be monitored?

Another sign of inadequate breathing is a high level of carbon dioxide (CO₂), the waste gas we normally breathe out. When breathing is inadequate, the carbon dioxide may rise and cause sleepiness or coma. It is possible to measure CO₂. There are two ways:

1. this measures carbon dioxide in the exhaled air from the nose or tracheostomy (end-tidal CO₂), or
2. by a heated probe placed on the skin (transcutaneous CO₂)

Patients will usually have carbon dioxide measured in the hospital or during a sleep study. Some patients have their own carbon dioxide monitors for use at home. Sometimes this may be used to guide changes in the settings on the ventilator.

Pulse oximeters and other devices also measure the heart rate. There is a wide range of normal heart rates, which vary with age. Usually low alarms will be decided with your physician.

In patients suffering from CHS, the minimum home monitoring is the pulse oximeter. Monitoring must be carried out during sleep and every time the individual is asleep or left alone.

Services and Follow-Up

What help and support is available to care for my child at home?

Most parents manage to look after their children at home, either alone or with help from carers and community nurses, sitting in the home overnight. The decision to have carers in the home is affected by parental preference, the severity of the child's condition and associated problems, and the ease of obtaining funding to pay for night carers.

What equipment is needed at home?

Children will need oxygen monitoring when asleep, and while still very young, when falling asleep, particularly if left unattended. Some families also have home carbon dioxide monitors to help ensure adequate ventilation, identify if the child is becoming less well and allow adjustments in ventilator settings. Most families will have two ventilators and back-up power systems. Despite all the equipment, it is possible for families to organise holidays abroad.



Pulse oximeters & carbon dioxide monitors

What happens before we are first discharged from hospital?

In order to look after your child at home, you will need a number of issues to be organised. This is best done by a specialist health professional working with you to co-ordinate all the services you need.

Before leaving the hospital, the following activities need to be completed:

- order and purchase of equipment
- installation of oxygen
- appointment of additional carers
- training of parents and carers in:
 - use of ventilator
 - use of monitoring equipment
 - care of tracheostomy (if present)
 - resuscitation
- modification of housing, if needed
- transfer of responsibility of care to community / home care team
- application for available financial support
- agreed plans for dealing with emergencies
- agreed plans for community and hospital follow-up

Many of these will need review at regular intervals (for example, initially every few months and falling to annually) and this is best achieved with the help of a specialist health professional, such as a clinical nurse specialist or social care team leader.

Will we need to come back to the hospital?

This will be needed for the following reasons:

- for emergencies, see the separate section
- for regular review – see below

What regular follow up will my child need?

Children with CCHS have regular reviews to check for a number of issues. ***The exact time interval for reviews will be decided between the family and physician.*** Review of the following will be needed:

- to assess the adequacy of ventilation
the interval will depend on the age, severity of condition and the centre
- to check the mask fitting, tracheostomy or phrenic nerve pacing
- to determine whether there have been significant respiratory problems, such as chest infections (reflecting either inadequate ventilation or other lung problems)
- to check on growth and learning
- to assess for any of the associated problems (*see page xx*), and
- to make sure all care needs are being met.

The latter will often be helped by having a local care co-ordinator to oversee the care, and a regular multi-disciplinary meeting to review the care package organised for the family.

Which professionals may be involved with us?

- Specialist to review CCHS (who may be one of the following two)
- Specialist to look after ventilation, eg respiratory, anaesthetic or intensive care consultant
- Paediatrician to look after development and deal with any neurological problems
- Sleep study technicians
- Nurse specialist to co-ordinate care
- Therapists, such as physiotherapists, speech and language therapists (SALT)
- Social care / services to help with home care and financial support
- Psychologist / counsellors

Daily Life

What do people with CHS need to carry with them?

For most children and adults who need ventilation at night only, there is no need for any equipment to be carried with them in the day, apart from that needed to look after the tracheostomy: ie suction and emergency tube change. For infants and young children who still have daytime naps, or those who need ventilation during part of the day, the individual should have their ventilator, tubing (and facemask, if applicable) and a self-inflating bag. When used, patient monitoring will also be needed, ie pulse oximeter.

Patients may wish to carry a 'disease identification' card, 'patient passport' or list of emergency contact numbers, or wear a medical alert bracelet in case of emergencies.

Are different modes of transport safer, or unsafe, for people with CHS?

Individuals with CHS may travel by any means. However, some preparation is needed before undertaking long haul flights, including contact with the airline if ventilation is likely to be needed. Most adults and children have lower oxygen levels during commercial airline flights, including individuals with CHS. Whether oxygen is needed for CHS patients is uncertain, but pulse oximetry may be applied in flight and, if planned, ventilation commenced if SpO₂ falls, eg <90%.

Do children with CHS need extra help at school?

There is an increased likelihood of special educational needs for individuals with CHS. These should be assessed before beginning full-time schooling and at intervals thereafter. Children should not be disadvantaged if they have any special needs, eg dyslexia or shortened concentration.

All school staff who come into contact with the child with CHS should be aware of the condition, especially in relation to any emergency needing airway clearance or assisted breathing, eg reduced consciousness. Additional staff or training for staff may be needed for younger children with tracheostomies.

Can children with CHS play sports?

Individuals with CHS should avoid underwater swimming, as severely low oxygen levels may develop sufficient to produce loss of consciousness, but without a perception of this developing. Individuals with CHS should be closely supervised while swimming by a carer aware of their condition and the risk of low oxygen levels and altered consciousness.

Some children with CHS, and specifically any who are symptomatic, may need specific assessment of their exercise tolerance in order to guide what activities they may be included in.

Do children with CHS need the same immunisations as others?

Yes – all the usual immunisations should be given. There are additional immunisations that can be given to help reduce the risk of influenza respiratory infections, and to protect against some types of bacterial (pneumococcal) pneumonia (pneumococcal polysaccharide vaccine).

Palivizumab is a course of monthly injections of antibodies against respiratory syncytial virus (RSV), a virus which produces chest infections in the first year or two of life and may become serious in the child receiving long term ventilation. Palivizumab should be considered in children who are on long term ventilation (LTV) aged less than 12 months at the start of the RSV season.

Are there any other measures that need to be taken for the child with CHS?

Children with CHS are at particular risk if they acquire lower respiratory infections, as this may adversely affect their respiratory drive and lower oxygen levels. Exposure to tobacco smoke is closely linked with increased rates of respiratory infections, so measures to exclude smoke from the environment of children with CHS are advised.

Can people with CHS take medicines as usual?

Medicines with a 'sedative' effect should be avoided, unless ventilation has already been considered and planned for. Alcohol presents particular dangers because of the social use of this sedative.

Becoming Independent

Do people with CHS need to have someone nearby while they are asleep?

Individuals with CHS need some system whereby their sleep position, airway or ventilator settings may be manipulated in the event of an alarm on either the pulse oximeter or their ventilator. Such a system needs to either alert a carer, parent or partner, or ensure the individual is woken. The proximity of the carer, parent or partner who responds will depend on the layout of the home and use of electronic surveillance, intercom or monitors.

Can people with CHS drive?

There is no reason why individuals with CHS cannot drive.

Can people with CHS work?

Individuals with CHS can undertake work, ie paid employment, according to their abilities. As with any child at school, the employer should be made aware of the medical condition, so that appropriate interventions can be taken in the event of emergencies.

Can people with CHS have sex?

Yes, and they have had pregnancies and their own children.

Can people with CHS have children?

Yes, although there should usually be counselled by a doctor with expertise in genetics before becoming pregnant, in order that they can learn about the risks of the new infant having CHS. If pregnant, the mother with CHS should have increased monitoring of their condition.

Can people with CHS drink alcohol?

Alcohol has been shown to be linked to sudden death in people with CHS, and it should be drunk sparingly, if at all.

Alcohol is dangerous for patients affected by CHS and deaths have been reported in this population with the assumption of alcohol: teenagers are particularly at risk since they commonly drink alcohol without adequate awareness. Also little quantities can cause sleep and respiratory

arrest. Friends must also be aware of the diagnosis of CHS and of the need of mechanical ventilation in case of sleep so they can give an help. It is very important that patients affected by CHS avoid the assumption of alcohol in any case.

Can people with CHS smoke cigarettes?

Smoking of any type is discouraged in CHS and any other condition affecting breathing and the lungs.

Anaesthesia, Medicines & Immunisations

Is it possible to perform general anaesthesia in a patient with CHS?



Yes, an individual with CHS can have a general or a local anaesthetic. Specific supervision will be needed from the anaesthetist in order to plan care before, during and after the procedure. It is especially important to monitor the adequacy of breathing before and after anaesthesia.

Is it possible to perform local anaesthesia for an individual with CHS?

Local anaesthesia can be performed normally, as would be done, for example, in dental procedures and minor procedures in the emergency department. The doctor, dentist or nurse must be informed about CHS in order to avoid the use of certain anaesthetic drugs like nitrous oxide (an anaesthetic gas) or sedatives.

Are there any drugs that must be avoided?

The medical literature reports harmful events with the use of propofol for anaesthetic procedures for patients with CHS. Propofol is an intravenous anaesthetic that is commonly used in the operating room for anaesthesia. This drug can cause problems with the cardiac rhythm, particularly causing excessive slowing of the heart rate and should therefore be avoided.

Are there specific tests that must be performed before anaesthesia?

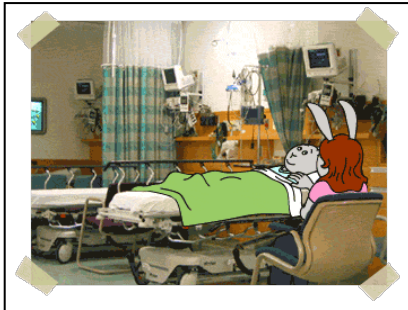
CHS patients should follow all the procedures needed by other patients, including a detailed pre-anaesthetic assessment. This should help clarify for the anaesthetist the method and settings for the mechanical ventilation in use, the type of tracheostomy tube or the model of the mask. The anaesthetist should also learn whether other aspects of the autonomic system might be a problem, including the heart rhythm, blood pressure, circulation and body temperature. It may be necessary to have an ECG or 48-72 hour ECG recording (Holter) performed in

order to find out about the presence of disturbances of heart rhythm.

Is it necessary to choose a specific hospital for anaesthesia in CHS patients?

General anaesthesia (where the patient is put to sleep) should be performed by surgeons and anaesthetists who are used to special conditions, that is, disorders of the control of breathing and the body's autonomic nervous system. In addition, it is essential that there is a recovery room, where the patient can be closely monitored as the patient gradually wakens from the anaesthetic. During this period, the patient may return to using his or her own kind of mechanical ventilation and to discontinue it only after completely awakening. It is preferable to choose a hospital already used to treating patients with CHS.

What kind of care should be considered for the period after surgery / anaesthesia?



After anaesthesia, patients affected by CHS should be monitored in a recovery room with pulse oximetry (oxygen saturation or SpO₂) and electrocardiogram (ECG – heart rhythm). Regular observations should be made of the SpO₂, heart rate, respiratory rate, blood pressure, body temperature and blood sugar. Ideally, carbon dioxide levels (CO₂) should be monitored as well. The anaesthetist will decide on the duration needed before the patient can be discharged from the recovery room. This may extend to a few hours – longer periods will usually mean transfer to a high dependency or intensive care unit.

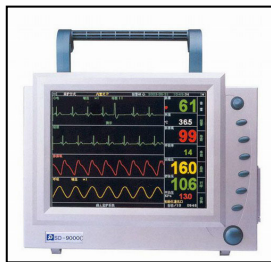
Is it possible to discharge home a patient on the same day as the procedure performed with general anaesthesia?

Whilst this is possible if they have fully woken and all observations have been repeatedly normal, it may be better to observe the patient in the hospital for at least 24 hours.



What kind of monitoring should be performed after pre-medication?

Pre-medication is the medicine given to patients before the surgery / anaesthesia. Sedative medication should never be used unless the patient is fully ventilated. If premedication is given, the patient should not be left alone. A trained nurse or the anaesthetist should stay close to the patient and monitoring of SpO₂ and CO₂ should begin. The patient's own mechanical ventilator must be available and may be started if oxygen and carbon dioxide levels begin to change from normal values.



And during general anaesthesia?

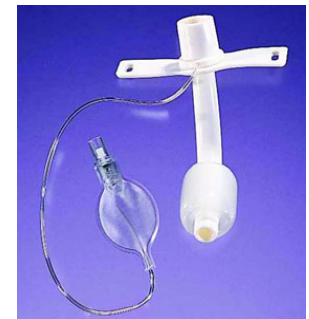
Some specific monitoring should always be available for CHS patients. Other monitoring can be utilized according level of invasiveness of the planned procedure. The standard monitoring will be: SpO₂ (oximeter); ECG (electrocardiogram); CO₂ (end-tidal or transcutaneous); non-invasive systemic blood pressure (BP); and body temperature (T°)

And after general anaesthesia?

All the monitoring will have to be applied also during the recovery period. The need for other monitoring should be assessed by the anaesthetist according to the condition of the patient.

Is it possible to use the patient's own ventilator during pre-medication and during recovery from general anaesthesia?

Patients affected by CHS will usually be asked to bring their equipment with them in order to have it available. It is possible that during the change over from anaesthesia to complete recovery, the equipment in use at home could be useful and needed. During the operation / procedure, a different type of ventilator is used.



Is it possible that the tracheostomy tube could be changed during the procedure?

Often uncuffed tracheostomy tubes do not fit well and make mechanical ventilation more difficult during general anaesthesia. It is possible that the anaesthetist will need to change the tube and use a cuffed tube during general anaesthesia. The uncuffed tube can then be re-inserted as the patient wakes.

Are there any problems with taking medicines?

Sedative medications should generally not be used in CHS unless specifically prescribed by a clinician with experience in managing CHS and monitoring with capacity to initiate ventilation is available. Most other medicines used in children on a daily basis are able to be used, but if there is uncertainty, check with your main CHS physician.

Is it safe to have all routine immunisations?

All routine immunisations should be administered, unless there is other specific reason for them not to be given.

Are there any extra immunisations that should be given?

Individuals with CHS are usually advised to have annual 'flu immunisation, as 'flu may cause a lower respiratory illness that can be serious. Other immunisations that may be considered include pneumococcal polysaccharide vaccine against pneumococcal bacteria, and in the first one or two years of life, palivizumab, which is a monthly therapy against respiratory syncytical virus.

Emergencies – Recognition & Response

What types of emergency can arise?

Individuals with CHS are at greater risk than other children of a number of emergencies, because of their condition and the treatments they need. Awareness of these and effective ventilation will lessen the likelihood of these happening. Early recognition of deterioration can lessen harm arising.

The main risks are breathing problems and cardiorespiratory arrest due to:

- i) problems with the airways or tracheostomy
- ii) fainting episodes or collapse (syncope)
- iii) breath-holding episodes (young children)
- iv) seizures (convulsions or fits)
- v) equipment failure, such as power failure or technical fault with ventilator

How do I recognise breathing problems?

As breathing is a vital function and this is the primary problem for individuals with CHS, it is especially important to be aware of how to recognise breathing problems.



Recession of the chest wall may not always show

In individuals **without** CHS, breathing difficulties are sensed as discomfort in breathing, chest tightness or breathlessness. In CHS, these sensations may not occur or occur late in an illness. Therefore reliance on these **symptoms** is not possible. Similarly, health professionals cannot rely on the usual **signs** of respiratory distress to indicate breathing difficulties, such as: fast breathing (tachypnoea), indrawing of the chest wall (recession), flaring of the nostrils, odd breathing noises and use of extra muscles of breathing.

In CHS, the most useful indicators of breathing problems include:

- looking pale, grey or blue
- sweating
- excessive tiredness
- any unusual breathing sensations
- falls in blood oxygen levels
- rises in carbon dioxide levels

It is important to have a pulse oximeter (saturation monitor; normal SpO₂ = 95-100%) ± carbon dioxide monitor available to use in the event of either respiratory illness (even colds) or with any respiratory symptoms.

How do I deal with breathing problems?

If an individual with CHS has the above symptoms or abnormal measurements of oxygen or carbon dioxide, either follow the emergency care plan you have been provided with or contact your health professional.



This is a risk in an individual with CHS

It is a risk to provide additional oxygen to breathe on its own without assisted ventilation, as this does not treat the under-breathing (as shown by the rise in carbon dioxide levels). In fact, giving oxygen alone may suppress breathing further, allowing carbon dioxide levels to rise even more and coma to follow. If oxygen is given, effective ventilation should always be provided and carbon dioxide levels should be monitored.

If the individual has stopped breathing or shows no signs of life, you need to perform cardiopulmonary resuscitation (also known as basic life support – BLS – or mouth-to-mouth) and call the emergency medical services. Health professionals will show you how to perform BLS and you should have practised on a manikin (dummy).

How do I manage problems with the airway (tracheostomy)?

If the individual has a tracheostomy, health professionals will show you how to manage problems with this, including what to do if it becomes misplaced or blocked. If you have a tracheostomy, there are changes to the usual BLS and health professionals will teach you these.

How do I manage a faint or a fit?

While these are more common in CHS, they are initially managed in a similar way to other individuals. In addition, it is important to ensure the individual is either breathing adequately, or they are ventilated. Usual first aid involves lying the individual down and free from any surrounding dangers, whilst keeping the airway clear, for example, by use of the recovery position.

Recovery position



If breathing is inadequate, as shown by no or poor chest movement or blue colour to lips, tongue and gums,, then assisted ventilation must be given. If a ventilator is not immediately available, use another way of giving ventilation, such as:

- a self-inflating bag
- mouth-to-mouth or mouth-to-tracheostomy lung inflations

Attempting to rouse the individual may increase ventilation.

Self-inflating resuscitation bag



How do I manage breath-holding episodes?

These are common in young children and often follow an unpleasant trigger, such as pain, fear or anger. Most are short lived and recover without treatment. However, some children have falls in oxygen causing blue lips (cyanosis) or slowing of the heart rate; these may cause loss of consciousness. Simple first aid is given, such as avoiding injury on objects surrounding the child. If breathing is inadequate, lung inflations should be given (as in basic life support or CPR).



Blue (cyanotic) breath holding with back arching

What equipment failures happen?

Your equipment will need to be serviced regularly to lessen the chance of it unexpectedly failing. Even so, you need to be prepared for the possibility that equipment does sometimes fail despite the best care.

Most equipment uses mains electricity and if this fails, each device should ideally run from a battery supply. This will include:

- the ventilator
- the pulse oximeter (sats monitor)
- suction (for tracheostomy)

In the event that the battery fails, it is important to have some way of providing lung inflations or suction mechanically. self-inflating bag is invaluable.



Self-inflating bag and mask

Other equipment failures are managed by having a second device or 24-hour access to technicians. Your physician will discuss this with you.

If you think that there are other emergencies that can occur, discuss these with your physician, as it is best for you and your child to be prepared for such occurrences.

Some do's and don'ts

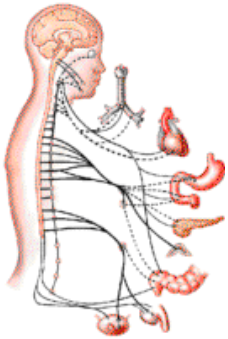
- ✓ Individuals with CHS should avoid sedative medication, including pre-medication before surgery, unless ventilation is planned for.
- ✓ Adults and young people should minimise alcohol intake, as its use has been associated with sudden death.
- ✓ Individuals may not perceive breathlessness and asphyxia and should be closely supervised when swimming. They are advised not to undertake underwater swimming.

Neurological Problems in CCHS

Why might my child have neurological problems?

CCHS is a genetic abnormality present from early in foetal life that affects the development of the autonomic nervous system (ANS). The ANS controls automatic functions such as breathing, circulation, heart rhythm, activity of the gut, body temperature and sweating, and so on, and is closely related to brain activity.

The main abnormality in CCHS involves a reduced ability to respond to changes in blood levels of oxygen and carbon dioxide by changing ventilation. Blood levels of oxygen may therefore fall and levels of carbon dioxide may rise, with harmful effects on the brain and heart. Some affected individuals may show evidence of other problems affecting the brain and development that are not necessary related to acute hypoxemic episodes and may be a direct result of the primary neurological problem associated with CCHS.



What are Seizures?

Seizures are symptoms of a brain problem. They happen because of sudden, abnormal excessive or synchronous neuronal activity in the brain.

How do they look like?

Seizures can cause involuntary changes in body movement or function, sensation, awareness, or behaviour. They are often associated with a sudden and involuntary contraction of a group of muscles and loss of consciousness.

Seizures can be provoked by acute hypoxemic episodes or can in some affected individuals occur unprovoked.

Optimal oxygenation and ventilation in CCHS patients reduces the chance for hypoxemic episodes but nevertheless in individuals with more severe forms of CCHS seizures may progress to persistent seizures disorder requiring anticonvulsive prophylaxis

Neurocognitive development

Will my child develop normal?

Children with CCHS are generally in the slow-learner range of mental processing abilities, compounded with suboptimal school performance and/or decreased intellectual function.

Neuropsychological function appears to correlate with a good ventilatory support and the severity of CCHS.

Most of children with CCHS attend regular classes in regular schools. However some affected individuals have significant learning disabilities requiring special education classes.

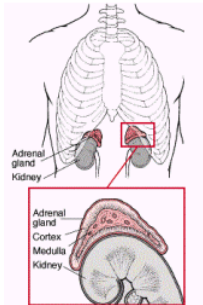
Can my child achieve normal intellectual functioning?

Most of children with CCHS attend regular classes in regular schools. However some affected individuals have significant learning disabilities requiring special education classes.

Normal intellectual function appears to be associated with an early diagnosis and optimal ventilatory support.

Regular and comprehensive intellectual testing can identify the problem and enable aggressive educational intervention that together with optimal ventilatory management can assure maximalization of child's neurocognitive

What about his/her motor developmental milestones?



It is a great chance that your child will achieve all motor developmental milestones in time but many CCHS infants present with lower muscular tone and/or major motor developmental delay needing inclusion of different neurophysiotherapeutical programs.

Neural crest cells are transient, migratory cells that during early foetal development give rise to diverse cells of ANS. Tumours of neural crest origin can frequently occur in individuals with more severe forms of CCHS. They may arise down either side of the spine, most commonly in the chest or abdomen, or in the adrenal glands just above the kidneys.

Vision

CCH patients frequently exhibit vision abnormalities reflecting neural control of eye function. Most have narrow pupils that react poorly to light. They can also have strabismus of various type and therefore problems with convergence on near looking.

Hearing

Some CCHS individuals can present hearing problems. These may be related to deficits in peripheral or central neural hearing pathways. It is important to diagnose hearing deficits early in the course of the disease to facilitate proper speech development in CCHS children that might be influenced by itself due to the need for the tracheostomy.

Many CCHS infants have swallowing difficulties. In order to facilitate nutrition they may require placement of the gastrostomy tube in their stomach. These can usually be removed at an older age.

CHS & the Gut

Why does CCHS affect the gut?

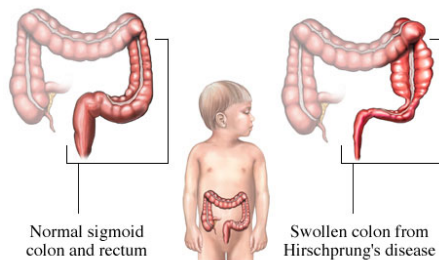
Yes, because CCHS involves the Autonomic Nervous System (ANS), which controls automatic functions such as breathing, circulation, heart rhythm, activity of the gut, body temperature and sweating. So problems can be expected in the gut, heart, and the eyes. And also certain tumors can occur more frequently.

What are the most common gut disorders?

The most common gut disorders are Hirschsprung's disease, gastro-oesophageal reflux disease and other motility disorders like diarrhoea without infection or swallowing problems.

What is Hirschsprung's Disease?

Hirschsprung's disease, also called congenital aganglionic megacolon is caused by defective bowel nerves. The length of the affected bowel varies.



The clinical presentation can be a delayed passage of first stool in the newborn period, a distended abdomen or different degrees of constipation. When it is more severe, it can present as bowel obstruction.

The treatment of Hirschsprung's disease consists in surgical removal of the affected part of the bowel and the two remaining ends of normal bowel are then joined up. Usually this is done in infancy. Occasionally, surgeons have to perform a colostomy, which means the bowel is brought to the surface of the abdomen, and the final repair is done at a later date.

What is Gastro-oesophageal Reflux Disease?

Gastro-oesophageal reflux disease (GERD) in children with CCHS is due to incompetence of the lower oesophageal sphincter, a ring-like muscle that tightens to prevent the passage of the stomach's contents back up into the gullet (oesophagus). If the barrier between oesophagus and stomach is not competent, gastric acid and other stomach contents reflux (flow backwards). This allows acid to inflame the oesophagus and the larynx (vocal cords) and even allow aspiration of food into the lungs.

Symptoms are variable, including repeated vomiting or respiratory symptoms like coughing. Affected individuals may also feel pain including heartburn or be irritable. Treatment is medication that reduces acid production and if this is ineffective, surgical intervention is possible.

What are Motility disorders?

Some of the children with CCHS suffer from motility disorders in absence of Hirschsprungs disease. Usually the food is moved through the digestive tract by rhythmic contractions (peristalsis).

In the presence of motility disorders these contractions don't occur in a coordinated fashion. Symptoms could be e.g. difficulty swallowing, vomiting, nausea, constipation and diarrhoea. Most of these symptoms could be treated by medication, special food and training. But in some cases, e.g. if the child isn't able to swallow it is necessary to use a feeding tube for a while. Most of the children will learn to swallow when they get older.

Cardiovascular Abnormalities In CCHS

What are the most common heart problems in CCHS?

The most common heart problems are arrhythmias and pulmonary hypertension.

What are arrhythmias?

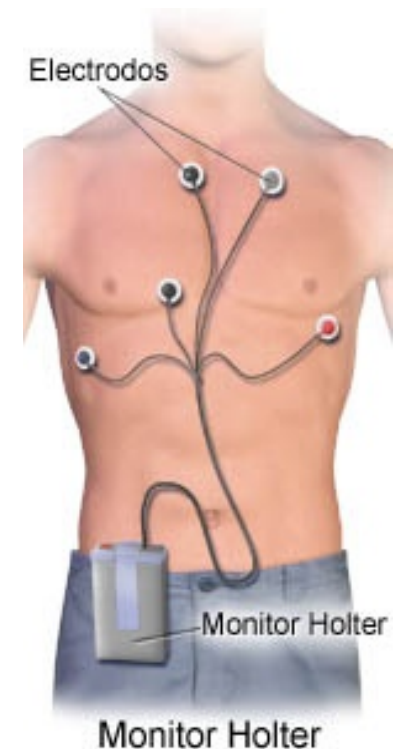
Arrhythmias are irregular heartbeats. The most frequent arrhythmias in CCHS are **bradycardias** in which heart beats at a lower rate or even stops during few seconds. These heart abnormalities can be asymptomatic or patients can have recurrent fainting episodes named **syncope** (a transient loss of consciousness and posture tone with fall down and spontaneous recovery). If these pauses are prolonged they can lead to cardiac arrest or even sudden death.

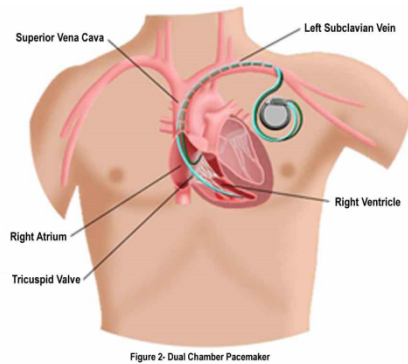
How to diagnose arrhythmias?

Abnormalities in heart rhythm can be detected by prolonged electrocardiography (ECG) monitoring lasting 24-72 hours that is also called Holter monitoring.

Can these problems be treated?

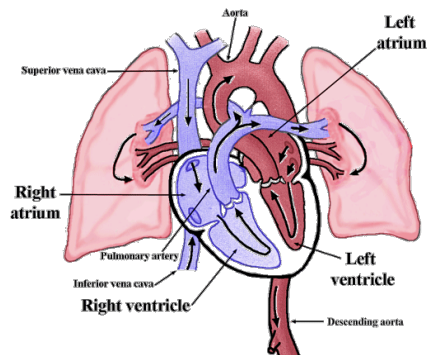
On the basis of Holter monitoring and symptoms cardiologist will decide on the need of medication or in severe cases a cardiac pacemaker. The pacemaker is a small device that is implanted under the skin. It has wires which analyses heart rhythm and if it's below a stablish value it sends electrical signals by wires to stimulate heartbeats.





What is pulmonary hypertension / cor pulmonale?

Pulmonary hypertension is high blood pressure in the arteries, that take the blood to the lungs to be oxygenated. Chronic low blood oxygen or high carbondioxide make these vessels to constrict their walls. Therefore the pressure in these vessels raises which is called pulmonary hypertension. Due to high pressure in these vessels the heart has to work harder to make the blood circulate through the lungs. If the pressure is too high the heart can't keep up, and becomes wider. This situation is called cor pulmonale.



How do I recognize pulmonary hypertension?

Mild pulmonary hypertension can be asymptomatic or cause bluish discolouration of the lips and skin, [fatigue](#) and [shortness of breath](#). When patients develop cor pulmonale those symptoms become worse and patients can have swelling around the ankles and feet (peripheral oedema), and abdominal swelling (ascites).



How to diagnose pulmonary hypertension?

Pulmonary hypertension can be diagnosed by a cardiologist using echocardiography (ECHO or cardiac ultrasound) and ECG, at physician agreed intervals

Can pulmonary hypertension be prevented or treated?

It can be prevented by avoiding low blood oxygen and high carbon dioxide levels. Therefore optimal ventilation settings need to be ensured early on.

Once, cor pulmonale has developed, it can be treated by different options like optimizing ventilation oxygen and different types of medication.

Are all fainting episodes due to arrhythmias in CCHS?

No, these children also can have fainting episodes related to orthostatic hypotension — also called **postural hypotension**. This is a consequence of low blood pressure that happens when you stand up. Postural hypotension can also make you feel dizzy or lightheaded, or causes blurred vision, also known as neurocardiogenic syncope.

Tumours in CCHS

Do CCHS patients often develop tumours?

No, but a few of the CCHS patients can develop tumours, which do not necessarily need to be dangerous.

The cells that transform and may build the tumours derive from nervous system cells. These cell bundles are called the neural crest. These tumours tend to present in early childhood.

Since the finding of specific changes in the genes of the CCHS patients, it has been found that not all patients have a high risk ever to develop a neural crest tumour



Especially those patients with longer polyalanine repeat expansion mutations, which means 20/28 to 20/33 and those with missense, nonsense or frameshift mutations, need to be assessed more closely. For further information please see the leaflet on genetic findings.

What are the symptoms?

Often the patient stays without symptoms in early stages, however later presentation depends mainly on the location of the tumour. In the abdomen, a tumour mass may cause a swollen belly or [constipation](#) or even chronic diarrhoea. In the chest a tumour may cause breathing problems. By pressing on the spinal cord a tumour may cause weakness and thus an inability to stand, crawl, or walk, or voiding problems

How to find tumours?

The tumours produce substances that can be found in the blood (like neurone specific enolase) or in the urine (catecholamine). Different imaging methods can also be very helpful.

Can these tumours be treated?

Yes, however the therapy of neural crest derived tumours varies according to their type, grade and location.

Surgery often is a choice and / or chemotherapy may be helpful. The therapy usually will be specific for the patient.

Reading List

Abbreviations and Glossary

Barium swallow – x-ray examination of the gullet (oesophagus) and stomach with a swallowed material that shows on x-rays

Echocardiogram (echo) – ultrasound scan of the heart

Electrocardiogram (ECG) – heart rhythm strip

Electroencephalogram (EEG) – brain wave recording

Holter – continuous ECG recording of heart rhythm, usually lasting at least 24 hours