VOLUME I

SLEEP DISORDERED BREATHING AND ITS TREATMENT IN CHILDREN

A Thesis submitted in fulfilment of the requirements for

Doctor of Philosophy

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SHORT TABLE OF CONTENTS

VOLUME II ACHONDROPLASIA

Abstract

PhD ABSTRACT

The establishment of a dedicated paediatric sleep unit over the past three years has allowed detailed investigation of a large number of children with sleep associated upper airway obstruction. This thesis explores the characteristics of upper airway obstruction and sleep associated breathing control abnormalities, in children who have been investigated in that unit. The "unit" began with three or four people performing children's sleep studies at the Sleep Unit (for adults) at RPAH; the results presented here include those studies. The methods used in this thesis have evolved through practical experience acquired in caring for children with breathing disorders in sleep.

This thesis is presented in two parts. The studies in the first section provide an overview of the presentation and treatment of the syndrome of obstructive sleep apnoea (OSA) as it occurs in infants and children. The second section is a more detailed exploration of OSA and its treatment in achondroplasia. These latter studies provide further insights into the disorder in this specific group, and therefore into some aspects of OSA in the broader population of children.

VOLUME I

More than seven hundred studies have been performed within the paediatric unit now. That we have been able to study this number of children within such a short time frame is one indication of how common sleep breathing disorders are in the paediatric population. Studying this number of children with upper airway obstruction has revealed some previously unidentified features which include the predominance of males even in the pre-pubertal age group.

Three chapters are devoted to studies which review treatments of OSA and patients responses to these. These studies demonstrate the need for conclusive investigation and treatment of children with OSA. Adenotonsillectomy may not always cure the disorder and nasal CPAP is a practical and viable treatment option. Effective treatment of OSA in children is associated with significant changes in their sleep architecture despite the apparent preservation of sleep structure when children have sleep associated breathing abnormalities.

Additional treatment has been required in 40% of the children where adenotonsillectomy was initially recommended and nasal mask CPAP has been used in eighty children to date. The development of a behavioural program which introduces children to nasal CPAP therapy gradually is one distinct factor in the successful use of CPAP in children. The second important factor has been the development of a range of paediatric nasal masks which allow for a universal good

fit and seal. There are unique aspects to using CPAP in paediatrics, including a maximum CPAP pressure. This phenomenon, and its potential mechanisms have not been previously described.

Repeat overnight sleep studies were performed in a total of thirty children after treatment (with either CPAP or adenotonsillectomy). Apart from the changes in respiratory status in these children there are also some striking trends in the sleep architecture following treatment. The most marked change is an increase in the percentage of slow wave sleep (SWS) seen, with proportionate reduction in stages one and two sleep.

Studies in eight children with spina bifida and associated brainstem dysfunction have revealed a high prevalence of OSA. Three of these children were commenced on nasal CPAP therapy and details of their results are presented.

Finally; a reminder that unusual disorders may masquerade as OSA. Acquired central hypoventilation has been regularly diagnosed in this paediatric unit and while this may indicate serious underlying pathology, it is possible for children to live an entirely normal life when adequately treated with nasal mask ventilation. The unique experience of establishing these children on nasal mask ventilation in sleep, in the home environment is detailed.

VOLUME II

Studies of 30 individuals with achondroplasia have confirmed a very high incidence of sleep associated upper airway obstruction in this population. Sleep architecture appears to be preserved even without treatment. Obesity was prevalent in this group and may underlie the high incidence of OSA.

Detailed pulmonary function testing in eight young adults with achondroplasia has failed to reveal any significant abnormalities which may contribute to, or result from, OSA. In fact, these pulmonary function test results demonstrate better function overall than the single previous report, and provide new information about pulmonary distensibility in these subjects.

Overnight growth hormone assays in nineteen subjects with achondroplasia provide a baseline of normal data, not previously available in this disorder. Five subjects had repeat overnight studies and these results indicate that growth hormone secretion is reduced during SWS in the presence of OSA even when sleep architecture was apparently preserved.

Current thinking is that respiratory abnormalities in achondroplasia are most likely secondary to compression of the brainstem at the level of the craniocervical junction. Measurement of somatosensory evoked potentials have been recommended to screen for this abnormality. A high prevalence of abnormal test results was confirmed in

this group. However, repeat studies performed after conventional treatment for upper airway obstruction demonstrated a reversible component to the neural conduction abnormalities seen in achondroplasia.

Follow-up sleep studies were also performed in eleven of the subjects with achondroplasia. A clear increase in the proportion of SWS was again demonstrated in association with improved respiratory status. One important feature, revealed in this group with achondroplasia, was that the adult subjects had a marked increase in the proportion of REM sleep which was not matched by their paediatric counterparts.

Acknowledgements

ACKNOWLEDGMENTS

This study spans a period of four years from inception to completion. The aims of my work have seemed impossible on more than one occasion. It could not have been completed without the invaluable help of people who have been prepared to support and encourage me during that time. I take this opportunity to acknowledge and thank all of those people.

I came into this work with the encouragement of a number of people at the Children's Hospital, Camperdown (RAHC). I thank Dr. Jonathan Gillis for the encouragement he gave me from the time I commenced work at RAHC. I recall a pivotal conversation with him, which he has probably long since forgotten, when he first mentioned the area of sleep disorders medicine. Professor David Sillence from Medical Genetics for his unswerving support. Much of this work could not have proceeded without his assistance and the co-operation of the patients from the Skeletal Disorders clinic. The team in the Department of Respiratory Medicine were my backbone as this work got underway. Drs. Craig Mellis and Peter Van Asperen in particular. Drs. Liz Fagan and Chris Cowell have also given generous support.

My early discussions with Professor Colin Sullivan led to the vision of a dedicated, research oriented, Paediatric Sleep Disorders Centre. This dream has since become reality, and the results presented here attest to this. One of the key features I have come to value in my work with Colin is something I first learned from my father. I

have been taught and encouraged by both of these friends to dream impossible dreams. Both gave their unconditional support while I went out to realise these dreams.

The process of developing the expertise necessary to perform so many studies of high standard with children has required a committed team. Fay Everett is a colleague and friend. I thank her for the many hours spent teaching myself and others the intricacies of sleep studies and the standards we should aspire to. Through Fay's expert care, we now have a team of five trained nurse technologists who handle these studies with true expertise.

The team at the Sleep Disorders Unit at the Royal Prince Alfred Hospital have all contributed to my work in an individual and collective sense. They welcomed me into the unit from the start and tolerated my intrusions and idiosyncrasies while they were introduced to the world of paediatric syndromes. I truly appreciate the friendship which has been offered. I particularly thank Michael Berthon-Jones for the thoughtful expertise he has provided along the way. His introduction to statistical methods and his listening and clear thinking skills continue to be very much appreciated.

Cheryl Cochineas, Peter Donnelly and Mark Jiminez require special thanks for their contributions to the technical aspects of the evoked potential, pulmonary function and endocrine studies in achondroplasia. Their work was performed with great care.

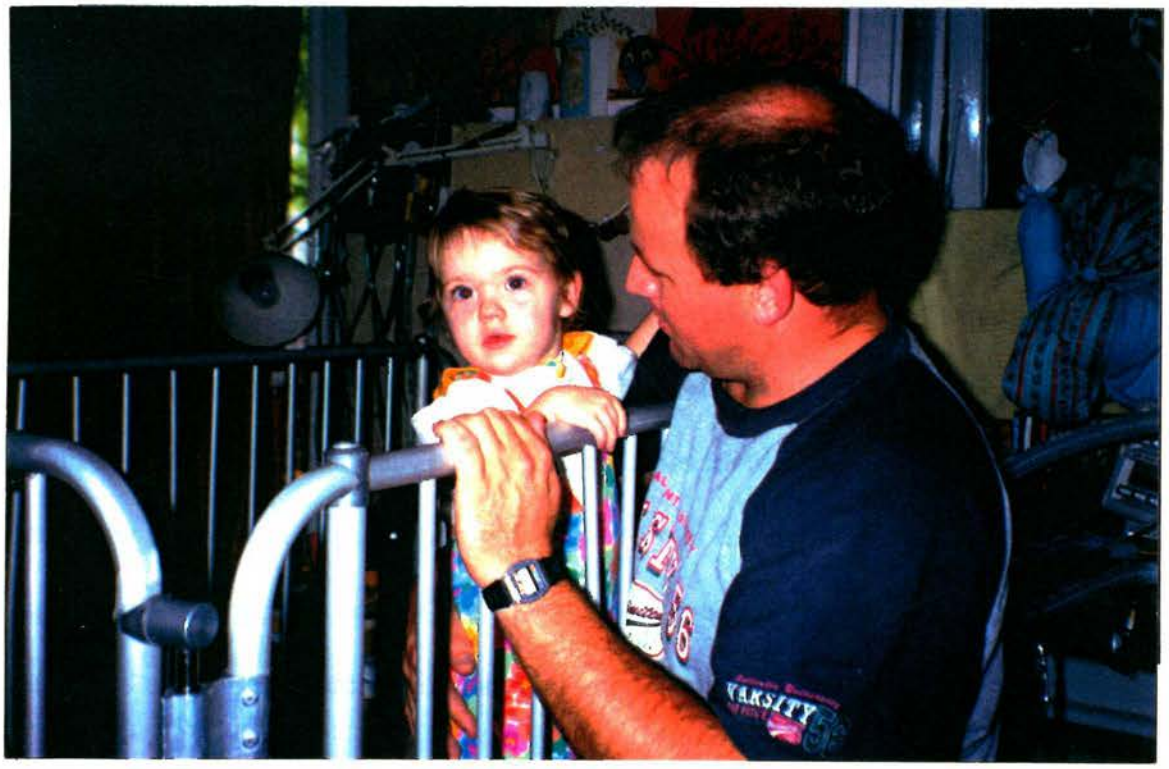
Cheryl's willingness to help with this research has been constant and I thank her for those extra special efforts made in order to achieve some of these studies. I thank Mark for the time which he has contributed to this project, and hope that his health has not suffered as a result of the extra coffee and cigarettes consumed on my behalf.

A progressively larger crowd seems to have been enlisted as the thesis drew to its conclusion. Simon's assistance has been invaluable and he seems to have taught me some English on the way. The sleep unit team were again enlisted for the proof reading process and then a new group arrived and came to the fore. Gus Cooper has managed to read the whole document from beginning to end - so it can be done!

I have a number of friends and loved ones who require special thanks. I thank my parents for their unerring support in all of my endeavours, this no less than any of the others. Jeanette, who has taken on this thesis as a project of her own. Geoff, who has encouraged me to the end. The Kathys, who were always willing to listen to my sometimes arduous sagas, and Louise, who acted as my trail-blazer in many respects.

The Canteen Fund at the Children's Hospital Camperdown, and the NH&MRC of Australia have provided my salary, for which I am grateful. I also thank the National SIDS Council of Australia for their financial support which saw the "David Read, National SIDS Council, Paediatric Sleep Disorders Centre" become reality. I trust that this thesis warrants the support that has been given to me by all of these people and groups in its making.

Introduction



1 INTRODUCTION

There is no doubt that sleep disordered breathing occurs in children, as well as adults. It is now important to identify the implications of these disorders for children, as a group distinct from the adult population. Research into these paediatric disorders is in its own childhood. The eclectic nature of these disorders, and their sequelae, is the subject of this thesis.

Until recently, there were two main routes to obtaining information about breathing disorders, in sleep, in children. Studies in neonates and young infants were primarily directed towards the identification of risks and correlations with the Sudden Infant Death syndrome. An important point made by these investigations is that any pathology in children is superimposed on the normal developmental and maturational aspects of the group. As part of this development process, there is a plasticity of the responses and reflexes present in children which sometimes dominates the final expression of the disorder.

Older children have generally been studied in units established for the investigation of adults and the results were, therefore, interpreted from this perspective. At this end of the age spectrum, there is more likely to be other underlying disease, which highlights some of the sequelae of the sleep disorder. It is much easier to identify the important sequelae of sleep disordered breathing in this group.

Studies of normal development of breathing and sleep have been performed. As increasing numbers of children are identified with obstructive sleep apnoea, the unique nature of their responses has emerged. The questions which I have addressed are

1. What is the nature of OSA in children?
2. What is the efficacy the available treatments?
3. What are some of the factors which predispose children to OSA?
4. What information about the pathophysiology of the disorder can be gleaned from studies of groups with a high prevalence of OSA?

The studies presented here are undertaken in children. They have been performed in a unit which caters specifically to children. It is only by taking this approach that these questions can be answered. This thesis provides new data about the disorders of breathing which occur in sleep in children. This first section looks primarily at the experience of obstructive sleep apnoea in a paediatric sleep unit and then a further examination of the treatments available.

Volume I

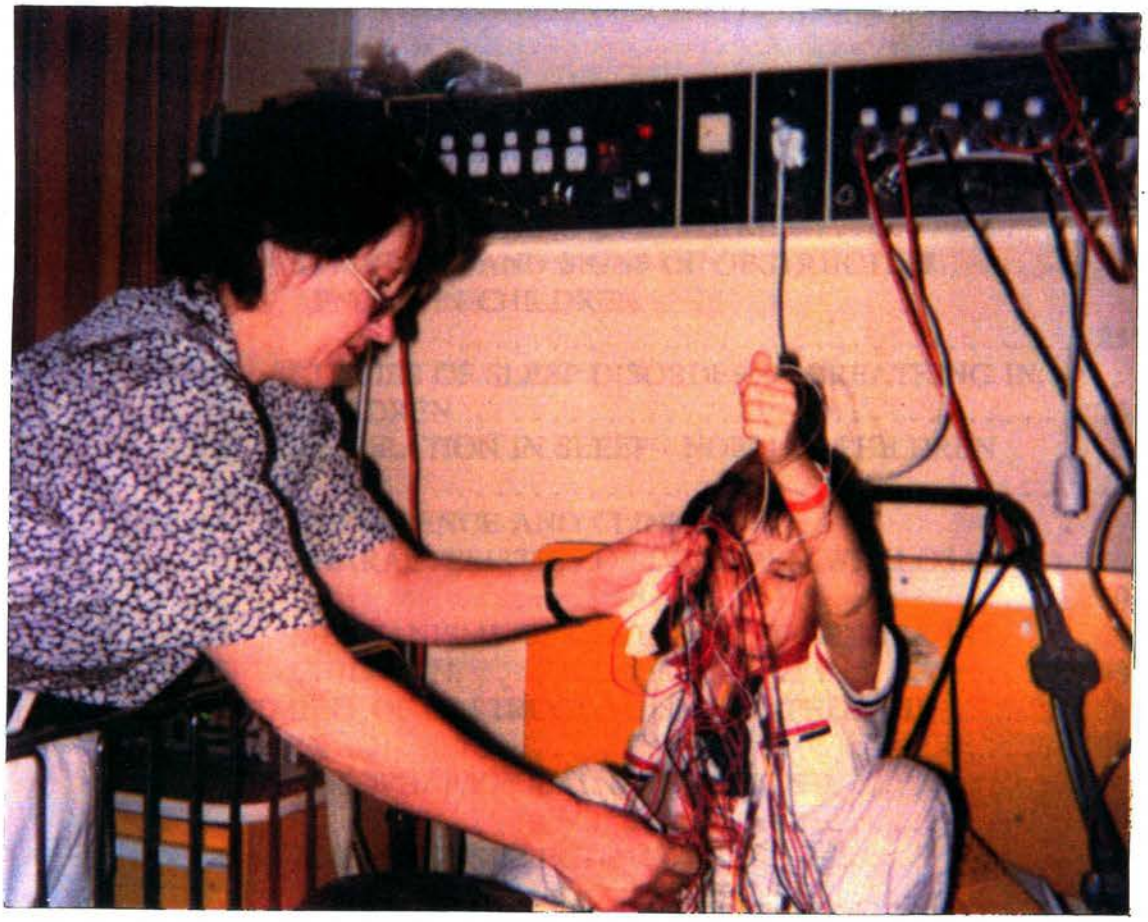


TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CRDI	- central respiratory disturbance index
EEG	- electro-encephalogram
EMG	- electromyogram
EOG	- electro-oculogram
GH	- growth hormone
CPAP	- nasal mask continuous positive airways pressure
mmHg	- millimetres of mercury
ORDI	- obstructive respiratory disturbance index
OSA	- obstructive sleep apnoea
pCO2	- partial pressure of carbon dioxide
RDI	- respiratory disturbance index
SaO2	- oxygen saturation
REM	- rapid eye movement sleep
S1-2	- stages one and two sleep
SEM	- standard error of the mean
SEPs	- somatosensory evoked potentials
SWS	- slow wave sleep
TST	- total sleep time

Chapter 1.

Introduction

1 INTRODUCTION

Sleep disordered breathing occurs in infants and children and it is associated with serious sequelae when not treated. Upper airway and respiratory dysfunction have are examined in the following studies. These studies were undertaken in a paediatric sleep disorders unit and examine the nature of sleep disordered breathing in children.

In this volume the studies concentrate on the nature of sleep disordered breathing in children, particularly obstructive sleep apnoea. Treatment of these disorders with nasal CPAP is one of the major developmental aspects of this thesis. The use of nasal CPAP in children has had limited success in previous reports. In the studies presented here CPAP has been shown to be an effective and practical treatment in children.

The wider use of this CPAP equipment has also been an important component of these studies. The nasal masks developed for children have been used successfully to treat OSA, even in children with an underlying disorder such as spina bifida. The masks were also adapted successfully for the delivery of nasal mask ventilation in young people where this therapy was required.

Chapter 2.

Literature Review

2 SLEEP DISORDERED BREATHING IN CHILDREN

2.0.1 SYMPTOMS AND SIGNS OF OBSTRUCTIVE APNOEA IN CHILDREN

In the adult, a combination of snoring and excessive daytime sleepiness (EDS) constitute a diagnosis of OSA until proven otherwise. Symptoms may also include early morning headache, cognitive impairment, impotence and systemic hypertension (Sullivan 141, McNamara 95). Up to ninety percent of adults with OSA are male (Shannon 131).

In children the presentation depends on parental observation. Disordered nocturnal breathing often commences in the first year of life but delayed diagnosis has been common. An average delay in diagnosis of up to 23 months has been seen in previous reports with 70% of children suffering serious sequelae (Brouillette 17, Gordon 47). More recently, the reported age at which children present varies from 7 years with 5 years of symptoms (Mauer 91, Marcus 87) to 14 months (Butt 22) presenting 6-12 mths after symptom onset. The incidence of snoring (91%,100%) and witnessed apnoea (81%,60%) has been high in those groups of children with subsequently documented OSA (Jeffries 72, Brouillette 18). Snoring is much less common in normal children (9% to 27%) (Hunt 66, Dyson 24)

Older children tend to present with daytime symptoms and behavioural disturbances. These include excessive daytime sleepiness (EDS), daytime fatigue, abnormal

daytime behaviour, learning disabilities and morning headache (Guilleminault 55). Less than five years of age the presentation tends to be with difficulty breathing while asleep, heavy snoring, witnessed apnoea, restless sleep, nightmares, night terrors, or nocturnal enuresis (Guilliminault 51). The major presentation is noisy breathing in sleep or snoring (continuous, heavy) occurring in almost all cases. This may begin as young as six months of age. Other symptoms in sleep include witnessed apnoeic episodes (60% to 88%), or irregular breathing and difficulty breathing when asleep (95% to 96%). Mouth breathing and abnormal or increased activity in sleep (restlessness) occur in 70% to 78%. Frequent waking (up to 87%), or insomnia, abnormal sleep positions (including upright, or on hands and knees) and sweating when asleep (68% to 96%). Nocturnal enuresis (18% to 38%) may be of recent, secondary onset. There may be difficulty waking, nightmares (up to 24%), associated sleep walking and/or night terrors (10%). (Gordon 47, Butt 22, Brouillette 18, Guilleminault 55, Lancet Editorial 32, Silverman 133, Leiberman 83, Krabath 77, Guilleminault 58, Potsic 117, Buckstein 20, Frank 39).

Chronic night time cough may be one of the symptoms, caused by intermittent aspiration of small amounts of pharyngeal secretions. OSA can aggravate other conditions such as asthma. Other disabilities may be made more severe by OSA. One frequent complaint is decreased stamina during athletic activities, with the child running out of energy before their peers (Dyson 31).

The complications of OSA in children can be severe and life threatening. Acute respiratory failure may be precipitated by upper respiratory tract infection (URTI) (Thach 143, Serratto 130). In early studies, up to 73% had serious sequelae at presentation, including pulmonary hypertension (Levy 84) which may result in secondary congestive cardiac failure. Systemic hypertension (8%) may be a symptom of patients older than 10 years (Krabath 77, Gaultier 43). OSA is one cause of failure to thrive (Brouilette 17) occuring as a complication in 27% to 56%. Other complications include developmental delay or behavioural disturbance in 5% to 23%, while 10% have massive obesity. Recurrent respiratory infections occur in up to 26%, and pectus excavatum has been reported. (Brouillette 17, Gordon 47, Guilleminault 55, Editorial 32, Silverman 133, Guilleminault 51, Buckstein 20, Frank 39, Dyson 31, Gaultier 43, Guilleminault 54). Anoxic seizures may occur as a complication, usually associated with CNS pathology, eg cerebral palsy or a recognisable syndrome with permanent neurological damage in 2 - 9% (Brouillette 17, Guilleminault 51). There is an increased incidence of sudden death, possible due to cardio-respiratory arrest (Potsic 117, Southall 136). Raised intracranial pressure (ICP) up 400mm of cerebrospinal fluid (CSF pressure) may occur secondary to hypercapnia (Seratto 130).

Other features which may be present include exacerbation with upper respiratory infections (Editorial 32). Lower respiratory tract infections, may be common with 25% having more than three in the past 12 months (Butt 22). Chronic upper-airway obstruction may result in craniofacial developmental changes that cause orthodontic

malformation. Craniofacial abnormalities are also recognised as a predisposing factor, but are not present in most (Carroll 23). Children who habitually snore did not have increased incidence of abnormal ears or facial dysplasia.

2.0.2 STUDIES OF SLEEP DISORDERED BREATHING IN CHILDREN

The diagnosis of sleep disordered breathing can be made by a variety of methods. Sleep wake patterns per se, may be reliably identified by the actigraph (a movement detector), or other ambulatory techniques (Sadeh 126). Simple observation of a child in sleep may reveal apnoeic events (Gordon 47) - particularly those at the severe end of the spectrum, with either frequent or prolonged apnoea. In order to document the frequency and severity of the obstruction accurately some form of quantitative study is required. Polysomnography is the most accurate diagnostic method (Brouillette 18, Potsic 117, Gaultier 43). Other investigations may be directed towards the demonstration of an abnormal upper airway, in either a static or dynamic manner (Gordon 47, Guilleminault 55, Dyson 31, Levy 84, Gunn 59).

Standard polysomnography includes recordings of sleep staging using electroencephalogram EEG (C_3-A_2) and/or (O_2-A_1), electro-oculogram (EOG), and submental electromyogram (genioglossus) via surface electrodes. Respiratory variables include inductance plethysmography of chest and abdomen, airflow and diaphragm electromyogram (EMG). Electrocardiogram (ECG), is generally recorded using chest leads. Oxygen saturation (SaO_2) and pCO2 may also be recorded. This

full study will be able to show partial upper airway obstruction which can lead to clinical symptoms without evidence of apnoea (Hunt 67). This technique may be modified (Guilleminault 58, Guilleminault 52, Carskadon 24) according to the research need, and available resources.

The syndrome of obstructive apnoea has been recognised to cause hypoventilation and cor pulmonale (Gastaut 42). Many children have predominantly obstructive hypoventilation, with long periods of continuous partial airway obstruction, associated with long periods of continuous snoring, without intervening silent (apnoeic) episodes (Southall 136, Carroll 23, Hunt 67). The criteria for defining apnoea in children are still being debated. For adults, apnoea is defined as failure to respire for longer than 10 s, with a duration greater than 10 s, with arterial oxygen desaturation of 4% or more. Hypopnoea refers to a fifty percent reduction in tidal volume (Guilleminault 51). The most important factor influencing the severity of symptoms is thought to be the amount of sleep disturbance; not the amount of oxygen desaturation.

Most children would fail to meet the minimum diagnostic criteria as stated for adults and there is a general consensus that using adult scoring criteria will underestimate the severity of obstruction seen in children (Marcus 125). The previously defined criteria of severity are also inapplicable; two of the four major criteria of severity in adults are EDS, and cardiac arrhythmia, which are generally not seen in children

(Carroll 23). However, there is no consensus yet about which criteria are sufficient to warrant surgery (Mauer 91, Guilleminault 58, Hunt 67).

2.0.3 RESPIRATION IN SLEEP - NORMAL CHILDREN

Studies have characterised sleep in normal children for age. Apnoea of 5 sec duration occurred with a mean total of 19 per night in girls, and 17 in boys. If longer apnoea (of 10 seconds duration) were evaluated, a mean of 3, and 5.5 total occurred respectively (Kahn 73, Guilleminault 51). All apnoea in these normal studies lasted less than 30 seconds and all were central in type. More than 50% occurred in stage one (S1) and NREM sleep. The 20 sec limit for defining pathological apnoea duration, which is used in infants, is not applicable in these older children (Guilleminault 51). A respiratory disturbance index (RDI) of > 5 apnoea per hour is abnormal for a young child 2-6 year old as these children have very few apnoea under normal circumstances (Guilleminault 55, Marcus 125).

Normal subjects have lower ventilation in sleep than awake, with minimum ventilation in REM sleep. In quiet sleep (QS) there is lower pCO_2 responsiveness, and minute volume is less for the same pCO_2 level. Hypoxic responses appear unaffected in QS. The normal pCO_2 increase in sleep is 2-8 mmHg. The changes in pO_2 are less, usually with a range of 3-11 mmHg. Normal SaO_2 variability is 2% or less. There may be a significant exacerbation of these abnormalities in children with chronic lung disease (Hunt 67). REM sleep is normally associated with phasic events.

A lower lung volume in active sleep (REM) may contribute to more rapid desaturation in this state, compared to an equivalent duration of apnoea in other states (sleep or wake) (Krieger 79).

2.0.4 PREVALENCE AND CLINICAL CHARACTERISTICS OF CHILDREN WITH OSA.

The prevalence of OSA in children is unknown, but estimated at 1.75 - 3.4% of the population depending on the age group surveyed and the method used (Gaultier 43). The estimated prevalence in adults is between 1.6% and 8.5% (Young 156, Bearpark 4) of the population, with increased morbidity and mortality in untreated disease (McNamara 95). More than 95% of patients with OSA have snoring. In a survey of 355 children 27% snored, and 6% had difficulty breathing in sleep (Brouillette 18). Other studies have estimated the incidence of snoring in children at 9-21% of the population (Dyson 31).

A preponderance of boys has been found in children with OSA in two studies of children with OSA, including one comparison with controls. The proportions and distribution of sleep architecture may be also be altered in children with OSA. Previous studies suggest that children with OSA slept less at night but more in the day than controls with 8.7 (8.1 hours), vs 10.2 hours of night sleep (Brouillette 18, Frank 39). Sleep disturbance may be recorded with considerably more stage one and two sleep (S1-2) (average 55.2%), but less stage 3-4 (SWS) (varying from none to 28.4%) compared to controls. Sleep is fragmented and associated with shorter REM periods. In severe cases sleep stage may only ever resemble stage 1 & 2 sleep. Studies have shown decreased REM sleep in up to 22% of affected children compared to age-matched controls. Children with OSA had 15.9% REM of the total

sleep compared to 20-25% in normal children. In 14% of affected children a paradoxic increase in the proportion of stage 4 sleep was seen. Total movement time also increased by 100-250%. Complete apnoea are said to be uncommon and usually not seen in SWS. Progression to SWS was delayed or precluded by the occurrence of repetitive apnoea. Marked sinus arrhythmia was always associated with sleep apnoea. (Guilleminault 55, Leiberman 83, Guilleminault 51, Frank 39, Guilleminault 54).

The most severe falls in oxygen saturation are reported to occur in those children with an underlying cause such as obesity, syndromes and severe facial dysmorphia (Guilleminault 55, Guilleminault 54) and OSA is common in children with a structurally small upper airway. Impaired ventilation in the Pierre Robin syndrome may be exacerbated by position - especially when supine. Other abnormalities associated with OSA are isolated mandibular hypoplasia, and syndromes of Treacher-Collins, Crouzon's, Apert's, Downs and Mucopolysaccharidoses where there is a high incidence of obstruction (Potsic 117). In patients with adenotonsillar hypertrophy, URTIs may precipitate or exacerbate obstruction (Thach 143). Persistent stridor from the perinatal period may also result in sleep related hypoventilation, and sequelae such as slow development (Levy 84). The incidence of congenital skeletal abnormalities contributing to upper airway obstruction has been reported from 27% to 50% (Hunt 66).

Electromyographic activity of accessory muscles and its association with upper airway obstruction has been formally evaluated by studying integrated EMG signals.

Sternomastoid, genioglossus and abdominal muscles were all recruited during sleep related airway obstruction in children. Sternomastoid muscles are active during inspiration, genioglossus in maintenance of airway patency, and abdominal muscles during expiration. The recruitment of the abdominal muscles suggests that there is increased expiratory, as well as inspiratory, resistance (Jeffries 72).

2.0.5 MECHANISMS OF OBSTRUCTIVE APNOEA IN CHILDREN.

Classic adult obstructive sleep apnoea consists of repetitive obstructed breaths, resulting in desaturation, followed by recovery. The associated hypoxia causes arousal, improved dilator muscle tone and relief of the obstruction. The resulting sleep fragmentation produces the daytime symptoms of sleepiness and poor cognitive function. The two cardinal features of sleep apnoea in the adult are snoring and excessive daytime sleepiness.

The mechanism of both obstructive apnoea and hypopnoea are the same. The immediate cause of the obstruction is upper airway collapse, as the muscular oropharynx collapses under negative pressure. Factors determining airway patency include airway size, neuromuscular tone and neuromuscular coordination. Tonsils and adenoids contribute to airway size. There is sleep associated loss of neuromuscular tone but there may also be secondary damage to the airway after snoring because of the trauma to the soft tissues of the upper airway (Sullivan 141). Any increased in the negative pressure of inspiration may shift the balance towards airway collapse. This includes upstream resistance which is not matched by increased muscle activity; retrognathia, adenotonsillar hypertrophy and other causes of increased upstream resistance. Increased respiratory effort then compounds the obstruction (Sullivan 141, Gunn 59).

Brainstem areas of respiratory control regulate both inspiratory pressure-generating muscles and the upper airway dilators. Either resistance to inspiration or decreased activity of the dilator muscles can result in airway collapse (Hunt 66). Both structural (genetic) and additional soft tissue mass, for example hypertrophied tonsils and adenoids. There is sleep associated loss of neuromuscular tone, but this may also suffer secondary damage after snoring because of the trauma to the soft tissues of the upper airway. Dis-coordinated upper airway respiratory function may be secondary to failure to coordinate with externally imposed ventilation.

Central apnoea may result from several mechanisms. Local causes include forebrain damage with loss of inhibitory input to brainstem reflexes. Reflex inhibition occurs in response to stimulation of local reflexes by upper airway closure for example the tongue touching the posterior pharynx (Sullivan 141). When the feedback loop is disrupted a delayed signal from the peripheral chemoreceptors may result in central apnoea. This may occur if the the carotid body responses are depressed or circulation time is delayed.

In children tonsils and adenoids have a much greater role in pharyngeal obstruction than for adults where the abnormality is typically functional (Hunt 66). Underlying conditions, other than adenotonsillar hypertrophy, may affect the age of onset, and also the severity of the obstruction which occurs (Dyson 31). There is further reduction of airway size in sleep, and additional factors such as an URTI, may make the difference to whether apnoea occurs or not. Sleep fragmentation secondary to an

URTI may then further alter the patency of the airway, and the response to apnoea (Guilleminault 58).

Partial or complete obstruction may occur in children without adenotonsillar hypertrophy, and may persist after adenotonsillectomy (Editorial 32). The peak incidence of obstruction has been presumed to be in the 2-5 year old age group, when the adenotonsillar hypertrophy which occurs normally at this age would be a plausible explanation (Dyson 31). Since symptoms begin prior to the second birthday in 57% of children, factors other than maximal adenoidal and tonsillar hypertrophy must contribute (Potsic 116).

The pharyngeal airway of the infant is easily collapsed by the negative pressure generated by the diaphragm and inspiratory intercostal muscles. Immature control in infants is due to their immature CNS. Infants are unable to vary tonic and phasic activity of skeletal muscles of respiration to mechanical and chemical stimuli. The result is instability of respiration, variable expiratory time (Te), and relative inefficiency of the respiratory pump. This may be due to peripheral chemoreceptor instability resulting in unstable feedback control. The small and unstable lung oxygen stores in infants also lead to marked fluctuations in the blood gases, even with brief respiratory pauses (Spear 137).

Reflex responses important in protecting upper airway patency include those which occur within a single breath and those occurring over a number of breaths. The acute

response mechanisms active in infants include vagal mechanoreceptors in the lung, proprioceptors in the rib cage, and upper airway mucosal chemosensors. Slower responses (occurring over a number of breaths) include carotid body and medullary chemoreceptors, and reflexes conveyed by the Vagus (Hunt 66, Krieger 79, Guilleminault 55, Henderson-Smart 61)

Vagal responses in newborns are vigorous in reaction to load changes, but they have less effect on the rate and depth of breathing in active sleep. Trigeminal afferents also have a marked effect on breathing, and cold exposure stimulates breathing. Cortical inhibition of trigeminal afferents is present and greater in wakefulness and active sleep than during quiet sleep. Premature infants may have laryngeal activity or laryngeal chemoreceptors playing a part in the initiation of apnoea, and laryngeal stimulation by liquids produces apnoea in the young pig, lamb, and monkey. These responses are more marked in the newborn than in adults. If arousal responses are depressed, then the apnoeic events can be life threatening (Hunt 66, Guilleminault 55, Henderson-Smart 61, Thorpy 144).

The medullary chemoreceptor input is also important, particularly during quiet sleep. Without feedback control by pCO_2 there is progressive hypercapnia, hypoxia, and apnoea. The total response of the medullary chemoreceptors is a consequence of interaction with central drive and other reflexes. These include those with vagal input, peripheral chemoreceptors, hypothalamus, proprioceptors, sleep control centres, adrenal, thyroid and other metabolic and behavioural variables (Shannon 131).

Activation of inspiratory muscles probably originates in brainstem areas which also drive airway maintenance muscles. The function of the pharyngeal musculature is important to prevent collapse of the upper airway during inspiration. Obstructive apnoea occurs when airflow is not maintained in spite of respiratory effort (Gordon 47). Apnoea may result from inappropriate response to occlusion such as defective tone regulation in genioglossus and geniohyoid muscles. Poliomyelitis, may result in this poor coordination, and such CNS lesions may cause both obstructive and hypoventilating syndromes (Hunt 66). Hypoxia may cause depressed tone of the upper airway muscles (Shannon 131). Poor coordination and timing of reflexes and muscles in inspiration and expiration may be secondary to hypoxia, hypercapnia, or other respiratory disorders persisting in sleep (Guilleminault 55, Guilleminault 51).

Pulmonary hypertension in response to OSA in children is most likely secondary to exposure to hypoxaemia during lung growth. The underlying mechanism is hypoxic vasoconstriction in the pulmonary arteriolar bed, but there is variability in the pulmonary vascular response to hypoxia and hypercarbia. Pulmonary vascular hyper-reactivity to hypoxia is seen in 20% of normal children and some children with left to right shunts for example with ventricular septal defects. Pulmonary vasoconstriction can be mediated by the hypoxia and hypercarbia provoked by upper airway obstruction. In infants who have a higher metabolic rate there may be more rapid desaturation and pCO_2 retention and increased sympathetic tone may also contribute. Vascular development is altered, and pulmonary hypertension is accelerated in the postnatal period, in the presence of these precipitants (44). Right

ventricular hypertrophy is the result of initially intermittent, and subsequently sustained, pulmonary hypertension as a result of hypoxia (Serratto 130, Levy 84, Guilleminault 54, Berman 7).

2.1 TREATMENT OF OBSTRUCTIVE SLEEP APNOEA IN CHILDREN

The longterm significance of mild to moderate respiratory abnormalities in sleep are uncertain. A significant increase in airway resistance in sleep, without apnoea, may lead to as many clinical complaints as typical OSA and treatment of this may be recommended (Guilleminault 58). Certainly, treatment should be undertaken when the signs and symptoms are adversely affecting the health of the child (Brouillette 17, Hunt 66). Until more is known about the natural history of the disorder the standard recommendation is that children be followed-up regularly up to and through puberty (Gordon 47, Mauer 91, Guilleminault 55, Guilleminault 51, Hunt 66, Thach 143, Dyson 31).

Medical treatments which are available include weight loss which may be helpful, but rarely so in children where failure to thrive (FTT) is the more common association (Guilleminault 55, Guilleminault 51). Treatment with respiratory stimulants may work in mild cases (Gordon 47, Silverman 133, Guilleminault 51, Hunt 66). Acute infection may require specific treatment including intubation, antibiotics (pharyngotonsillitis) and steroids (for infectious mononucleosis) (Potsic 116).

2.1.1 NASOPHARYNGEAL INTUBATION

Acute management of upper airway obstruction may require use of a nasopharyngeal airway or an endotracheal tube. Nasopharyngeal intubation has been recommended as a diagnostic method, and for pre-operative stabilisation and treatment of upper airway obstruction. As a functional test, it can be used for determining the site of obstruction, as well as acutely bypassing the obstruction. A nasopharyngeal tube is preferable to an endotracheal tube, because it allows the patient to eat, talk and sleep while it is in place. The nasopharyngeal tube has been recommended for both acute stabilisation and long-term treatment. The use of a nasopharyngeal tube has even been suggested for treatment of infants at risk of SIDS (Krabath 77, Hunt 67, Potsic 116).

2.1.2 ADENOTONSILLECTOMY

Where there is a narrow upper airway the treatment consists of eliminating the source of narrowing as much as possible. Otolaryngological assessment includes looking for all causes of obstruction in the head and neck region (Potsic 116). Most children respond to adenotonsillectomy and this is the first step in treating uncomplicated OSA. To date the criteria for adenotonsillectomy or other surgery are not clearly delineated. Adenotonsillectomy in children without craniofacial abnormalities is very effective management, for OSA, irrespective of the size of the adenoids and / or tonsils. The purpose of surgery is to relieve airway obstruction and increase the

cross-sectional area of the pharynx (Robertson 124, Butt 22). Excellent results have been reported, as removal of even normal size glands makes a critical reduction in this airways resistance particularly in children less than 2 years. The most likely effect of surgery is to reduce the airways resistance above the hypopharynx. As a result of this good response, adenoidectomy and tonsillectomy is recognised as standard treatment for OSA in children. Tonsillectomy may be undertaken alone, but usually not adenoidectomy alone (Gordon 47, Guilleminault 55, Hunt 66, Dyson 31, Attal 2).

Adenotonsillectomy is not always successful in children with underlying structural abnormalities eg retrognathia (Butt 22, Guilleminault 55, Krabath 77). Associated structural problems such as a long palate, associated deformity of the mandible, or soft tissue infiltration behind the tongue will predispose to apnoea (Guilleminault 58). The majority of children improve with surgery, but in the severely obstructed patient obstruction may be worse in the perioperative period because of post-surgical oedema. Respiratory support may be required for at least 12-24 hours. Children with neuromuscular disorders and craniofacial abnormalities may required extended hospital admission at the time of surgery (Potsic 117). Concurrent treatment of pulmonary and cardiac complications is important, and some patients may develop acute pulmonary oedema immediately after relief of the obstruction (Potsic 116).

Documented improvement after surgery includes increased weight and height. The surgery also controls sinusitis in 20% of cases, and middle ear disease in 8%, and

symptoms of both of these improved in children post-operatively after T & A's (Buckstein 20, Frank 39). Post-operative evaluation has demonstrated that school performance remained low in two cases even though sleep studies showed return to normal sleep structure, and normal proportions of sleep stages (Buckstein 20, Guilleminault 54).

Haemorrhage is the major complication of adenotonsillectomy. Pre-operative evidence of pulmonary hypertension on echocardiography is associated with an increased risk of complications after adenotonsillectomy. Upper airway obstruction, can increase the incidence of laryngospasm. The combination of laryngospasm and upper airway obstruction is a risk factor for the development of pulmonary oedema. More severe obstructive abnormalities and cardio-pulmonary problems, may not be corrected by adenotonsillectomy (McGowan 93). Insufflation of the nasopharynx has also been suggested as a means of treating upper airway obstruction (Klein 74). This consists of delivery of air or oxygen via a soft nasal catheter to the oropharynx, without any positive pressure.

2.1.3 NASAL CPAP (Continuous Positive Airways Pressure).

It has been clearly shown that partial or complete upper airway obstruction may occur in children without adenotonsillar hypertrophy, and may persist after adenotonsillectomy where the glands were enlarged. Nasal CPAP has been used for such children but has not been well tolerated (Robertson 124). CPAP and

tracheostomy are both effective in treatment in this circumstance (Southall 136), and tracheostomy has been regularly used in such situations (Southall 136, Silverman 133).

Reports of long term successful treatment with nasal CPAP in children are limited. The complications of CPAP in children have included difficulties because of the child's inability to understand and therefore cooperate with treatment. Also, parents may have difficulties in corroborating with and training the child to use the equipment. Finally, mask problems including air leaks, and skin allergies reacting to the cement used to fix the masks in place. The first two difficulties may well lead to discontinuation of treatment (Guilleminault 51). The major reason for failure of CPAP in children has been behavioural (Dyson 31).

Continuous positive airway pressure is delivered via a nasal mask. It provides a pressure splint to the segment of the airway vulnerable to closure. Active expiratory efforts occur, but the soft palate and tongue are held together providing a hermetic seal of the oral cavity (McNamara 95). There may be additional benefits as in the presence of other chest deformities (eg scoliosis), where ventilation for five minutes can reduce respiratory work for up to 3 hours subsequently, because of the increased lung compliance produced (Weibicke 151). The mechanisms of CPAP include reduced upper airway resistance by stimulation of mechanoreceptors that increase upper airway muscle tone, or alternatively dilatation of the upper airway that may be beyond its usual calibre in the awake state. CPAP also counteracts marked negative

inspiratory pressures and therefore eliminates the collapse of the upper airway. In adults it results in improved respiratory and sleep parameters, including central apnoea, in adults. Adults also show improvement in ventilatory control of blood gases, reduction of upper airway oedema, reversal of polycythaemia and heart failure, and improved daytime functioning (Kreiger 79).

2.1.4 OTHER SURGERY

There are other abnormalities which may lead to narrowing of the upper airway. These include: mandibular hypoplasia, abnormally long soft palate, retroposition of the mandible, soft tissue infiltration behind the tongue, and deviated septum (Mauer 91, Guilleminault 55, Guilleminault 51). Some abnormalities require specific surgical intervention on their own right such as nasal septal haematoma (Frank 39) and tongue lip adhesions for mandibular hypoplasia (Leiberman 83).

Uvulopalatopharyngoplasty (UPPP) is soft-palate surgery. It is most successful when combined with adenotonsillectomy in neuromuscular or tissue disorders, or where adenotonsillectomy alone has been unsuccessful (Potsic 117). It has been performed and reported in children. The complications of UPPP include nasal reflux, retraction of the palate, reduction of the airway, and impact on the vocal trill.

Other forms of upper airway surgery include UPPP in combination with tonsillectomy, epiglottoplasty, and stapphylorrhaphy (Attal 2). Orthodontics can be of

assistance. Sixty percent of the face is formed by age four, and ninety percent by the age of 11 years. Orthodontic intervention may help during this period of development (Mauer 91). Faciomaxillary surgery has been used as treatment since the 1970's, and the response of children with OSA, to this surgery, has been successful. While the majority improved with this surgery, around 40% required tracheostomy (Guilleminault 55). Reconstructive surgery of the oropharynx may also be required (Silverman 133).

Tracheostomy is occasionally needed where other surgery is unsuccessful (Potsic 117, Hunt 66, Dyson 31). Patent tracheostomy at night certainly relieves symptoms of OSA (Guilleminault 54). Depending on the unit, definitive treatment may still require tracheostomy because of limited experience of CPAP in children (Butt 22). Tracheostomy associated problems include local complications with incorrect tubes and low grade infections with granulation tissue. In older patients depression secondary to surgery is common (Guilleminault 51) and hence surgery tends to be used only in severe cases (Thach 143).

2.2 RESPIRATORY CONTROL

Respiratory rhythm is generated in the brainstem. Respiratory control is governed by feedback systems, which adjust the rate and depth of ventilation to meet changing metabolic needs during varied activities. Afferent information is modified by the various reflex and neural modulators and converted to appropriate efferent motor responses. The final result is the output to respiratory musculature which arises from these coordinating neural groups within the brainstem (Berger 6).

Respiratory rhythm is not generated from any single defined nucleus, or group of cells, but a number of cells within the brainstem are capable of generating a respiratory rhythm. Processing in the Dorsal Respiratory Group (DRG) results in a coordinated rhythmic output. The output of the DRG is further modulated through the Ventral Respiratory Group (VRG). The output of the VRG then projects to the cranial and spinal neurones driving the muscles of respiration (Berger 6).

2.2.1 BRAINSTEM STRUCTURE

Neural centres within the brainstem are the primary source of the respiratory rhythm. The brainstem is the site of integration of the multiple input signals and reflexes which may modify output to the respiratory musculature. Both upper airway obstruction and acquired central hypoventilation may be secondary to brainstem abnormalities (Cistulli 25).

The development of these nuclei is similar to other neurones. The dendritic spines of the Nucleus tractus solitarius (NTS) and of the reticular formation increase prenatally. The highest concentration of these dendritic spines occurs shortly before birth. After birth, the concentration of synaptic connections decreases gradually, with this process occurring slightly earlier in the reticular formation than the vagal nuclei. A higher concentration of dendritic spines in SIDS victims has been demonstrated, suggesting immaturity of the brain stem neuronal processes as an aetiologic factor in this syndrome (Lawson 82).

2.2.2 BRAINSTEM INFRASTRUCTURE

The location of the major brainstem respiratory groups of neurones are shown in Diagram 1a and 1b. These show a sagittal and coronal section of the brainstem, with the respiratory neuron groups identified and labelled.

Within the brainstem there are three major levels of respiratory activity. The function of these, can be demonstrated by sectioning the brainstem at the different levels. They are the pneumotaxic centre, the apneustic centre, and the medullary centre (Lawson 82).

The pontine structures include the pneumotaxic centre (PNC) and apneustic centre (APC). The PNC is the highest, and lies bilaterally in the rostral pons. The APC lies in the pontine reticular formation near the pontomedullary border (Berger 6).

The medullary centre is divided into expiratory and gasping centres (Berger 6). The main respiratory neurone groups in the brainstem are the dorsal and ventral respiratory groups in the medulla. The DRG lies in the ventrolateral part of nucleus tractus solitarius and is composed of primarily inspiratory neurones. Inspiratory input arises from the dorsal respiratory group. It projects to contralateral spinal cord to stimulate the diaphragm. The ventral respiratory group lies in the nucleus ambiguus and nucleus retroambiguus containing both inspiratory and expiratory neurones which project to the contralateral spinal cord to stimulate the intercostal and abdominal muscles (Berger 6).

2.2.3 RESPIRATORY RHYTHM

Respiratory rhythm generation is based on inspiratory cell rhythmicity. Those neurones generating the respiratory rhythm have been called the central rhythm generator (CRG). This group lies in the medulla oblongata but the exact populations and circuits are controversial, it may in fact be within the DRG. Inspiratory neurones depolarise during inspiration, post-inspiratory neurones depolarise immediately after inspiration. Expiratory neurones have a ramp depolarisation during the post-inspiratory period followed by a plateau of repetitive firing during expiration. Vagal motor neurones of the ventral respiratory group are also activated in the post-inspiratory phase. The driving force for oscillation between the various phases of the respiratory rhythm is from tonic excitatory inputs to the respiratory centres. This is primarily derived from the chemosensor inputs (Lawson 82).

The spinal cord is the final common pathway in respiratory control. The phrenic nucleus at C3-5 innervates the diaphragm. Additional anterior motor neurones at thoracic and lumbar levels innervate the intercostal and abdominal muscles. Movements of the pharynx and larynx are coordinated with those of the thoracic muscles in order to ensure smooth airflow. The nucleus ambiguus, innervates the skeletal muscles of the pharynx and larynx. The dorsal motor nucleus (the other vagal motor subdivision) provides parasympathetic stimulation to the smooth muscle and the glands of the respiratory tree (Berger 6).

2.2.4 RESPIRATORY MODULATORS

Input from reflexes mainly goes to the nucleus tractus solitarius (NTS) via the vagus nerve. The NTS has control over the respiratory neurones because of its intimate involvement with the DRG. Other significant inputs arise rostrally, and are able to override the brainstem respiratory rhythm when necessary for emotional and functional activities (Bogousslavsky 12).

Rostral to the brainstem other inputs exert regulatory roles. These include the limbic, hypothalamic subthalamic regions and thalamic regions which have all had respiratory related activity recorded. These centres do not generate respiratory rhythm, but do stimulate changes in the rate and depth of respiration in coordination with other motor and autonomic behaviours (Davidson-Ward 28).

Caudal input arises from stretch and irritant receptors in the lung and upper airway and transmit sensory information to the medulla via the vagus, and initiate the afferent limb of many respiratory reflexes. Chemoreceptors on the ventral surface of the medulla and in the carotid and aortic bodies relay information, via the vagus and glossopharyngeal nerves, about blood pO2, pCO_2 and pH. The nucleus of the tractus solitarius (NTS) in the medulla is the sensory vagal nucleus, receiving the input information (Berger 6).

Rostral output is via axons projecting from the DRG, VRG, cortex and other supraspinal sites into spinal white matter and influence phrenic, intercostal and abdominal motor neurones of respiration. Expiratory neurones project to the contralateral spinal cord segments T1-L3 and to the intercostal and abdominal respiratory motor neurones. Ninety percent of inspiratory neurones project to the contralateral cord. All of these go to the thoracic segments of the cord, and 25% go to phrenic motor neurones. The premotor neurones in the medulla project to spinal cord motor neurones which drive the respiratory skeletal muscles. The bulbospinal neurones are concentrated in the dorsal and ventral respiratory groups. Spinal respiratory motor neurones integrate the descending influences as well as local spinal reflexes (Newsom-Davis 104).

2.2.5 CHEMORECEPTORS

The medullary chemoreceptors control ventilation changes in response to hypercapnia, hypoxia, acidosis and exercise. The pCO_2 response is linear (Read 120), but the decrease in response to hypoxia is hyperbolic, and only responds when pO_2 is less than 60 mmHg (Weil 153). The normal ventilatory response to pCO_2 is 2-5 l/min/mmHg, with a mean of 2.6 l/min/mmHg, which decreases with increasing age (there are normal reference values produced within each laboratory). A change of arterial pH from 7.45 to 7.25 will double ventilation (Berger 5).

The carotid bodies primarily control hypoxic responses. The reaction is near linear in response to a fall in SaO_2 under isocapnic conditions. The mean response is 0.1 - 1.35 l/min/% desaturation (Rebuck 121,122, Weil 152). In the absence of carotid bodies, hypoxia depresses ventilation through a direct depressive effect on the respiratory centres. Weak responses make the individual more prone to hypoxic pulmonary oedema, vessel muscularisation in response to chronic hypoxia, and more susceptible to respiratory-depressant effects of narcotics (Marcus 85).

2.2.6 INFLUENCE OF AROUSAL ON RESPIRATION

It has been established that an awake individual has more respiratory "drive" than when asleep. The reduction of respiratory drive in sleep occurs centrally, and involves activity in a reduced number of neurones, as well as decreased output from

those which are active. Many of these are part of the reticular-activation system. In REM the output from the DRG and VRG increases, along with some of the associated brainstem nuclei, in proportion to the amount of Ponto-geniculo-occipital (PGO) wave (a characteristic feature of REM) activity (Orem 107).

The responses to hypercapnia and hypoxia allow maintenance of arterial blood gas tensions with little variation in sleep. These responses tend to be reduced in sleep, to varying degrees. The chemoreceptors are powerful promoters of arousal from all stages of sleep. The type of arousal response is important in the pathogenesis of breathing disorders of sleep in response to airway changes. The carotid body probably forms the most important element of the arousal responses to breathing (Phillipson 113).

In non-REM sleep the ventilatory response to pCO_2 shows a 50% decrease in slope and a right shift compared to awake. In REM there is a further decrease, and there may be differences between phasic and tonic REM sleep. The mechanism is a combination of reduced reflex drive and increased upper airway flow resistive load. Adult males have the most change in ventilatory responses, and also the most increase in resistive load (Cistulli 25).

2.2.7 VENTILATORY RESPONSE CHANGES IN SLEEP

There is an increase of approximately 2 mmHg in arterial pCO_2 in non-REM (NREM) sleep compared to wakefulness (Douglas 29), despite a 10-30% decrease in metabolic rate. REM is associated with irregular respiration, and an increased mean respiratory frequency. In NREM there is an increase in inspiratory intercostal activity compared to wakefulness and a decrease in expiratory intercostal muscle activity. Both the diaphragmatic EMG and intrathoracic airway resistance remain similar (Hudgel 65).

Hypoxic ventilatory responses fall in sleep, with a drop of around 33% in non-REM and 67% in REM compared to wakefulness (Grunstein 48). Hypoxia produces a poor arousal response in normal humans (Berthon-Jones 9), with no difference between REM and non-REM. The arousal response is poor in response to hypoxia alone but is improved when combined with high pCO2. The major difference is likely to be the sensitivity of the carotid body to the different gases and the result of combined interactions of pCO_2 and pO_2 (Grunstein 48).

Arousal occurs in response to progressive hypercapnia in REM or NREM, presumably mediated by the medullary chemoreceptors. It is possible that mechanoreceptors produce arousal through their response to the increased work of breathing induced by the pCO_2 response or that the airway may be directly sensitive to inhaled carbon dioxide (Grunstein 48).

2.2.8 THE AIRWAY IN SLEEP

Airway resistance is at its minimum in wakefulness, and still contributes half the total airflow resistance in breathing. There is a twofold increase in both inspiratory and expiratory airway resistance in non-REM sleep. Tracheal smooth muscle tone increases in NREM in dogs, and shows large fluctuations during REM. Some genioglossal motor units increase firing in NREM, but in general genioglossal EMG activity is diminished in non-REM and markedly reduced in REM sleep. The genioglossal response to hypercapnia is also reduced in sleep, and markedly inhibited in phasic REM sleep (Parisi 110). Load compensating mechanisms are diminished in sleep (Kreiger 78).

Lying supine results in an increase in intrathoracic airway resistance, increased upper airway resistance, decreased functional residual capacity and decreased lung compliance. In REM postural muscles drop out, therefore respiratory muscles with dual roles also drop out, including the intercostal, abdominal, and parasternal muscles. Tonic activity of these muscles is lost, but not phasic. In REM the diaphragm is not inhibited except in the pattern of firing, and both frequency and intensity may be altered (Muller 102).

Airway occlusion during sleep results in arousal. This occurs earlier from REM than NREM (6.2 vs 20.4 seconds). This response is the combined result of pressure

receptors in the upper airway and progressive chemoreceptor stimulation by hypercapnea and hypoxia (Bowes 14).

Neuromechanical stimuli include added airflow resistance, airway occlusion, airway irritation and lung inflation. Added resistance to flow in sleep results in reflex load compensation, which is diminished in both NREM and REM compared to wakefulness. Where chemical drive is not taken into account, the response in NREM is the same as awake. One measure of the response to external loads, mediated by chest wall or bronchopulmonary reflex receptors is the P0.1 (mouth pressure at 1 msec after occlusion). These measures show no change in sleep responses compared to awake. In the presence of hyperoxic hypercapnia the responses are reduced in REM sleep but remain unchanged in NREM (Berthon-Jones 10).

The cough reflex is mediated via the vagus and is depressed in sleep. Airway irritation results in arousal before the normal reflex responses of tracheal smooth muscle contraction and cough are seen (Sullivan 142). Apnoeic and airway dilator responses to lung inflation are seen normally and without arousal. Depression of the cough reflex means that there is poor protection of the bronchial tree in sleep (Jamal 70).

Loss of peripheral chemoreceptors results in dependence on central chemoreceptors - with longer apnoea and less adequate recovery. Where peripheral chemoreceptors are

defective there is poor recovery. Another possible abnormality is of heightened arousal responses, resulting in increased arousability to hypoxia (Millhorn 98).

2.2.9 CONTROL OF BREATHING IN THE INFANT

Nasal resistance in infants accounts for a smaller portion of total airway resistance than in adults. In infants, pulmonary resistance varies with nasal resistance, but mostly in the opposite direction to the nasal resistance so that total airway resistance remains constant. Phasic changes in upper airway dimensions occur during breathing; the upper airway dilates during inspiration and constricts during expiration (Mathew 89).

Glossopharyngeal afferents can stimulate respiration and alter respiratory frequency. Expiratory braking occurs at both laryngeal and pharyngeal levels. Human infants demonstrate extreme diaphragmatic braking during expiration in NREM sleep. Respiratory frequency increases in response to increased pCO2. This occurs through a decrease in the duration of expiration and is largely vagally mediated (Mathew 89).

In the lamb, quiet sleep is associated with little reduction of thyroarytenoid activity, but in active sleep the active retardation of expiratory airflow is lost. The result of relaxing expiratory braking is a reduction in end expiratory volume (Mathew 89).

2.2.10 UPPER AIRWAY OBSTRUCTION IN INFANTS

Upper airway collapse, thought to be at pharyngeal level, can be seen in 50% of the central apnoea in infants. With the neck in neutral position, post-mortem closing pressure is virtually at atmospheric pressure in infants. With the neck flexed the airway may close at positive pressures. Other factors facilitating collapse include posterior displacement of the epiglottis by the tongue as the tongue loses its tone in sleep and posterior displacement of the epiglottis by the soft palate when the palatal muscles become atonic. There is no direct evidence for either pharyngeal or laryngeal collapse (Mathew 89).

Recovery from obstruction can occur in infants without arousal. Airway stimulation produces apnoea, and spontaneous periods of apnoea in active sleep are characterised by sustained activation of adductor activity in experimental animals. The post-inspiratory phase is readily activated in the developing animal and during active sleep. Other unknown events may be able to activate the post-inspiratory phase during active sleep (Mathew 89).

2.2.11 DISORDERS AFFECTING RESPIRATORY CONTROL

Hindbrain malformations are usually complex and not limited to the brainstem. The Arnold Chiari Malformation (ACM) may be associated with hypoventilation, sleep apnoea, prolonged breath-holding, vocal cord paralysis and laryngeal stridor. These

may be associated with intermittent apnoea or rapid, shallow, or Cheyne-Stokes respirations. Neuronal depopulation in the nucleus ambiguus and vocal cord paralysis both suggest intrinsic involvement of specific respiratory related loci in brainstem in this condition although there may be other, associated pathology (Holinger 63).

In the congenital central hypoventilation syndrome, histologic lesions may not be demonstrable in the brainstem even after serial sectioning, and lesions of neuronal loss and gliosis may be secondary to prolonged or recurrent hypoxia and ischaemia, rather than the primary abnormality. There may be associated signs of brainstem dysfunction with any of these lesions, including absent gag or swallow, and atrophy of the tongue (Brazy 15).

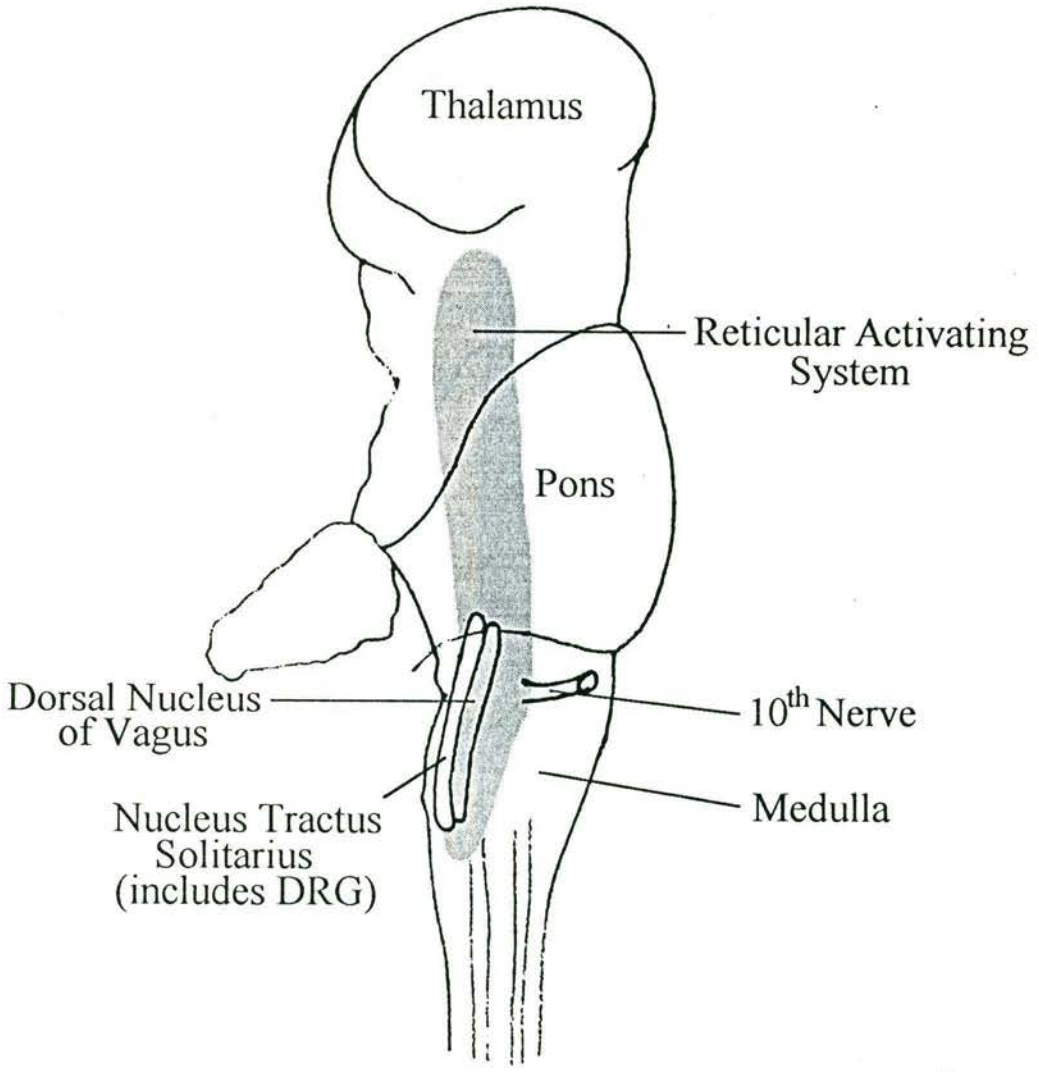


Figure 1. Lateral view of the brainstem with the Respiratory nuclei marked. The shaded area represents the Recticular activating system. DRG = dorsal respiratory group, VRG = ventral respiratory group. (Adapted from Nieuwenhys R, Voogd J, van Huijzen Chr. The Human Central Nervous System. Springer-Verlag, Berlin. 1988).

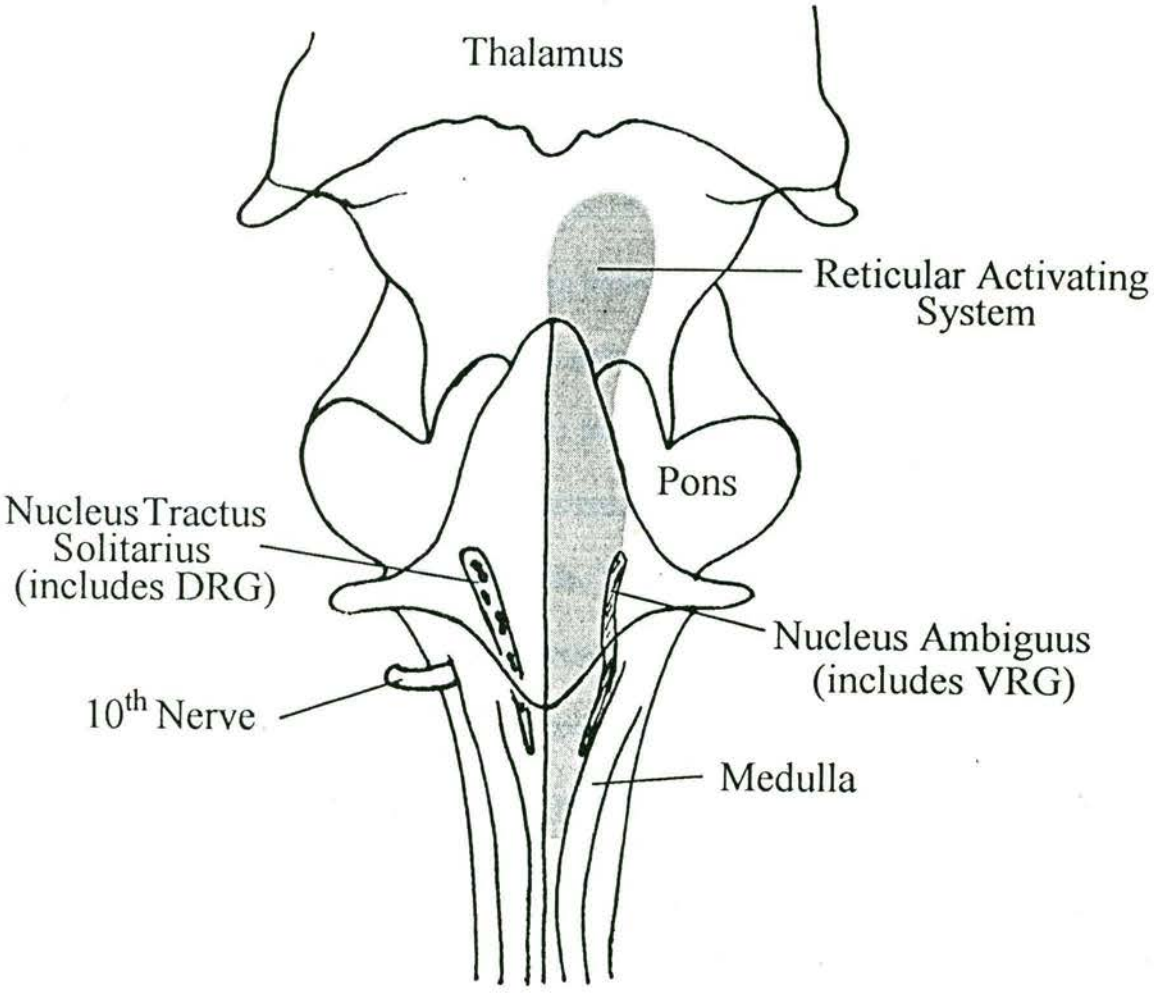


Figure 2. Ventral aspect of the brainstem. The Respiratory nuclei are marked. The shaded area represents the Reticular activating system. DRG = dorsal respiratory group, VRG = ventral respiratory group. (Adapted from Nieuwenhys R, Voogd J, van Huijzen Chr. The Human Central Nervous System. Springer-Verlag, Berlin. 1988).

2.3 SPINA BIFIDA AND MYELOMENINGOCOELE - KNOWN NEUROLOGICAL AND RESPIRATORY ABNORMALITIES.

The malformation of spina bifida occurs during embryogenesis in the induction period i.e. occurring before the fourth week of gestation. The malformation results from a time specific insult. Spina bifida results from a failure in fusion of the posterior midline of the vertebral column. This results in a bony cleft through which varying quantities of spinal cord tissue protrude. The lesion is called meningocoele or meningomyelocoele (myelomeningocoele) depending on whether the meninges herniate alone, or associated with spinal cord parenchyma and nerve roots. Major abnormalities of neural cellular migration are part of the disorder, along with the secondary mechanical deformities of the nervous system. The incidence of myelodysplasia varies from 0.2 per 1000 to 4.2 per 1000, with a recurrence rate of 10% in affected families. (Gabriel 41, Oren 108).

80% of lesions are confined to the lumbar and lumbosacral region with a mixed upper and lower motor neuron lesion below. The outcome of myelomeningocoele has been affected very little by the use of selection criteria for the decision whether or not to actively intervene and treat at presentation (McLone 94).

2.3.1 ASSOCIATED MALFORMATIONS

Hydrocephalus and the chiari malformations (type 2 or 3) are present in 90% of cases of spina bifida. There is also an associated malformation of the craniobasal bones (Gabriel 41). The type 1 ACM consists of the caudal displacement of the medulla into the spinal canal. The inferior pole of the cerebellar hemispheres is herniated through the foramen magnum, extending in some cases as far as the third cervical vertebra (Naidich 103).

The Type 2 ACM is the most common type. It is defined by the presence of additional herniation of part of the fourth ventricle into the spinal canal. In 90% of affected patients, spina bifida cystica and hydrocephalus are combined with the malformation. All patients with spina bifida cystica and hydrocephalus are said to have the type 2 defect, including dorsal overriding of the medulla on the cervical cord (Sieben 132).

The presenting symptoms of the ACM may be quite varied. They include central hypoventilation (Bullock 21, Oren 108), respiratory distress, apnoea, vocal cord paralysis and inability to swallow (Papasozomenos 109). Multiple lower cranial nerve abnormalities may be present resulting in absent gag and cough reflexes and downbeat nystagmus (Sieben 132). Clinically the patient may have prolonged expiratory breath-holding, central apnoea, stridor (Oren 108), absent hypoxic ventilatory responses (Bokinsky 13), and obstructive sleep apnoea-hypopnoea. There

can be abnormal upper limb function associated with the ACM (Bluestone 11, Brown 18). In young infants the presentation may be with swallowing difficulties, weak or poor cry, inspiratory stridor, arching of the head, lower brainstem problems and/or facial weakness (Oakes 106). Persistent head lag may occur due to involvement of the 11th cranial nerve (Sieben 132).

Syringomyelia and hydromyelia may also be associated with spina bifida. The incidence of these lesions in association with spina bifida is reported to be 32-33% (Azimullah 3). A syrinx may affect the vagal nerve and produce stridor and laryngospasm. If the nucleus ambiguus is affected, then there may be chronic stridor and vocal cord paralysis. Complications of syringomyelia/bulbia include vocal cord paralysis, diminished ventilatory responsiveness to hypercarbia, central alveolar hypoventilation and aspiration pneumonia. Other associations include sleep related stridor, nocturnal dyspnoea, irregular breathing snoring, and apnoea (Haponik 60). Bilateral diaphragmatic paralysis, sleep associated hypoventilation, decreased vital capacity, respiratory failure (Bullock 21), and associated central nervous system tumours (Peter 112) have also been reported.

2.3.2 PATHOPHYSIOLOGY

The severity of the anatomical abnormality on MRI does not correlate with the severity of the functional disability (Oren 108). The functional abnormalities may be tested for, using evoked potential or ventilatory response testing (Haponik 60). Post

mortem studies have demonstrated decreased neuron density (Oren 108) and brainstem dysgenesis (Holinger 63). Shrunken and atrophic neurones are common in the cranial nerve nuclei with the choroid plexus severely fibrotic. The nerve roots have not been shown to have demyelination (Sieben 132).

Vascular abnormalities may contribute to the dysfunction seen. Vascular lesions of the lower medulla have been found in 86% of those with a history of clinical dysfunction of either respiratory or lower cranial nerves highlighting the precarious nature of the blood supply to this region in the ACM (Papasozomenos 109, Morley 99). The blood vessels and the cranial nerves have an abnormally elongated and sometimes tortuous course at post-mortem. Ischaemia may result from kinking and herniation of brainstem itself or of the vessels as they traverse their abnormal course resulting from the abnormal brainstem anatomy (Holinger 63). The lesions may be beyond the resolution of MRI (Morley 99).

Dysfunction may be a consequence of direct compression of the medulla and cranial nerves, especially at the level of the foramen magnum. Displacement of the cerebellum and 4th ventricle may add to the bulk of the brainstem, and so produce compression of both the brainstem and cranial nerves (Sieben 132). Blood vessels displaced in association with these structures further add to the bulk of tissue in the foramen magnum and upper cervical cord, and the vessels themselves may be vulnerable to compression. The structural damage seen at brainstem level may be a

primary developmental problem or secondary to caudal displacement of the structures causing stretching.

Raised intracranial pressure, also common because of the high incidence of associated hydrocephalus, may exacerbate all of the above pathologies by causing traction. Increased ICP transmitted to the hydromyelic cavity may mean that relief of ICP gives relief of cranial nerve dysfunction (Sieben 132).

2.3.3 RESPIRATORY ABNORMALITIES IN SPINA BIFIDA.

The associated malformations at the level of the brain stem are very likely the most important in affecting respiratory function. The ACM is symptomatic in around 30% of spina bifida patients, although this proportion probably increases with increasing age. Thirteen percent have severe neurological associations. This malformation is the cause of 79% of deaths in spina bifida (McLone 94). Compression of the upper cervical cord can impair motor function of the respiratory system by interference with phrenic nerve and diaphragmatic dysfunction. Structural derangement can affect the ponto-medullary respiratory controller, afferent and / or efferent pathways.

Decreased sensitivity to hypoxia and hypercapnia are associated with the ACM (Oren 108, Bokinsky 13, Haponik 60). When ventilatory control is defective it may be expressed by hypoventilation, sleep apnoea, or prolonged breath-holding spells. Hypoventilation may be acute or chronic (Bullock 21). Prolonged breath-hold in

expiration can proceed to severe hypoxia and seizures. Apnoea may not be relieved by tracheostomy, and may be associated with an otherwise abnormal respiratory pattern and cyanosis. Not all cases respond to decompression (Holinger 63). Lack of carotid body input may prolong apnoeic spells (Bokinsky 13). Hypoxia secondary to the absent hypoxic respiratory drive may exacerbate the severity of dysfunction.

Brainstem dysfunction may cause faulty activation of upper airway muscles - including loss of phasic activation and therefore inspiratory collapse. Again this may be local or due to afferent and /or efferent pathways abnormalities. The presence of brainstem abnormalities is supported by abnormal brainstem auditory evoked potentials.

Absent ventilatory sensitivity to hypercarbia, and variable hypoxic response suggest a primary abnormality of central chemoreceptors. Hypoventilation results in progressive hypercarbia and hypoxaemia in quiet sleep (Oren 108). Abnormal vagal activity may contribute to respiratory dysfunction through afferent / efferent dysfunction and some patients have responded to treatment with atropine (Oren 108). Decreased sensitivity of the respiratory centre, a carotid body defect or a defect of the neural afferent, (via 9th cranial nerve or medullary centres) will produce similar effects.

Posterior fossa decompression may be indicated when control of ICP does not relieve upper airway obstruction. Decompressive surgery to treat infants with ACM and respiratory distress from a variety of causes (apnoea, vocal cord paralysis or inability

to swallow) resulted in 35% improvement, 35% no change, and 27% irreversible neurological damage for a group of 14 patients (Papasozomenos 109).

Damage of descending spinal pathways can occur and affect both voluntary and involuntary respiration. Thoraco-lumber lesions results in lower motor neuron lesions of intercostals and abdominal muscles. These lesions reduce respiratory reserve, by causing inefficient cough and reduce the effectiveness of the accessory muscles of respiration (Oren 108). Secondary deformity with kyphoscoliosis, and restrictive thoracic deformity, will also affect the lower respiratory tract. Combined respiratory muscle dysfunction and increased airflow impedance by vocal cord paralysis can accelerate respiratory muscle fatigue.

2.3.4 UPPER AIRWAY DYSFUNCTION

Transient respiratory obstruction through upper airway dysfunction or bilateral vocal cord paralysis can occur. This may affect up to sixteen percent of children with spina bifida and ACM. Hydrocephalus can exacerbate the symptoms and in the majority of cases of vocal cord paresis there is raised intracranial pressure (Oren 108, Brown 18, Haponik 60, Holinger 63). Sleep apnoea has been demonstrated (Oren 108).

Dysfunctional innervation of the upper airway muscles may be due to damage of the brainstem respiratory centres or their connections (Brown 18). Localised medullary haemorrhages have been seen at the level of the olivary nuclei and posterior to them

ie innervation of tongue pharynx and larynx (Morley 99). Faulty innervation of the posterior cricoarytenoid muscle may be involved. Bilateral abductor vocal cord paralysis may be secondary to vagal nerve dysfunction. Upper airway dysfunction can also be caused by dysfunction of other cranial nerves and the ACM may be associated with multiple lower cranial nerve dysfunction (Sieben 132, Morley 99, Emery 36).

There are a number of mechanisms which will produce a combination of both upper airway dysfunction, and disordered respiratory control. Some lower respiratory problems may be secondary to upper airway dysfunction. Absent gag and cough, oropharyngeal incoordination, gastro-oesophageal reflux and abdominal muscle weakness all contribute. Combined chronic aspiration and sleep hypoventilation can result in chronic alveolar hypoxia, pulmonary hypertension, and cor pulmonale (Oren 108). The phrenic neurones in the medial part of the anterior horn are vulnerable to compression by an expanding syrinx (Bullock 21).

Prevention of respiratory complications or vascular compromise includes control of intracranial pressure (shunting hydrocephalus), and posterior fossa decompression (Papasozomenos 109). A syrinx may be relatively silent in children where the neurological symptoms can be subtle or absent. Apnoea in sleep may be one of these symptoms (Dure 30).

2.3.5 SLEEP APNOEA IN SPINA BIFIDA

There are few cases of spina bifida associated with sleep apnoea documented in the literature. There are no specific reports of the use of nasal CPAP in this disorder. Cited cases, have been treated with either adenotonsillectomy alone, or tracheostomy for relief of their symptoms (Haponik 60, Brown 18, Pasterkamp 111).

2.3.6 SPINA BIFIDA - SUMMARY

Spina bifida is associated with severely disrupted respiratory function. In some cases this may lead to early death (Papasozomenos 109), and in others a congenital central hypoventilation syndrome (Weese-Mayer 149). Cranial nerve dysfunction can lead to obstructive sleep apnoea. Obstructive sleep apnoea may be a significant contributing factor to the respiratory or neurological presentation. To date the treatment measures recommended to treat this apnoea include adenotonsillectomy, posterior fossa decompression and tracheostomy. The use of nasal CPAP is not documented in infants with apnoea secondary to involvement of the brainstem and cervical spine in association with myelomeningocoele.

2.4 CENTRAL HYPOVENTILATION

Alveolar hypoventilation in the absence of lung or neuromuscular disease is uncommon, and the first description in the literature was given the descriptive name of "Ondine's curse" in 1962 (Weese-Mayer 148). Central hypoventilation is the presence of alveolar hypoventilation in the absence of any pulmonary or neuromuscular cause and is the result of deficiency in the automatic respiratory output from the brainstem. Patients with central alveolar hypoventilation lack ventilatory responsiveness to pCO2. This is associated with partial or complete loss of ventilatory response to hypoxia. Sleeping ventilation is insufficient, but awake (voluntary) ventilation is normal. Both ventilatory and arousal responses to hypercarbia and hypoxaemia are affected (Weese-Mayer 148).

Even those patients with adequate ventilation when awake, lack normal pCO_2 responsiveness if tested while awake and fail to have adequate ventilatory response to other physical phenomenon such as exercise, and emotion (Fleming 38). Because of the abnormal ventilatory responses, which have been demonstrated in both the congenital and acquired forms, the defect is attributed to a primary abnormality of the medullary chemoreceptors (Mellins 97, Weese-Mayer 148). The cause is thought to be loss of chemosensitivity, but may be in the brainstem integration of these signals (Marcus 86).

Mellins first reported an analysis of the congenital syndrome of hypoventilation in 1970 and reviewed those thirty cases of acquired central hypoventilation in the literature at that time. In this review there was only one case of a child with the acquired syndrome. This child was aged three and a half years (Mellins 97).

The clinical picture is of sleep induced hypoventilation, usually worst in slow wave sleep. Overt apnoea is uncommon, but tidal volumes may be reduced to levels which would only ventilate the respiratory dead space. Generally, reduced tidal volumes occur only during sleep. Patients may present with inadequate responses and inadequate minute ventilation only in sleep but in the more severe form, the disorder may affect control in the awake state as well. Importantly, significant respiratory acidosis may occur without tachypnoea or respiratory distress (Weese-Mayer 150).

The severity of the hypoventilation is state dependent, and may only be evident in slow wave (stages 3 & 4) sleep. In moderately severe cases REM sleep will be affected as well. All patients with congenital central hypoventilation follow the pattern of maximal severity in quiet sleep, less severe in REM and best in wakefulness (Fleming 38). Respiratory and heart rates also show reduced variability (Woo 155).

Experience at RPAH suggests that arousal responses do become less sensitive if hypoventilation remains untreated. Oxygen (pO2) needs to become progressively

lower to cause arousal, and pCO_2 higher. Desensitisation of chemoreceptors eventually results in inability to maintain normal awake gases (Ellis 33).

2.4.1 KNOWN CAUSES & CLINICAL ASSOCIATIONS

The largest clinical groups are those with the congenital idiopathic form, and those associated with the ACM. There are reports of the congenital syndrome presenting at up to 3 to 4 months of age (Guilleminault 57).

The congenital syndrome can be associated with Hirschsprungs disease (Weese-Mayer 148, Guilleminault 57). The acquired form may be associated with congenital malformations, tumours, trauma or infections (Brouillette 16, Moss 100). Other miscellaneous causes include arteriovenous malformation (Mukhopadhyay 101), birth asphyxia, hypoxic-ischaemic encephalopathy, Leighs disease, Shy-Drager syndrome, pyruvate dehydrogenase, and carnitine deficiency. Complete or partial Moebius syndrome may also be associated (Fujita 40, Bogousslavsky 12). All of these disorders may be associated with generalised neurological dysfunction. There have been a number of clinical abnormalities associated with the acquired form (Weese-Mayer 149). The precise location of the neuronal injury affecting respiration is often unknown in secondary cases because of the associated widespread neurological damage (Brouillette 16).

Acquired lesions of the medulla are rarely demonstrated to account for central hypoventilation. Brainstem infarcts have shown that unilateral involvement of pontomedullary reticular formation and nucleus ambiguus is sufficient to cause loss of automatic respiration. If this is associated with a lesion of the nucleus tractus solitarius then it may lead to loss of both automatic and voluntary control (Bogousslavsky 12). A congenital slow growing astrocytoma involving the brainstem has been reported (Mellins 97).

Thirteen percent of infants with ACM develop a syndrome of central hypoventilation and inability to swallow. MRI is now considered the most reliable imaging for evaluation of brainstem. Studies of children with acquired central hypoventilation have generally shown a high incidence of abnormal studies (Weese-Mayer 149).

2.4.2 TREATMENT OF CENTRAL HYPOVENTILATION

Mechanical ventilatory support is usually necessary in sleep for treatment of central hypoventilation. No respiratory stimulants have shown persistent effectiveness in the treatment of this disorder (Moss 100). A combination of tracheostomy and positive pressure ventilation is the most common method for providing assisted ventilation at home (Weese-Mayer 150).

Cuirass ventilation (negative pressure chest shell or wrap ventilator) relies on generation of negative pressure to expand the chest and upper abdomen proportional

to tidal volume. This may eliminate the need for tracheostomy in the older child, younger children may still need the tracheostomy because of the tendency for upper airway collapse. This method is less effective where the patient has less compliant lungs. The device also needs refitting with growth, and is not very portable. Upper airway obstruction may be precipitated by cuirass (negative pressure) ventilation (Ellis 33).

Diaphragm pacing has been used in a number of patients now for periods of up to 14 years. Some periodic replacement of the implanted components is required with a mean time to failure of 56 months. There has been no chronic nerve damage secondary to electrical stimulation. Where there is awake hypoventilation this may be used during the day, with ventilation via a tracheostomy at night. Less stimulation is required with maturation and this eventually allows 24 hours a day use. Decannulation of tracheostomy has not been possible in children before 5-6 years of age with diaphragmatic pacing (Weese-Mayer 148).

Ventilation can be maintained via the nasal CPAP mask, for use with a small portable home ventilator. Lung volumes do not improve with treatment but blood gas analysis does. Physiologic changes occur between 48 hours and 10 days, while whole body improvements continue for months (Ellis 34).

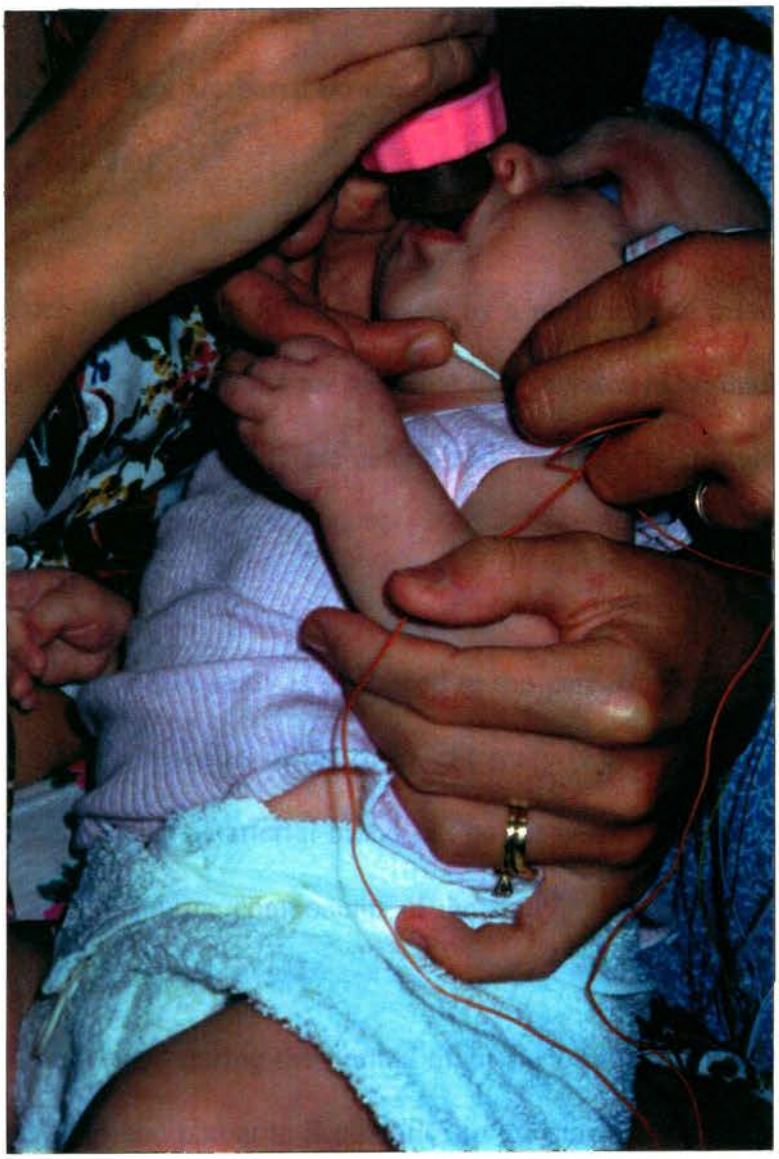
2.4.3 PROGNOSIS

There is no evidence to suggest that children will outgrow this respiratory control deficiency. Only one child has been reported who was able to be weaned off the ventilator, and this child still hypoventilates (Hunt 27). However, there is markedly improved morbidity and mortality. Long term morbidity has related to the development of cor pulmonale in the absence of other significant congenital abnormalities (Weese-Mayer 148). A majority of children are now successfully cared for in their parents homes. A lengthy initial hospitalisation is often required but then little subsequent hospitalisation (Marcus 88).

There has been a high incidence of pulmonary hypertension in children with central hypoventilation which suggests that current management could be further improved (Weese-Mayer 150). There is a broad range of intellectual test results at follow-up Median full-scale IQ 81 and median performance IQ 75 (Silvestri 134).

Chapter 3.

Methods



3 METHODS

3.1 SLEEP STUDIES.

The methods used for these studies in children were developed in the David Read Sleep Disorders Units (at the Royal Prince Alfred Hospital, and The Children's Hospital Camperdown). They are based on the standard sleep study methods used with adults in the same unit.

It is standard practice for the child to be reviewed by a paediatrician prior to the overnight study. The child is assessed for potential sleep related abnormalities, and the indications for the overnight study are determined. During this consultation a physical examination is performed.

The procedure of the overnight study is explained to the parents, and an information sheet which details the components of the overnight study is provided, including potential extra elements, such as arterial blood gas or oesophageal pressure monitoring which are not routine components of the study.

The sleep study is performed during the normal night sleep period. Early arrival allows time for the child and parent to acclimatise to the surroundings, and for the set-up to be completed before dinner time. Children arrive in the unit at, or before, 3 pm on the afternoon of their study, unless there are extenuating circumstances. A

parent or familiar relative is strongly encouraged to stay for the duration of the study, with the child. A bed is provided for the parent, in the same room as the child.

Because the equipment can be intimidating the equipment and observation room have been located along the hallway, well apart from the bedroom. The parents and child are introduced to this area after arriving and settling in, as part of their orientation to the unit.

All studies were performed without sedation, and recorded on a Grass® Model multi-channel recorder. Standard components of sleep staging include the variables electroencephalogram EEG (C_3-A_2), (O_2-A_1), electro-oculogram (EOG) (ROC-A_1) (ROC-A_2), and submental electromyogram (EMG_{sm}). Sternomastoid (EMG_{st}) electromyogram and or abdominal muscle activity (EMG_{abdo}) is also monitored via surface electrodes.

The respiratory variables which are monitored include inductance plethysmography via Respitrace® of chest and abdomen (uncalibrated), nasal airflow via pressure transducer, and diaphragm EMG (EMG_d). Oxygen saturation (SaO_2) is monitored using a finger probe attached to an Ohmeda Biox 1000 saturation monitor. Transcutaneous CO_2 ($TcCO_2$), is recorded using the Radiometer® (TINA, Copenhagen) monitor. Electrocardiogram (ECG), is recorded using chest leads.

3.2 SLEEP STUDY SCORING

All of the sleep study results reported in this thesis were scored manually, by the author. Sleep stages are scored using the staging criteria of Rechtschaffen and Kales (1).

Results are given for combined apnoea and hypopnoea index (RDI), central apnoea index (CRDI) and obstructive apnoea index (ORDI). The apnoea index is the total number of apnoea during sleep divided by the total number of hours of sleep recorded. An obstructive apnoea is one where there is absence of airflow, but persistent respiratory effort, indicated by diaphragm EMG activity, and chest and abdominal movements (Respitrace). Central apnoea are those where the absent airflow is accompanied by absent diaphragmatic activity, and lack of thoracic and abdominal respiratory movement.

The criteria used to define a respiratory event are that it resulted in a) arousal, b) a change in SaO_2 (> 3%) on transcutaneous measures or, c) disruption of two or more of the regular respiratory cycles. As a result, apnoea duration varies markedly across the age range of our patients. In a 12 month old infant an apnoea covering three normal breath intervals, but lasting only three seconds and resulting in a 4% O_2 desaturation would be included. We included hypopnoea (half average respiratory excursions) only if this occurred in association with an arousal or desaturation, and subsequent return to baseline respiratory excursions.

3.3 SOMATOSENSORY EVOKED POTENTIALS.

3.3.1 POSTERIOR TIBIAL NERVE

A transcutaneous stimulus was applied over the posterior tibial nerve at the ankle. The stimulus was adjusted to motor threshold (indicated by twitch of the great toe). A stimulus range of 4 - 9 mAmp was used, for 200 microseconds, at 2.1 Hz. The potential was recorded at the lumbar spine (referred to the iliac crest) and the cortical response was recorded at C_z^1 referred to F_{pz} (ground plate of leg). The data was analysed using the Nicolet Compact Four, evoked potential system. Sensitivity set at 25 microvolts, and filter 30 - 3000 Hz were used. Studies were performed without sedation; chloral hydrate (single dose 25 mg/kg) was used in two cases where the subjects were toddlers, unable to co-operate.

3.3.2 MEDIAN NERVE

The stimulus site for this test was at the wrist. The stimulation rate was 1.1Hz with a 200 us duration and analysis time 200ms (45). The amplitude of the stimulus was 4-9 mAmp, with a duration of 100 microseconds. Gold (Ag/AgCl) electrodes were positioned using the international electrode system at Erb's point, C_3^1, C_4^1 and Cervical C5, and referenced to F_{pz} with a ground on the arm. 64 artefact-free trials averaged for each recording, and recording duplicates measured to ensure reproducibility.

Impedance was 5k Ohms or less. Sensitivity 50uV and filters set at 30Hz and 3KHz. The 50Hz filter was off. Analysis time 50 ms, 2.1Hz, and 256 potentials were averaged.

Neonate recordings were only from the cortex and recorded at a bandpass of 5Hz to 1.5KHz, and 30Hz to 3KHz with a sensitivity 50uV full scale. The stimulation rate was 1.1 Hz with a 200 microSec duration and analysis time of 200 msec.1

3.4 VISUAL EVOKED POTENTIALS.

Visual evoked potentials were performed using a Nicolet Compact Four. Ag/AgCl electrodes were positioned using the international electrode system at O_z, O^1 and O^2, referenced to F_{pz} with a common electrode at C_z. Electrode impedance was 2K Ohms or less. Butterworth type filters were set to provide a bandpass of 1-100 Hz and sensitivity was 100 uV full scale. Automatic artefact rejection was used and duplicates were always recorded to ensure reproducibility. Analysis time was 250 ms and 128 artefact-free trials were averaged for each recording. Stimulation was either pattern shift (PS) stimulation or in babies light emitting diode (LED) goggles were used.

The PS stimulator was a Nicolet 1015 visual stimulator at a rate of 1.9 Hz and subjects were constantly monitored to ensure that good fixation and concentration were maintained throughout the recording. Visual acuity was tested and PS stimulation was recorded with glasses if normally worn. Check size was 61 inches or larger if required.

The LED stimulus was a red light presented monocularly using Nicolet 105 A goggles, positioned over closed eyes in a sleeping child, at a rate of 1.9 Hz.

3.5 BRAINSTEM AUDITORY EVOKED POTENTIALS.

Brainstem auditory evoked potentials BAEP's were recorded using a Nicolet compact Four. Ag/AgCl electrodes were positioned using the international electrode system at A^1, A^2 referenced to C_z, with a common electrode at F_{pz}. Impedances were 3 kOhms or less. Butterworth type filters were set to provide a bandpass of 100 Hz - 3KHz and sensitivity was 50 uV full deflection. Automatic artefact rejection was used and duplicates were recorded to ensure reproducibility. Analysis time was 10 Ms and 2000 artefact-free trials were recorded. Rarefaction stimulation was delivered through Nicolet headphones at 11.4 Hz and contralateral masking was presented at -40 dB. Babies were tested in natural sleep while older children were tested while lying relaxed in a warm softly lit room.

3.6 STATISTICAL METHODS

The standard presentation of data is as mean +/- standard error of the mean (SEM). This is used in the presentation of values from studies of large groups.

Where children were studied before and after treatment a paired t-test was used to compare results.

Differences between groups were studied using unpaired t-tests.

For comparison between non-parametric values, log or rank transformation was performed on the raw data for the subsequent statistical analysis.

4 SLEEP BREATHING DISORDERS IN CHILDREN

4.1 INTRODUCTION

Awareness of the wide spectrum of obstructive sleep apnoea (OSA) in children is increasing (Gaultier 43). The complications of the disorder have been considered infrequent until recently, with only occasional reports in the literature of children suffering growth failure, or presenting in cardiac failure as a consequence of upper airways obstruction (Levy 84, Guilleminault 54). It is increasingly apparent that the disorder is both common, and potentially life-threatening. Children do die suddenly in sleep from this disorder (personal communications). Equally, there are other disorders, particularly acquired central hypoventilation, which may present with an indistinguishable clinical history and examination (Ellis 35).

The mechanism of upper airway obstruction in children has largely been attributed to a structurally small airway (Singer 135). The basis for this assumption has been the common association with craniofacial malformations and adenotonsillar hypertrophy. However, the dynamics of upper airway respiratory control play an active and important role in protecting normal airway patency and dysfunction of these mechanisms must contribute to the disorder. It appears to be the predominant factor in at least half of the children affected. Since children with anatomically small airways may not experience obstruction at all (Stebbens 138), the dynamic function must play a part in the pathophysiology of all cases.

The fact that obstruction may occur solely in sleep is no accident, as normal sleep physiology will further contribute to respiratory and upper airway instability, or dysfunction. Children can be assessed accurately during normal sleep times, using appropriate clinical and investigative procedures. To date, treatment has largely consisted of uncontrolled adenoidectomy and/or tonsillectomy (Butt 22) but such surgery may be associated with significant risk and morbidity if there is not adequate pre-operative assessment and management (Potsic 117, Koopmann 76, McColley 92). While adenotonsillectomy is the appropriate initial treatment for the disorder, further treatment is required in a significant number of children. While nasal CPAP has had limited use in the paediatric population to date, our experience clearly shows that with appropriate equipment and behavioural management, it is a practical and effective means of intervention.

Three and a half years ago, a specialised paediatric sleep disorders service was established. The aim of this chapter is to examine the demography of the children who have undergone sleep studies for sleep related upper airway obstruction. Features of OSA which have been seen on overnight sleep studies in these children are also highlighted.

4.2 PATIENTS

The data in this chapter refers to patients studied in the David Read Sleep Disorders Unit since a specialist Paediatric service was established three years ago. All of the children studied in the unit had been reviewed by a paediatrician. The only criteria for inclusion in this analysis was that the child had undergone a diagnostic sleep study at age 15 years or less. The majority of the studies were performed on clinical grounds. Some children were studied as part of specific research protocols and they have also been included in the analysis.

4.3 METHODS

The data in this chapter was compiled from the admissions records of the sleep disorders unit. The period from January 1990 to 30 June 1993 is covered. A database was not established for the unit at this time. Details of patient attendance and relevant information were taken from the admission record and entered into a spreadsheet program (Column Oriented Language ©). Statistical analysis was performed on this aggregated data.

The details of the sleep study methodology is described in chapter 3. Sleep studies were performed according to standard procedures, with both sleep stage and respiratory variables recorded for each patient. Where a neurological abnormality was suspected the number of EEG leads was increased to six and the distribution altered

to provide EEG mapping. Left and right sided recordings were made of frontal (outer canthus to A), parietal (A to Cz) and occipital (A to O) areas. In some cases specific research protocols required the insertion of either an intravenous cannula or oesophageal pressure transducer. The majority of children had a standard sleep study directed towards the identification of sleep associated respiratory abnormalities.

Results are presented as mean +/- SEM (range). The groups are:

Total = all children who have undergone overnight sleep studies.

OSA_t = all children studied for OSA including those with other abnormalities.

OSA_o = those children studied for OSA alone

OSA_s = those children studied for OSA plus other sleep problems

Treated = those children treated for OSA

CPAP = those children treated with nasal mask CPAP.

4.4 RESULTS

A total of 455 children have undergone 766 overnight sleep studies (**Total**). Figure 1 shows the number of studies performed in each six month interval covered by this report. Four hundred and thirteen children (**OSA_t** = 90.8%) have been studied to diagnose OSA either as a an isolated sleep problem (**OSA_o**, 267 = 58.7%), or to diagnose OSA in association with other sleep related problems (**OSA_s**, 146 = 32.1%). The two other major groups of studies are those for children at risk of SIDS (21 = 4.5%) and for neurological abnormalities (19 = 4.1%). Of the children studied for OSA, 129 (31.2%) were identified as having been treated.

The mean age of all children studied was 5.04 +/- 0.21 years (**Total**) (0-15.9). From this group the children found to have OSA had a mean age of 5.1 +/-0.22 years (**OSA_t**). Those children studied for OSA alone had a mean age of 5.7 +/-0.26 years (**OSA_o**), (0.05 - 15.9). In the group (**Total**) there were 179 (41.2%) females and 255 (58.8%) males. Of those studied for OSA (**OSA_t**) there 160 (40.6%) females, and 234 (59.4%) males. Where OSA was isolated (**OSA_o**) there were 99 (39.1%) females and 154 (60.9%) males.

One hundred and twenty nine (31.2%) of the children with OSA were treated (**Treated**) with adenotonsillectomy or CPAP (31 = 24% in this group). In this group (**Treated**) there were 66 (37.7%) females and 109 (62.3%) males. Of those treated

with CPAP the mean age was 6.9 +/- 1.1 years (**CPAP**) and there were 12 (39.6%) females and 19 (61.3%) males. See Table 1.

Seventy-two of all children (**Total**) studied (15.8%) had an associated syndrome and 54 (11.9%) had a major congenital malformation. These 126 children represented 27.6% of the total and they were all studied for OSA. Those with syndromes represented 17.4% of this group (**OSA_t**) and those with malformations 13.1%. Of the children with OSA alone (**OSA_o**), 52 (19.5%) had syndromes and 30 (11.4%) had malformations. A total of 45 (34.9%) of the children requiring treatment (**Treated**) had a syndrome or malformation. Twenty-nine 29 (22.5%) (**Treated**) had a congenital syndrome and 16 (12.4%) had a malformation. Of the 19 (61.3%) children treated with CPAP, 11 (35.5%) (**CPAP**) had a syndrome and eight (25.8%) had a malformation. See Table 1.

Some distinct abnormalities were seen either on history, examination or sleep study in children with obstructive sleep apnoea. See figures 2-6. Notably 23 (5.6%) in this group (**OSA_t**) were identified as obese - 52% female and 48% male. Only 3 (0.7%), two boys and one girl were failing to thrive. Excessive daytime sleepiness occurred in 22 (5.3%) children (**OSA_t**) of whom 14 (64.6%) were girls. Asthma was present in 30 children (7.3%) of whom 20 (66.7%) were boys.

Through overnight sleep studies we have been able to identify several features of OSA in children. These include prolonged partial obstruction (Figure 2a) often with

associated CO2 retention in SWS (Figure 2b). Cycles of mixed apnoea/hypopnoea tend to recur (Figure 3). Repetitive complete obstruction does occur in some cases (Figure 4a) and arousals are generally not associated with the apnoea. These are usually associated with acute changes in SaO2 and CO2 (Figure 4b). Children frequently demonstrate phasic EMG activity throughout REM sleep in the presence of obstruction (Figure 5).

4.5 DISCUSSION

The number of children studied in this unit gives an indication of the frequency of sleep disorders in children. Ninety-point-eight percent of all these studies were for evaluation of sleep disordered breathing and 267 of 455 children (58.7%) were performed specifically because of concern about obstructive sleep apnoea. The larger group includes those children with associated chronic lung disease, central hypoventilation, or anatomic abnormalities such as tracheomalacia or vocal cord paresis. Figure 1 shows the increase in numbers of studies which has been limited by the capacity of our facility.

The predominant age group is less than 3.5 years. Children less than one year of age can, and do, present with symptoms of upper airway obstruction. Common symptoms have not been quantified in this study. Children present with snoring and witnessed difficulty breathing in sleep with or without witnessed apnoeas. Excessive daytime sleepiness and obesity are both uncommon affecting less than 6% of children in each case. Unusual symptoms have included cyclical vomiting (one severe enough to require recurrent hospital admission), polyuria/nocturia, and insomnia. All of these have occurred in school-aged children.

Through all of the subgroups of this study there is a significantly greater proportion of boys than girls. There are an even greater proportion of boys who are studied for OSA than have sleep studies in general, and a further increase in the proportion of

boys who were treated for OSA. Finally, the proportion of boys who were treated with nasal CPAP was greatest. This was not shown clearly in these figures, as children who have not had CPAP pressure determination studies were not included in these figures (see chapter 5).

A large proportion of the studies performed in this unit have shown significant respiratory abnormalities. Thirty-three percent of all children studied for OSA have received treatment, and a minimum of 19.3% of this group have had ongoing treatment with nasal CPAP. Because of the limitations of this data collection, it is likely that there were more children treated than were identified in this study. Regardless of this, the important feature is that these studies can, and do discriminate which children require treatment for sleep disordered breathing, and that at least one third of those children currently being studied go on to require some form of intervention. Also significant is the different age distribution of those children treated for OSA compared to those presenting with symptoms (Figures 6 & 7). The median and mean ages of children studied, and children treated, are not different.

The common "causes" and expressions of obstructive sleep apnoea in children are not the same as those in adults. Congenital syndromes and malformation are frequently associated with sleep disordered breathing in children. Of children assessed in our unit for obstructive sleep apnoea, 28% (**Total**) have a congenital syndrome or malformation. Thirty five percent of those children treated for sleep disordered breathing ($\mathbf{OSA_t}$) had a syndrome or malformation. Of all children assessed for

obstructive apnoea (**OSA_o**) 49.6% have a syndrome or malformation. Severe sleep disordered breathing is also more likely to occur in children who have a syndrome or malformation. Forty percent of those children requiring re-assessment after surgery, and 70% of those children requiring treatment with nasal CPAP therapy (**CPAP**) have a syndrome or malformation.

Sleep associated breathing disorders in children are diverse and vigilance for associated or alternative disorders has been important. Since obstructive apnoea and hypoventilation in sleep are abnormal, and detrimental to health, there is presumably some underlying abnormality in all cases. Structural abnormalities have been highlighted in children (Singer 135, Laurikainen 81), but there is also clear evidence for functional abnormalities causing or contributing to this disorder in both adults and children (Sullivan 139, Southall 136). Fifty percent of children had no apparent structural abnormality.

Obstructive sleep apnoea was associated with another respiratory or neurological abnormality in 146 (35.4%) of children with sleep disordered breathing. Amongst these are children with cystic fibrosis, spina bifida, chronic neonatal lung disease and cerebral palsy. For example, the nocturnal episodes of children with cerebral palsy may be seizures or obstructive episodes. There have been several children studied in order to make the final diagnosis with both possibilities confirmed in different cases. Seven cases of acquired central hypoventilation have also been identified (see Chapter 10). Children with an underlying chronic lung disease may have disordered

breathing in sleep due to their pulmonary disease alone (Gaultier 44) and tolerate upper airway obstruction poorly.

The responses of children to airway occlusion are different to those seen in adults. Children sleep through apnoeas, including those associated with hypoxia, without repeated arousal. These studies do not show apnoea terminating with arousal in children. Perhaps as a sequelae of this, only two, of all the children diagnosed with OSA, had abnormal sleep architecture and both were teenagers. Despite severe apnoea the majority of children maintain normal sleep architecture and distribution. Sleep studies showing severe OSA, or associated with chronic lung disease have continued to show all sleep states including slow wave sleep and REM.

This may relate to neurological development and the increased or decreased activity of various reflex systems. The presence of accessory muscle activity in REM sleep presumably indicates the activity of upper airway reflexes, maintained in children in this sleep state (Henke 62). Accessory muscles of respiration are recruited where there is increased respiratory resistance (Mathew 90), and with upper airway obstruction, increased activity can be seen in both inspiratory and expiratory phases of the respiratory cycle. Activity of the sternomastoids and abdominal muscle groups can be recorded in sleep. The degree and duration of this increased muscle activity can be used to quantitate the severity of the obstruction occurring (Jeffries 72).

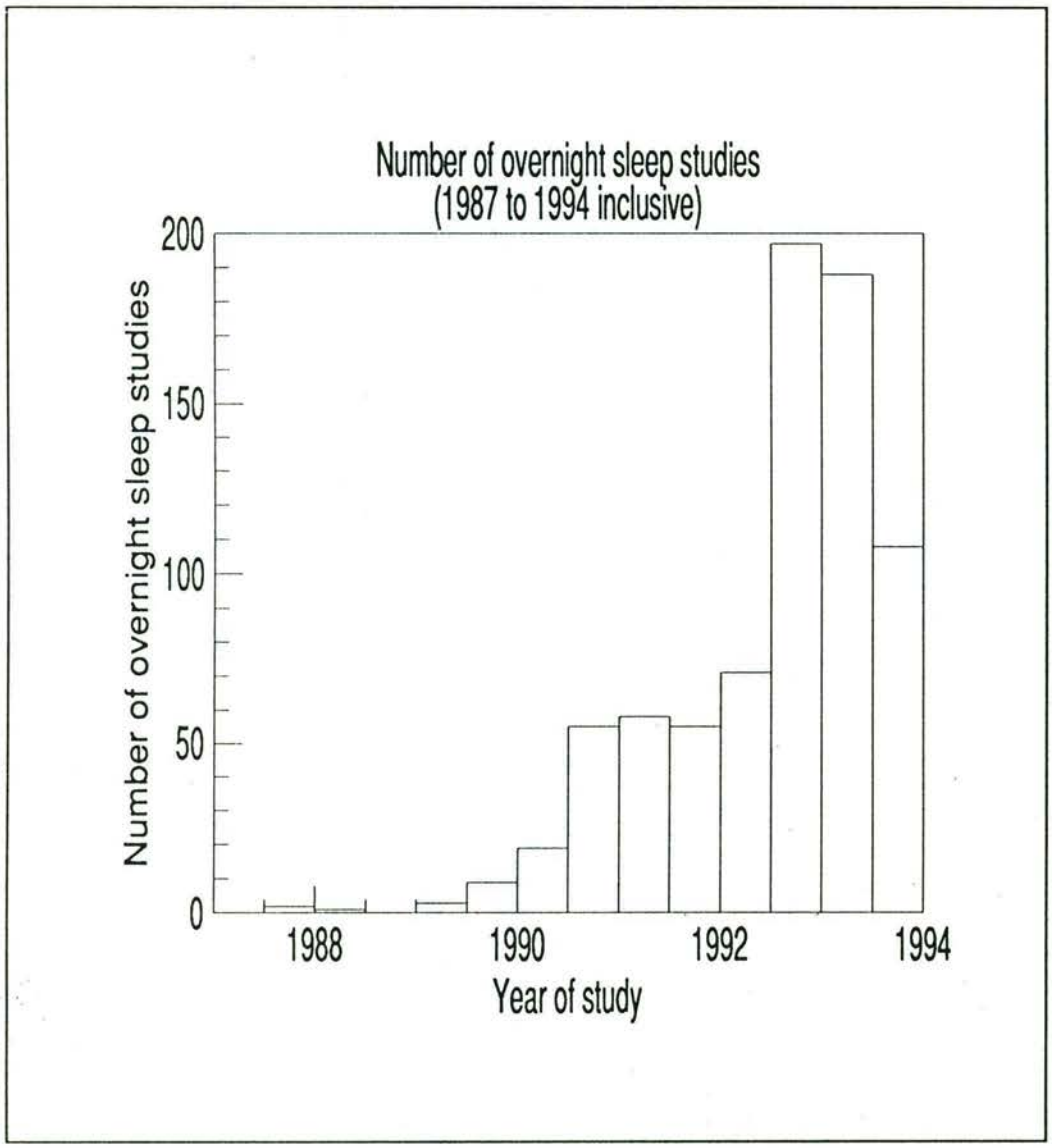
The role of partial upper airway obstruction is key to the understanding of obstructive apnoea as it occurs in children. Partial upper airway obstruction does appear to be stable and circumvent the most dramatic sequelae of obstructive apnoea seen in adults. The frequency of arousal and levels of desaturation which occur in children with OSA are greater than controls, but do not approach those levels seen in a typical adult patient. This mechanism of coping with upper airway obstruction appears to be common in children despite the negative consequence of CO2 retention.

Periods of cyclical mixed apnoea or hypopnoea have also been frequent in children with upper airway obstruction. Presumably there is an "undamped" reflex control system operating in this situation. It is possible that the central chemoreceptors are sluggish in their responses. Sniffing is seen during upper respiratory tract infections, with loss of repetitive sniff, coinciding with the recurrence of obstructive events. It appears that both chemoreceptor drive to the upper airway and upper airway pressure sensitive reflexes participate in the response of children to upper airway obstruction in sleep.

Table 1. Group numbers and sex ratio of the children studied in four subdivisions. The important feature here is that the percentage of boys increases with each subsequent group. Finally, the proportion who had an associated syndrome or malformation also showed a progressive increase through these subdivisions. There is a significantly greater proportion of boys with OSA, and more boys have severe OSA. More boys require treatment. The groups presented are a. all sleep studies, b. all OSA c. those treated for OSA d. those treated with CPAP. P values are given for chi-squared test for goodness of fit.

Feature	All studies N=455	OSA studies N=413	Treated N=175	CPAP N=34
Age	5.04 +/- 0.21 (0 - 15.9)	5.7 +/- 0.26 (0 - 15.9)	5.1 +/- 0.22 (0 - 15.9)	6.5 +/- 1.0 (0.1 - 15.9)
Sex ratio	M255 : F179(41%) $p < 0.001$	M234 : F160(41%) $p < 0.001$	M109 : F66(38%) $p < 0.001$	M21 : F13(38%) NS
Syndrome /	72 (15.8%)	72 (17.4%)	45 (25.7%)	12 (35.3%)
Malformation	54 (11.9%)	54 (13.1%)	27 (15.4%)	8 (23.5%)
Total	126 (27.7%)	126 (30.5%)	72 (41.1%)	20 (58.8%)

Figure 1. Number of children studied by years (1987 to 1993 inclusive) in 6 month intervals. There has been an exponential increase in the number of children studied each year. This has been limited only by the capacity of the facility.



Figures 2-5. Examples of the sleep study tracing abnormalities observed in children.

Figure 2a. Prolonged partial obstruction in SWS. The important features include inspiratory flow limitation on the airflow pressure trace, phasic inspiratory activity of the sternomastoid EMG and phasic expiratory activity of the abdominal muscles.

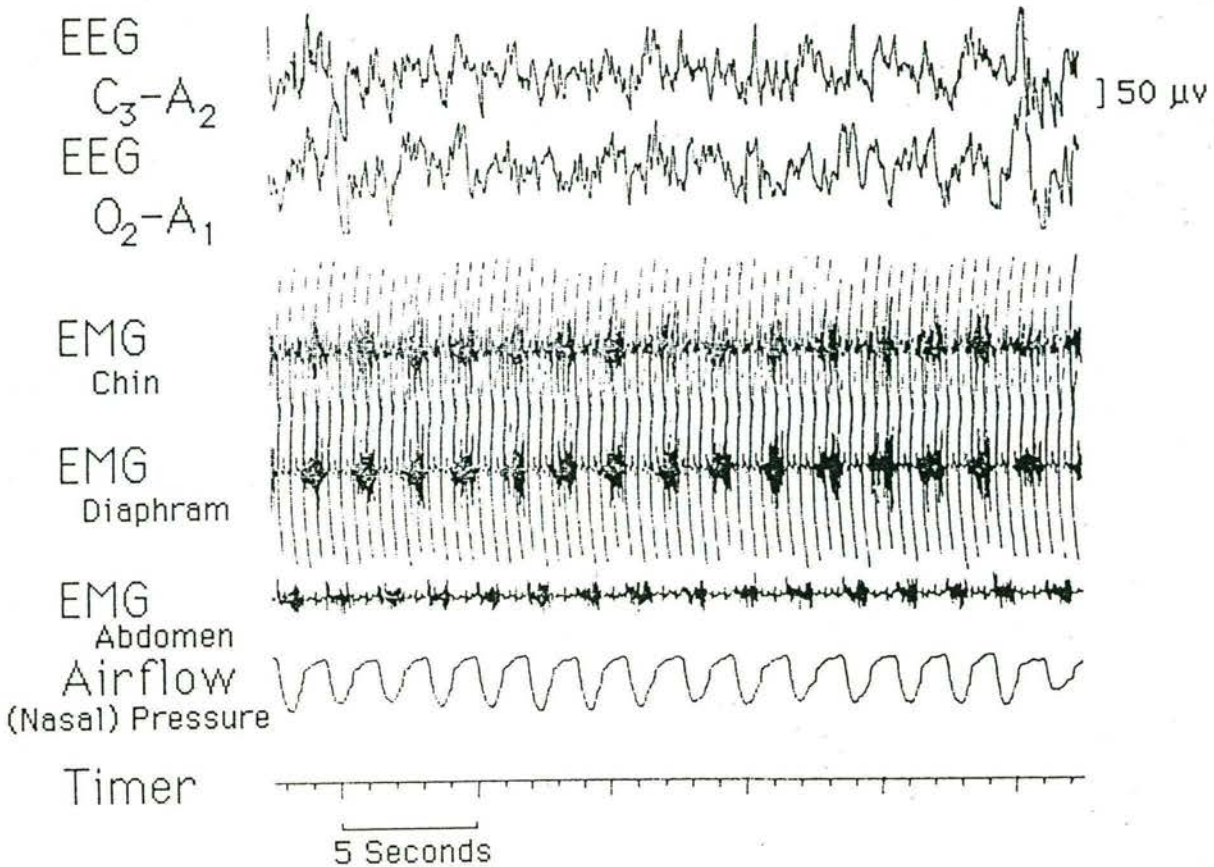

EEG
C_3-A_2
EEG
O_2-A_1
] 50 µv
EMG
Chin
EMG
Diaphram
EMG
Abdomen
Airflow
(Nasal) Pressure
Timer
5 Seconds

Figure 2b. CO_2 retention associated with sleep onset and SWS. The record commences at the time of sleep onset, with a further acute rise of $TcCO_2$ and fall in oxygen saturation SaO_2 at the onset of SWS (arrow). The scale is 30 - 100 with SaO_2 measured as percent, and $TcCO_2$ measured in mmHg.

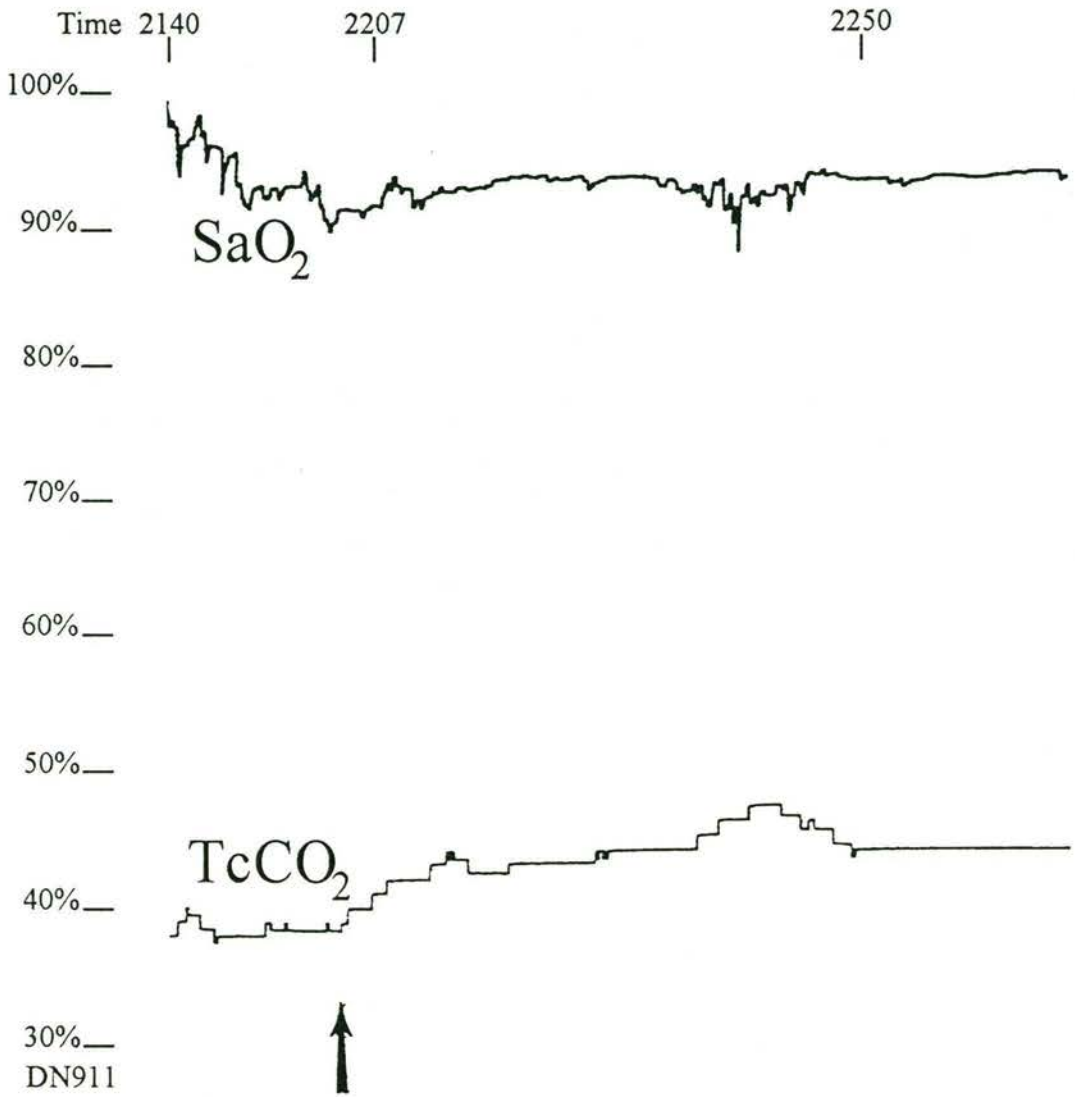

Time 2140
2207
2250
100%
90%
80%
70%
60%
50%
40%
30%
DN911
SaO2
TcCO2

Figure 3. Repetitive cycles of mixed apnoea / hypopnoea during light sleep. There are falls of oxygen saturation recorded in association with these events.

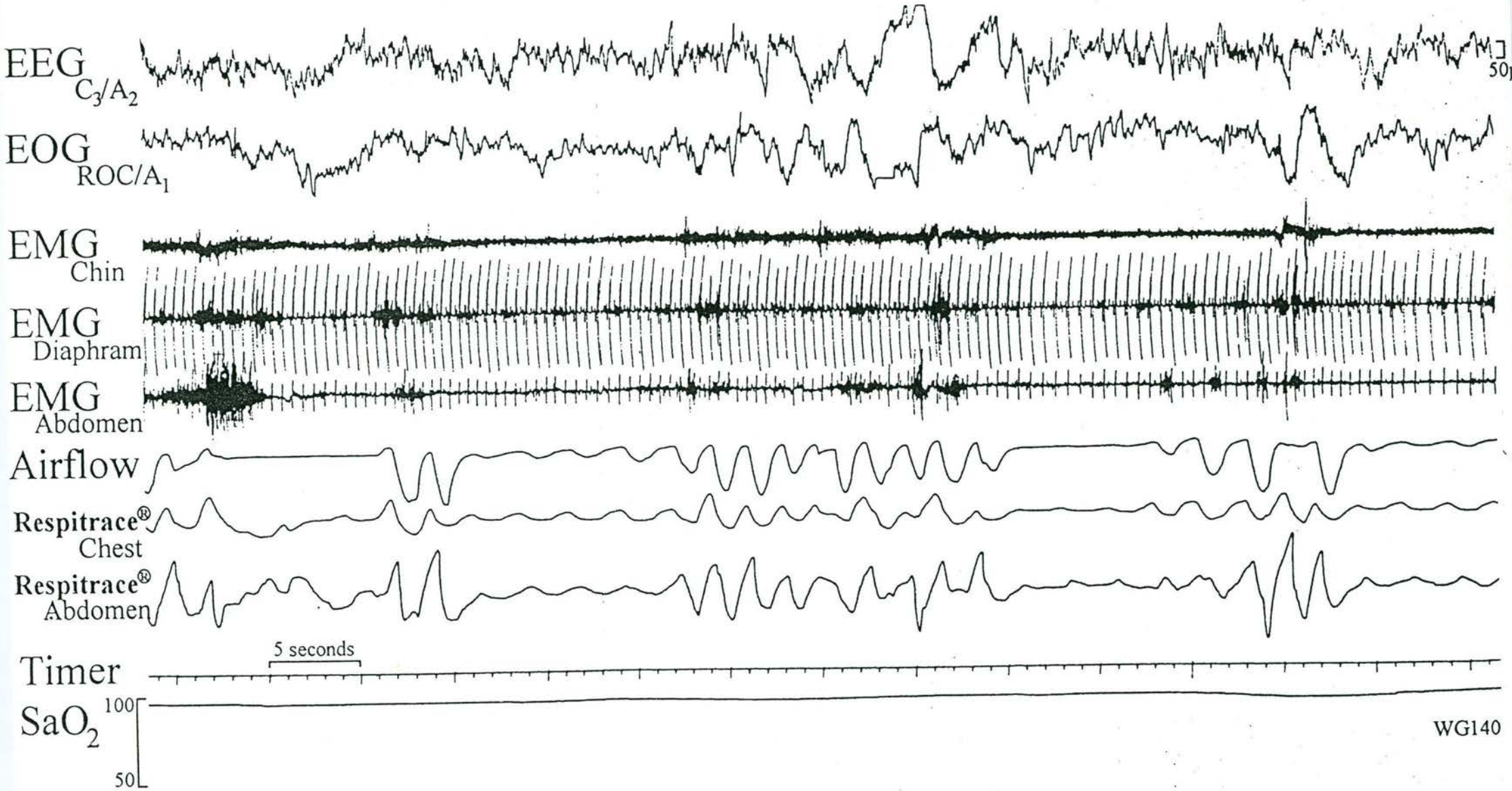

EEG C3/A2
50
EOG ROC/A1
EMG Chin
EMG Diaphram
EMG Abdomen
Airflow
Respitrace® Chest
Respitrace® Abdomen
5 seconds
Timer
SaO2
100
50
WG140

Figure 4a. Repetitive obstructive apnoea. Complete cessation of airflow is associated with continuing diaphragmatic activity, and paradoxic movement of the chest wall and abdomen. The acute events are associated with a fall in oxygen saturation (SaO_2), but no arousal on the electroencephalogram (EEG).

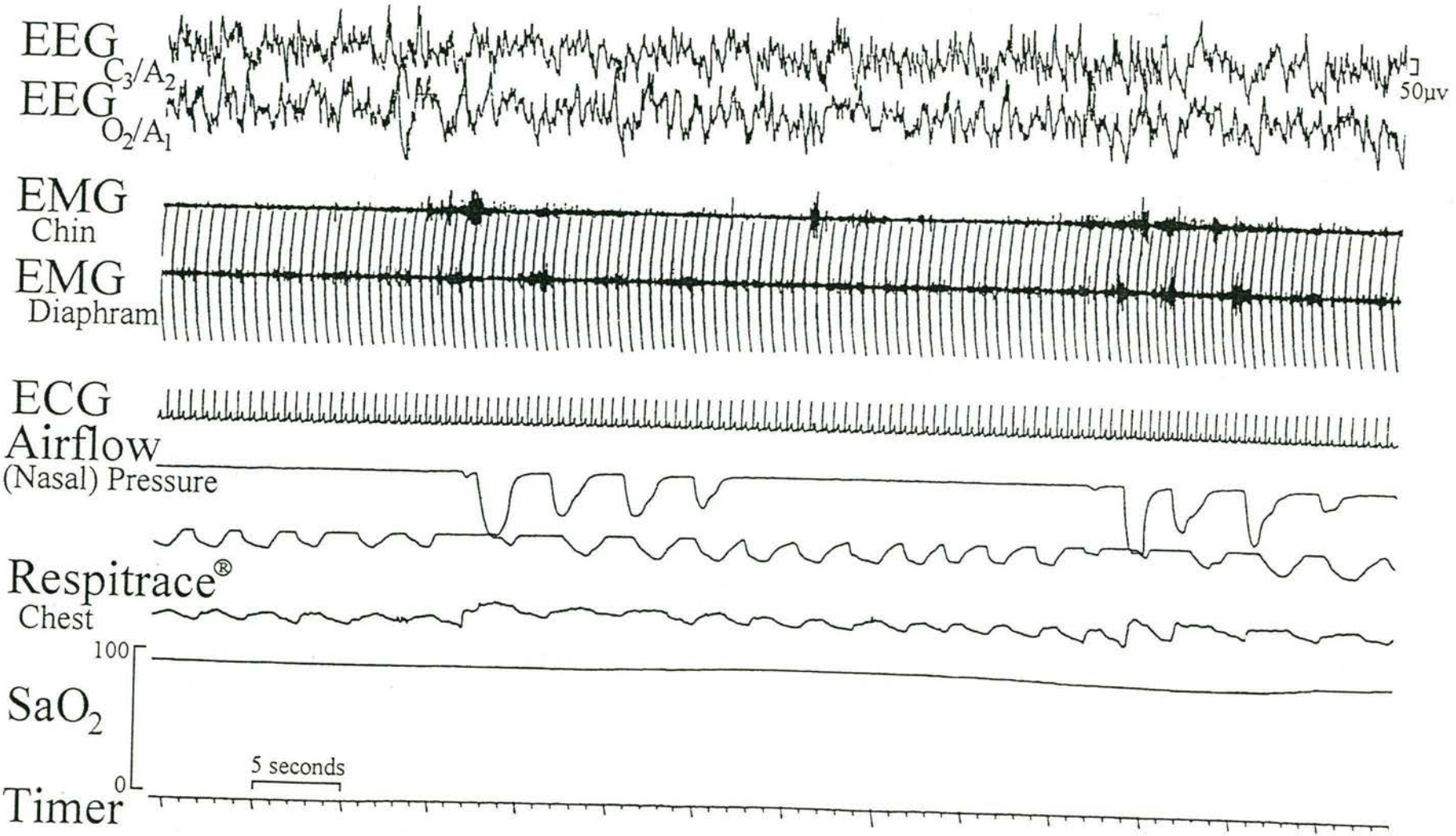

EEG C3/A2
EEG O2/A1
50µv
EMG Chin
EMG Diaphram
ECG
Airflow
(Nasal) Pressure
Respitrace®
Chest
100
SaO2
0
5 seconds
Timer

Figure 4b. Oxygen saturation (SaO_2) and (CO_2) changes associated with repetitive obstructive apnoea. These episodes are more frequent in REM sleep. The periods of rapid eye movement (REM) sleep are underscored.

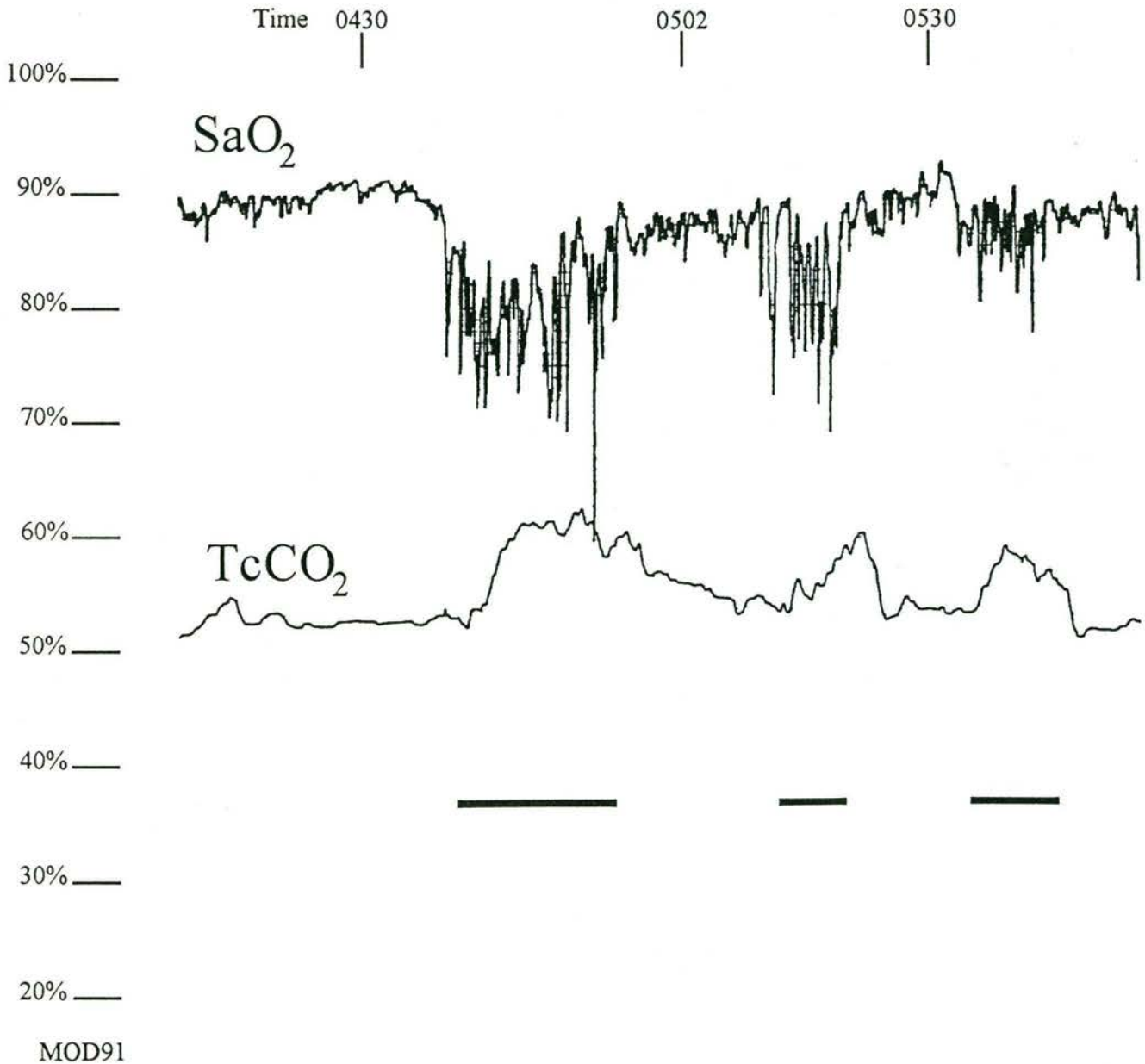

Time 0430
0502
0530
100%
90%
80%
70%
60%
50%
40%
30%
20%
SaO2
TcCO2
MOD91

Figure 5. Increased activity of chin and accessory muscles during REM sleep, with apparent "sleeping through" an obstructive event. There is loss of tonic activity, but phasic bursts of activity occurs with respiration. There is an increase in activity during the obstructive event (marked with an arrow) without an EEG arousal. It is likely that this represents a level of arousal which is not able to be detected on this form of sleep study recording.

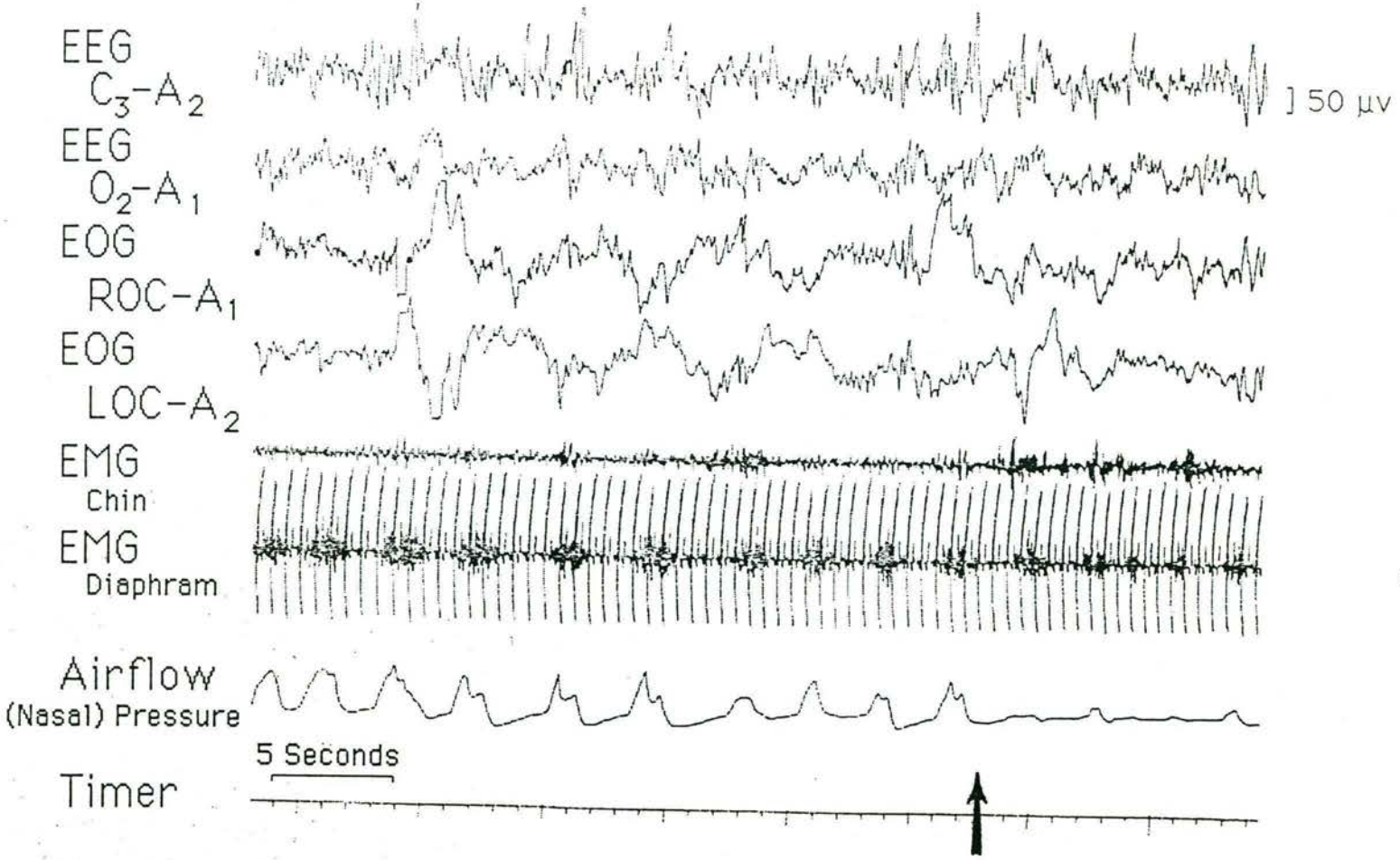

EEG
C3-A2
] 50 µv
EEG
O2-A1
EOG
ROC-A1
EOG
LOC-A2
EMG
Chin
EMG
Diaphram
Airflow
(Nasal) Pressure
5 Seconds
Timer

Figure 6. Histogram (6 month intervals) of the age of children studied for sleep disordered breathing. There is a skewed distribution, the peak age-group are those children less than six months old.

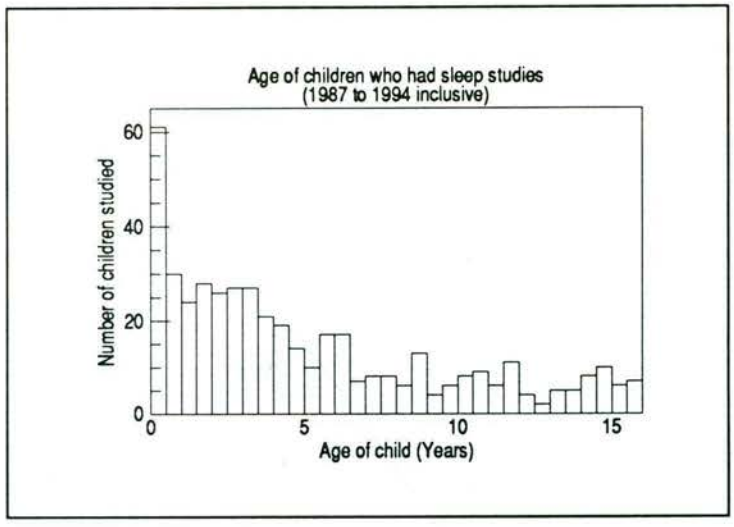
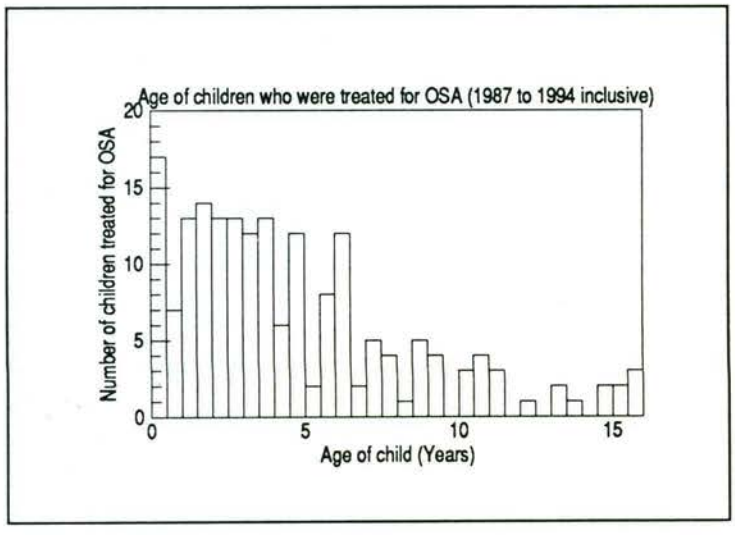
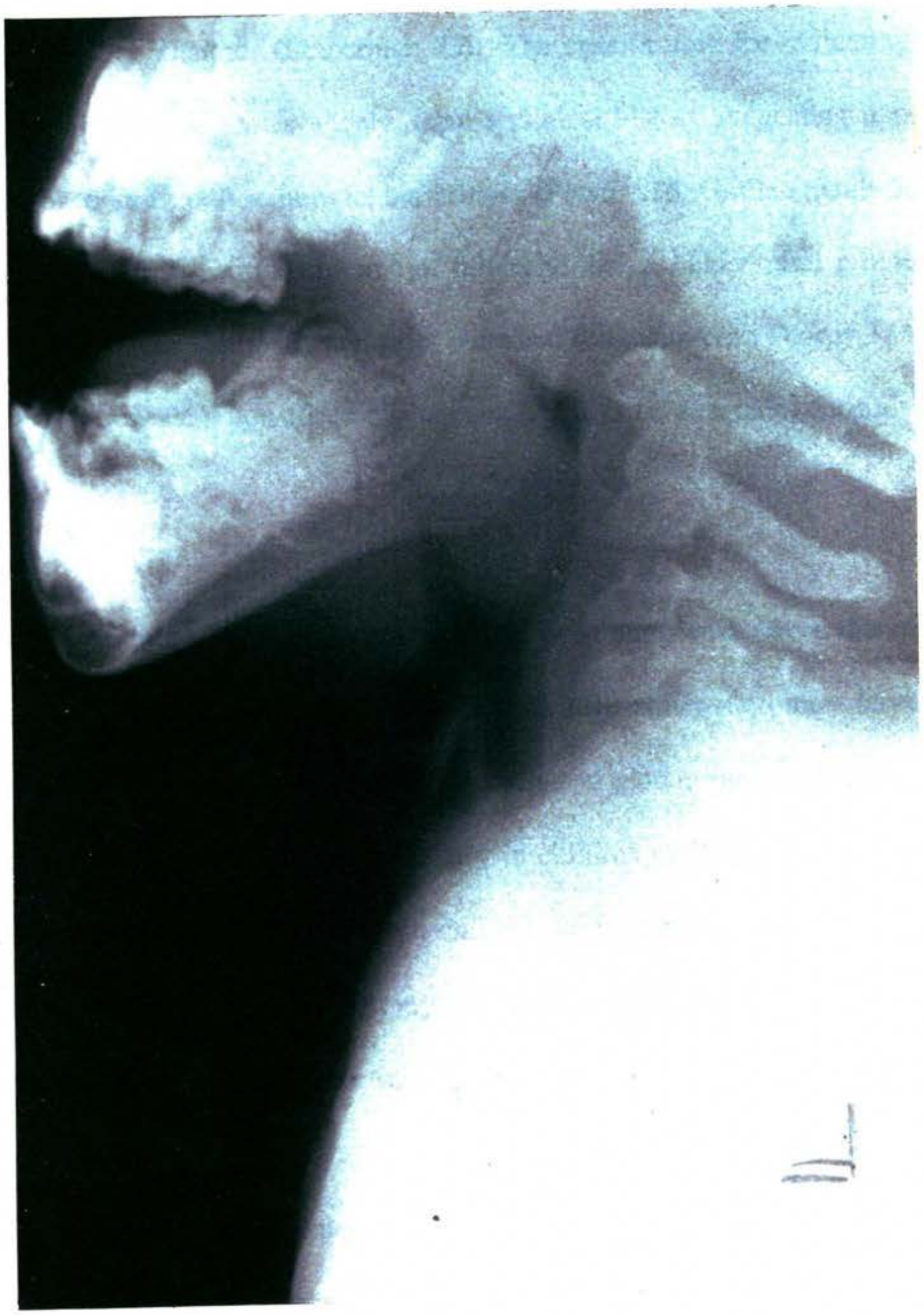


Figure 7. Histogram of the age distribution of children treated for OSA. The peak in the age group from birth to six months of age is no longer prominent. Sixty-one percent of these children were between the ages of one and four years.



Chapter 5.

Response of OSA to Adenotonsillectomy



5 RESPONSE OF OSA TO ADENOTONSILLECTOMY

5.1 INTRODUCTION

In children, the standard treatment of obstructive sleep apnoea (OSA) is the removal of the tonsils and adenoids (Leiberman 83). The criteria used for indicating the need for adenotonsillectomy varies widely, from a clinical history suggesting upper airway obstruction, to strict polysomnographic criteria (Potsic 116, Guilleminault 56). The association of apnoea with symptoms of failure to thrive, behavioural problems, or excessive sleepiness, definitely indicates the need for treatment (Thorpy 144). In the majority of cases, adenotonsillectomy is considered to be adequate, definitive treatment.

The use of adenotonsillectomy in children, has been suggested where there is evidence of hypertrophy of the glands (Editorial 32). However, others have also emphasised that removal of apparently normal sized glands can result in a critical reduction of airways resistance, particularly in children under the age of 2 years (Leiberman 83, Robertson 124). Even children with craniofacial abnormalities will often improve after adenotonsillectomy although they are less likely to respond fully to this surgery (Potsic 116, Robertson 124).

Follow-up studies following adenotonsillectomy in children have been limited (Frank 39). Significant clinical improvement is frequently noted (Leiberman 83, Brouillette

17, Serratto 130). Documentation shows that the frequency and severity of apnoea, also improves (Guilleminault 56). Past studies suggest that the quality and distribution of sleep has also been shown to change following adenotonsillectomy for treatment of OSA in children (Frank 39, Guilleminault 56). Significant consolidation of sleep is demonstrated by improved sleep efficiency, also inferred by improved indices of movement, and arousal.

In this study children who had diagnostic sleep studies which resulted in a recommendation of adenotonsillectomy were followed up with repeat overnight sleep studies an average of 1.5 years later. The aim of this study is to clarify the longterm response to this surgery for treatment of childhood OSA.

5.2 PATIENTS

The study group includes thirteen children, six females and seven males. At the time of the initial diagnostic study the age of the group was 2.72 +/- 0.46 years (0.92 - 6.13). The time between the first and second studies was 1.57 +/- 0.2 years (0.67 - 2.86).

5.3 METHODS

All of the subjects in this study had attended the sleep disorders unit because of a clinical suspicion of OSA. Full overnight sleep studies were performed in order to diagnose the severity of upper airway obstruction in each child. Following this study adenotonsillectomy was recommended as treatment of the upper airway obstruction.

These children had been assessed clinically as having a good response to treatment. The families were contacted by the unit and asked to participate in this study. The study group consists of those children where the family was able to be contacted by telephone and the parents consented to a repeat overnight diagnostic study. Nine children could not be contacted, and five did not agree to participate. As in the group who were studied, the parents in these cases felt that their child was well. In at least two instances other considerations (such as the mothers current pregnancy) were the main reason for not returning.

Both the initial diagnostic and the follow-up overnight sleep studies were performed within the David Read Sleep Disorders Unit. The methods for performing the sleep study and scoring the respiratory parameters are described in Chapter 4. There were no special diagnostic tools or methods used in either the diagnostic or follow-up studies.

Results are presented as mean +/- SEM (range a-b). Two way anova tests were used for statistical analysis sleep parameters. These results are presented as mean1 +/- SEM1, mean2 +/- SEM2 (p value / not significant (NS)). Respiratory variables were usually either log transformed or rank transformed for this analysis. Where variables which have been log transformed for statistical analysis the SEM is not presented.

5.4 RESULTS

All thirteen children snored at some time during their follow-up study. Other evidence of partial obstruction was frequent flow limited inspiration on the airflow trace (indicating increased upper airway resistance), use of accessory muscles of respiration and presence of obstructive apnoeas in the course of the study. Respiratory variables showed significant improvement in most areas, and the obstructive apnoea index fell from 77 to 14 ($p<0.01$)

There was clearly a persistence of upper airway obstruction on all measurable variables. See Table 1. CO_2 range was remained elevated showing a non-significant decrease from the first study mean of 15.5 to 14.1 +/- 1.8 mmHg (NS) at follow-up. Hypopnoea indices fell from 96 events per hour, but remained clearly elevated at 33 for the group ($p<0.01$). Nine of thirteen (69%) children had more than 20 obstructive events (apnoeas &/or hypopnoeas combined) per hour, and more than five obstructive apnoeas per hour, during their follow-up study.

Some trends in sleep architecture were apparent but only the change in total sleep time reached statistical significance. Total sleep time (TST) increased from 430 to 502 +/- 18.9 ($p = 0.02$). In this group of children the percentage of SWS showed no significant change and was 30.5 before treatment and 30.0 +/- 2.4% after treatment. The percentage of S1-2 increased from 47.6 to 52.9 +/- 2.9% (NS), and percentage of REM sleep decreased from 21.9 to 17.4 +/- 1.7% (NS). See Table 2.

Indicators of sleep disturbance include sleep efficiency (EFF), arousal index (ARI) and movement index (MVI). None of these variables had statistically significant changes. Indicators of respiratory insufficiency include respiratory rates in REM and SWS, and the sigh index. The frequency of sighs fell from 3.9 to 1.7 +/- 0.6 per hour ($p = 0.01$), but respiratory rates in SWS and REM were unchanged. Baseline oxygen saturation increased from 95.5 to 97.3 +/- 0.26 ($p < 0.005$) and although the range of oxygen desaturation fell from 19 it remained greater than normal. The mean fall was 11% ($p=0.07$) at follow-up. See Table 2.

5.5 DISCUSSION

Adenotonsillectomy is generally considered to be appropriate and definitive treatment for OSA in children. The aim of this study was to determine the longterm results of this surgery in a group of children who had full diagnostic sleep studies prior to, and then following, surgery.

This study has revealed evidence of persistent, partial, upper airway obstruction in a group of children with a past history of adenotonsillectomy for OSA. In general, they were considered clinically well by the primary care physician and parents. Follow-up studies had not been sought by the carers.

Clinical criteria have provided inadequate information for judging the persistence or progression of the disorder in this study group. It had been assumed that clinical criteria effectively screen for those children requiring ongoing therapy. In our unit, to date, children who required ongoing treatment with nasal CPAP were identified on clinical grounds using a combination of history, the documented severity of apnoea on diagnostic study and peri-operative course where adenotonsillectomy was undertaken. Repeat studies were prioritised on these criteria. Only one of the children in this study had been considered still symptomatic and in need of follow-up. There were no clinical concerns about the remaining twelve children when they were recalled specifically for this study.

Until more is known about the natural history of OSA this cannot be considered a curative operation. One possibility is that adult apnoea starts in childhood and that these are the individuals who will form the adult population of OSA. This concern is reinforced by these results. The persistence of CO_2 retention above the normal range and the persistence of upper airway obstructive events (both apnoeas and hypopnoeas) indicates that the majority of children treated by adenotonsillectomy for OSA achieve only partial correction of their upper airway obstruction in the long term.

There is a lack of paediatric data in the literature and these selection and scoring criteria for children are specific to our unit. Our treatment recommendations are based on these criteria. The clinical changes which occurred with treatment were represented by the general improvement in the respiratory indices at follow-up. The scoring procedure has produced discriminatory changes indicative of persisting, but generally not severe, sleep associated upper airway obstruction.

The severity of upper airway obstruction which should be treated in children remains unclear. Untreated OSA has been shown to have clearly detrimental sequelae in both adults (McNamara 95) and children (Levy 84). Adenotonsillectomy may also have an associated morbidity and mortality (McGowan 93). It is generally agreed that current criteria (established for adult populations) are not applicable to children (Carroll 23). It is unknown whether the level of upper airway obstruction which persisted in these children will have detrimental health effects in the long term.

There were no enduring sleep state changes in this group, even though differences between children with OSA and normal controls are reported (Guilleminault 56). Sleep architecture showed little response to the changes in respiratory variables. Some trends were identified and it may be that this group is too small for statistical significance.

The trends in sleep architecture observed in these follow-up studies do not consistently follow the changes expected for a group of children of increasing age. It is unlikely that the changes observed were "first night effects" since the normal data from other units was also recorded on the first study night, but normal data produced in other units may not be applicable in our setting. The proportion of SWS seen was stable (30.0 to 30.5%) and greater than expected for age (17.6 to 20.6%). There was an increase in total sleep time and in percentage of S1-2 sleep seen at follow-up without any change in the arousal index. Percent S1-2 sleep (47.6 to 52.9%) was consistent with normal values (44 to 50%), even though TST (430 to 501 mins) was reduced (N = 506 to 683 mins).

The reduction in percentage of REM sleep seen with time may be an age effect, but the percentage of REM sleep present in both studies was reduced. Normative data shows that 28.7 to 31% of REM sleep is typical for this age group (Williams 154, Kohler 75). The percentage of REM sleep in this study group decreased from 21.9 to 17.4% from diagnosis to follow-up.

It is possible that this group of children did not have apnoea severe enough to affect sleep architecture. All of the studies were scored by one person and so while absolute percentage of the different sleep states may be altered compared to other units, the trends shown are likely to be real through consistent disparity.

However, the values for percentage time in the different sleep states (including REM and SWS) and for sleep time and arousal parameters were consistent with other studies where a high proportion of children had upper airway obstruction. One other group of children was documented in our unit (Part II Chapters 2 & 7), and there is one previous report in the literature (Frank 39). A decrease in percentage of REM sleep compared to normal is also consistent with previous reports of OSA (Guilleminault 56). Presumably the changes in sleep architecture were both real, and persistent despite adenotonsillectomy in this group of children. It is possible that the changes in sleep architecture are linked with the underlying cause of OSA since each of the two studies demonstrating these changes have shown persistence in the differences in sleep architecture following treatment.

In conclusion, thirteen children had OSA diagnosed on overnight sleep study and underwent adenotonsillectomy as treatment for this. Follow-up sleep studies were performed 18 months later. Respiratory scores and clinical observations confirmed that the majority of these children had persistent partial upper airway obstruction.

Sleep architecture was assessed and showed that TST increased significantly. An increase in percentage of stages 1-2 sleep and decrease in percentage of REM sleep were not statistically significant. Percent SWS was unchanged, and there were no changes in any of the indices of sleep fragmentation.

The percentage of REM sleep seen, was persistently low, and of SWS was consistently increased compared to studies in normal children. The sleep architecture observed in this study may indicate persisting abnormalities associated with the presence of continuing upper airway obstruction in sleep despite some improvement in respiratory disturbance indices.

Table 1. Sleep parameters and their changes following adeontonsillectomy. The standard error of the mean is listed in parentheses following the values for the diagnostic study. The variables were compared using a paired t-test. The level of significance is presented in parentheses following the values for the follow-up studies. Where there is no significant difference this is presented as (NS). Sleep variables are presented in minutes (mins) or as a percentage of total sleep time(%). Efficiency indicates the amount of sleep during the entire study time. Movement, arousal and sigh indices are presented as events per hour (hr^{-1}).

There was an increase in the total sleep time (TST), but no significant change in the proportion of slow wave sleep (SWS) or stages one and two sleep (S1-2). There was a non-significant decrease in the proportion of REM sleep seen. There was a significant decrease in the number of sighs per hour of sleep time.

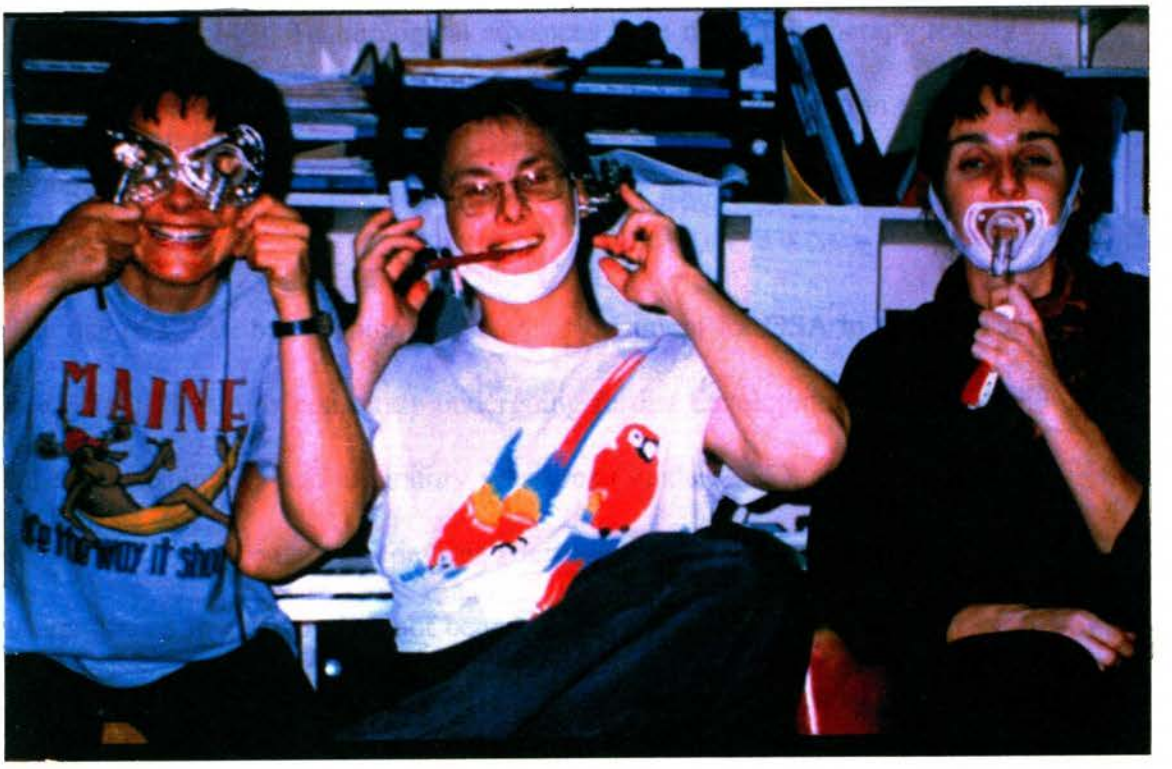
Variable (Units)	Diagnostic Study (SEM)	Follow-up Study (p value)
TST (mins)	430.6 (18.9)	501.7 ($p < 0.02$)
S1-2%	47.6 (2.6)	52.9 (NS)
SWS%	30.5 (2.4)	30.0 (NS)
REM%	21.9 (1.7)	17.4 ($p < 0.09$)
Efficiency (%)	86.9 (2.1)	91.4 (NS)
Moves (hr^{-1})	4.3 (1.0)	4.4 (NS)
Arousals (hr^{-1})	4.1 (0.6)	4.6 (NS)
Sighs (hr^{-1})	3.9 (0.6)	1.6 ($p < 0.02$)

Table 2. Respiratory variables and their change after adenotonsillectomy. The mean age of the group at the time of their diagnostic study was 2.7 years (0.9 - 6.1 years). The mean delay between studies was 19.2 months. The study was an average of 18 months following adenotonsillectomy for this group of fourteen children. These indices are given as events per hour. RDI = respiratory disturbance index and includes both apnoea and hypopnoea. OAI = obstructive apnoea index, OHI = obstructive hypopnoea index. Transcutaneous carbon dioxide levels (CO_2) are given in mmHg, and oxygen saturation (SaO_2) in percent.

Measurement (units)		Diagnostic Study (SEM)	Follow-up Study (p value)
RDI	Total (hr^{-1})	52.7 (7.7)	18.5 ($p < 0.001$)
	Obstructive (hr^{-1})	44.1 (6.0)	11.8 ($p < 0.001$)
	Central (hr^{-1})	8.6 (2.3)	6.7 (NS)
OAI	(hr^{-1})	76.7 (9.6)	13.5 ($p < 0.001$)
OHI	(hr^{-1})	96.0 (32.9)	32.9 ($p < 0.005$)
CO_2	Range (mmHg)	15.5 (1.9)	14.1 (NS)
	High (mmHg)	53.8 (2.5)	52.5 (NS)
SaO_2	Range (%)	18.5 (2.8)	11.3 (NS)
	Baseline (%)	95.5 (0.3)	97.3 ($p < 0.001$)

Chapter 6.

Use of Nasal CPAP in Children With OSA



6 USE OF NASAL CPAP IN CHILDREN WITH OSA

6.1 INTRODUCTION

Nasal continuous positive airways pressure (CPAP) therapy was introduced for the treatment of obstructive sleep apnoea (OSA) at the Royal Prince Alfred Hospital in 1980 (Sullivan 140). Technological advances have made this therapy readily available. The excellent response results in high patient motivation and compliance (Saunders 128).

The use of CPAP has become the standard treatment for OSA in adults (Thorpy 144). This therapy is constantly undergoing further development, including the use of different inspiratory and expiratory pressures (Sanders 127), and automatically responsive pressure delivery devices (Berthon-Jones 8). Nasal CPAP therapy for sleep apnoea in children has not been used extensively. The explanation for this difference likely relates to the widely held view that adenotonsillectomy cures OSA in children (Butt 22), and to the perceived greater difficulty in achieving patient co-operation.

Adenotonsillectomy is currently considered the appropriate initial treatment of OSA in children. Although it is claimed that this procedure is highly successful (Robertson 124), it is notable that virtually all such reports are based on post-operative clinical assessment. Reports in which both diagnostic and then follow-up studies have been

performed are notably lacking. There are individual reports in which tracheostomy (Wiebicke 151) and more recently nasal CPAP (Waters 146) have been used in patients with severe sleep apnoea where adenotonsillectomy has either failed or was not indicated in the first place.

Nasal CPAP as a more routine treatment alternative in infants has begun to occur (Tibballs 145). There are a few reports where it has been used successfully in older children in the home (Guilleminault 50, Schmidt-Nowara 129, Ellis 35, Dyson 31). Difficulties in establishing treatment successfully at home have prohibited its widespread practical use (Guilleminault 51, Gaultier 43).

One of the first five subjects treated with nasal CPAP at RPAH was a 13 year old boy (Sullivan 140). Since that time we have regularly treated a range of nose prongs and masks in an attempt to use nasal CPAP as a viable long-term treatment program in children. This report describes the development and use of this therapy in eighty infants and children. The characteristics of those children who have been treated with CPAP therapy and aspects of the therapy which have been found to optimise the chances of successful use in a paediatric population are described.

6.2 PATIENTS

The children analysed in this group were assessed and treated for OSA at the David Read Sleep Disorders Unit. All were diagnosed and commenced on CPAP treatment at age 15 years or younger.

Two hundred and fifty-two children have been studied to diagnose OSA in the David Read sleep disorders unit. Four hundred and thirty-three (68%) of the full overnight sleep studies performed on children to date have been for the assessment of OSA. The majority of patients were referred on clinical grounds with a suspected diagnosis of OSA. A small number of children were recruited under specific research protocols. Ninety-eight (39%) were female, and 154 (61%) were male. The average age of these children was 5.7 years (+/- 5.1 years) ranging 1 week to 15.9 years.

On the basis of the severity of apnoea found in the all-night sleep study and the clinical severity, nasal CPAP was recommended for the treatment of sleep associated upper airway obstruction in 80 children (32%). Where CPAP treatment was recommended 23 (29%) were females and 57 (71%) males. The age of the children treated with CPAP, was 5.7 years with a range from 12 days to 15.3 years (SEM 194 days). See Table 1, and Figure 1.

Treatment was recommended on a clinical basis and factors other than the apnoea index were taken into account. The majority of children underwent

adenotonsillectomy. The need for ongoing treatment with CPAP was based on the same criteria as the initial recommendation for treatment with adenotonsillectomy, and included an assessment of the severity of obstruction by overnight sleep study and clinical symptoms. Treatment was recommended if there was persistent partial obstruction associated with hypoventilation and CO_2 retention of 10 mmHg or more. Carbon dioxide retention was confirmed with arterial blood gases where possible.

6.2.1 ASSOCIATED CONDITIONS

The major indication for CPAP therapy has been OSA. A number of other conditions have had a major contribution to the final clinical presentation and need for ongoing treatment. The circumstances associated with our decision to use nasal CPAP are shown in Table 2.

Eighty (32%) of children assessed for the presence of obstructive apnoea 80 had a major congenital malformation or syndrome. Of the children recommended for CPAP, 42 (53%) had a major congenital malformation or syndrome. The syndromes or malformations in these children are listed in Table 3. Thirty two (40%) children had an associated syndrome and ten (12.5%) had a malformation.

Only fifteen (19%) of the children requiring treatment with CPAP had isolated adenotonsillar hypertrophy. Ten children (12.5%) had significant lower respiratory tract disease as well as upper airway obstruction. Six (7%) children were obese in

association with severe obstruction, and only one child (1.3%) presented as failing to thrive. Seven (8%) had cerebral palsy, and five (6%) had a history of prematurity with residual lung disease. Two children had cardiac lesions. One child with Down's syndrome had unexplained persistent pulmonary hypertension. Another child had corrective surgery delayed because of pulmonary hypertension but was considered suitable for this surgery twelve months after commencing CPAP therapy.

6.3 METHODS

6.3.1 SLEEP STUDIES

Full overnight sleep studies were performed within an established sleep disorders unit. The diagnostic studies included variables which provided measures of sleep stage and respiratory status.

A routine sleep study includes measurement of parameters as previously described (McNamara 96). These include measures of sleep stage, using electroencephalogram (EEG) C3/A2, and O2/A1. Electrooculogram (EOG): Right outer canthus/A1, Left outer canthus/A2, and electromyogram (EMG) submental. Respiratory variables were measured using nasal airflow via pressure transducer (Grass, or Validyne). A transcutaneous carbon dioxide monitor (Radiometer, Copenhagen) was placed on the upper chest. Oxygen saturation (SaO_2) (Ohmeda Biox 3700) was measured using a finger or ear probe. Thoracic and abdominal movement were monitored by

inductance plethysmography (Respitrace ambulatory monitoring). Electrocardiogram (ECG) was recorded using surface electrodes. In some cases further EMG recordings of either sternomastoid, or abdominal muscles were made via surface electrodes.

Sleep studies were scored using Rechstaffen & Kales (Rechstaffen 123), or Anders and Parmalee (Anders 1) criteria for sleep staging. Respiratory variables have been recorded using criteria developed for use in children (Waters 147). Apnoeic events were scored on the basis of respiratory cycle length, rather than absolute duration. An apnoea was scored if two or more respiratory cycles were perturbed. Hypopnoea were scored when there was a 50% or greater reduction in the amplitude of the respiratory flow signal.

6.3.2 NASAL CPAP THERAPY

The majority of children had a second overnight diagnostic sleep study following adenotonsillectomy or craniofacial surgery before the decision to commence CPAP therapy was made.

A behavioural program was used to gradually introduce children to the various aspects of this treatment. We found that it may take several weeks or months of training before CPAP is fully established. The program which we developed consists of gradual introduction of the child to the nasal mask. The CPAP mask is dismantled so that the manifold is open and not connected to any restrictive connections or

tubing, and there is no added respiratory dead space. We then encourage daytime practice sessions and games until the child is able to wear the open mask without fear or distress.

At the next stage the child is settled to sleep while wearing the mask. Once the child was able to wear the mask comfortably overnight, CPAP is commenced at the lowest machine pressure setting (3.5 to 4.5 cm H_2O). This is also introduced in the home environment. When the child is comfortable wearing the mask with low pressure CPAP during the night at home, a CPAP pressure determination study was performed in the sleep unit.

Our primary concern is always patient safety. In more severe cases CPAP is commenced in hospital, as soon as possible following the diagnosis. However, in less severe apnoea we found that a program of gradual introduction to the treatment was more appropriate. In very young or severely disabled children there was no obvious benefit gained from a behavioural program. During this introductory phase, close supervision allows any practical problems with mask fitting or mask attachment to be attended to.

6.3.3 NASAL CPAP EQUIPMENT

During the time period covered by this report, there have been a number of equipment revisions. The first infant commenced on CPAP used a specially

constructed mask and the second wore a range of custom designed nasal prongs for the first 2 years of her therapy. However, there are now commercially manufactured paediatric masks and manifolds available. Using this range of equipment we have been able to progressively reduce the number of individual modifications required for proper fitting and adaptation to take place. The headstraps used to hold the mask in place are still made by the hospital staff.

Nasal CPAP delivery has been via the Rescare CPAP machine including a number of new models. Commercially manufactured equipment has been available for use since the second child was commenced on this treatment, and to date we have made no unique modifications to this system. Humidification, where required, is delivered by the Fisher-Paykel system designed for home use in association with the CPAP system.

To date thirteen distinct varieties of CPAP masks/prongs have been used. The majority of children have worn one of four different mask sizes, with or without the "bubble" cushion. We have had such success with these masks that children originally established on custom designed nasal masks or prongs have all been converted to the newly designed systems. Examples of the smallest and largest mask manifolds are shown in Figures 2a and 2b. The features which best determine acceptability to patients and their carers (parents and staff) are mask size and ease of fitting. Development of equipment is still occurring.

6.4 RESULTS

The use of CPAP in children began in 1980 but the majority (84%) of children described in this analysis have been diagnosed and treated since the establishment of a dedicated paediatric service in 1990. Prior to 1990 there were ten children established on CPAP. Each of these ten children had custom made masks which they were able to use in the home environment. The first child presented in cardiac failure and commenced CPAP at the age of 13 years. He was later diagnosed with the Fragile X syndrome. The youngest child was a male infant established on CPAP in 1988 at the age of 9 months. This child presented in cardiac failure, with an underlying diagnosis of the foetal dilantin syndrome. Six of these ten children currently continue on CPAP therapy at home, one has died from progression of Morquio syndrome, one no longer requires CPAP, and two have abandoned the treatment. Of the children who no longer use CPAP, one had continued improvement following adenotonsillectomy, and the other child's problems were dominated by mental retardation. The parents of this child elected to cease treatment because they were concerned that the use of CPAP was detracting from the child's already limited quality of life (Waters 146).

Seven children are still being established on CPAP. Of the 73 children remaining, 63 (86%) were successfully established on CPAP therapy. Nasal CPAP was used successfully in 26 (36%) who no longer required this treatment. Twenty-nine (40%) children are currently using CPAP at home. The mean pressure used in this group of

63 children was 7.9 +/- 3.2 cm H_2O (range 4 to 16 cmH_2O). See Figure 3. The magnitude of the pressure required shows no correlation to the age of the child being treated, but tends to relate to the severity of the upper airway obstruction. Ten of the 73 children (14%) have failed to achieve adequate treatment using this therapy. Eight (11%) of those children who commenced CPAP have subsequently died.

The duration of CPAP usage has varied from several days to 12 years 8 months. The average duration of CPAP therapy for the group is 15 months. The shortest duration was 4 days when CPAP was used for preoperative stabilisation. The maximum duration is twelve years and eight months in a boy who was commenced on CPAP at the age of seven years, with an underlying diagnosis of Fragile X. This young man remains on CPAP therapy at the age of 19 years. The youngest child with documented obstructive apnoea was aged five days old and had an underlying diagnosis of spina bifida, with symptomatic bulbar dysfunction. Thirteen children have been on CPAP for two years or longer, and 21 children have been on CPAP for one year or more (Figures 4).

Those children who died had diseases which were life-threatening and this was taken into account at the time of commencing nCPAP. The details of these children's underlying illness and course are shown in Table 4. Five children died through progression of the underlying condition and three children did not respond to the treatment.

6.4.1 COMPLICATIONS OF NASAL CPAP THERAPY

6.4.1.1 Treatment Failure

The majority of children were able to be treated with nasal CPAP therapy over a long period provided the therapy was introduced slowly by trained staff. See Table 5. Of 80 children there has been a failure to establish treatment in 10. Treatment failure is the major problem with the use of nasal CPAP. The most common reason for failure is the inability of the child and/or carer to tolerate the use of the device. The reasons for intolerance have been diverse, but many appear to be linked behavioural mechanisms. A lack of motivation and fears of the caregiver about the treatment contribute to this.

The great need for careful introduction to the child is illustrated by the secondary failure of treatment in one infant. This infant had been effectively established on CPAP at home. Following several months of stable therapy a CPAP machine was purchased. The pressure set on this machine at purchase was 10 cmH_2O higher than that used previously. The parents attempted to use the machine but were alerted to the pressure difference by the marked distress and repeated refusal of the child to accept CPAP with this new device. The child has subsequently refused CPAP therapy even at previously tolerated pressures.

It has been necessary to use arm splinting in some children, albeit rarely, especially in those children with a behavioural age of 6-9 months up to 3 years. By pre-school

age most children become aware of their symptoms and the need for the use of CPAP. They are than able to reapply the mask themselves during the night if it shifts off the nose, rather than pulling it off deliberately. We have seen some cases where CPAP has been tolerated early in the treatment and the child has objected days or weeks later in the course of treatment.

6.4.1.2 Adverse physiologic responses to high CPAP pressure.

The pressure which may be used to treat children is limited as high pressure can be associated with hypoventilation, increased frequency or duration of central apnoeic events, and increased frequency of arousals. Progressive CO_2 retention can be seen acutely but resolves when the pressure is reduced again. Carbon dioxide retention or increased frequency of central apnoea has been seen in 26% of pressure determination studies. At each case this has limited the peak pressure which could be used for treatment. In younger children one of the signs indicating the potential for hypoventilation is abdominal muscle recruitment in expiration. The lowest pressure at which we have seen these limiting effects was 5.2 cmH_2O in a young child age 11 months.

The most serious medical complications of nasal CPAP at home have been changes in breathing during sleep induced by the nasal CPAP itself. One child, with severe neurological and respiratory dysfunction, was introduced to CPAP to treat upper airway obstructive events. However, within minutes of the mask and pressure being introduced, there was increased instability of her respiratory rhythm associated with

significant desaturation. Recovery ensued when the CPAP was withdrawn. Two other children have been restrained from commencing or continuing CPAP therapy by the specific instructions of their primary physician despite the demonstration of a positive response in sleep study parameters.

6.4.1.3 Nasal Complications

Local nasal complications may be very troublesome during the early phase of treatment. This is also seen in adults. The problems of induced nasal obstruction or rhinitis have been treated effectively in the majority with topical nasal sprays. Other measures are occasionally necessary, such as wrapping insulation around the CPAP tubing to ensure delivery of warm air. Where these measures have failed, humidification of the delivered air has resolved the problem.

Pressure areas around the points of mask contact have also caused some initial difficulties. These are treated with pressure care of the areas when the mask is removed. Although this has been seen during initial treatment in a number of children, it has not become a persistent problem in any of the children treated with mask CPAP. The tendency for patients or parents to apply the mask too tightly may exacerbate these early difficulties. In one child, hypoventilation was associated with the mask being applied so tightly (by the child) that it resulted in compression of the nose to the point that nasal ventilation was restricted.

6.4.1.3.1 Nasal Obstruction

Children on CPAP continue to contract upper respiratory tract infections. Often the CPAP cannot be worn during those times when their nose is severely obstructed by an upper respiratory tract infection despite the aggravation of their symptoms from upper airway obstruction and sleep fragmentation. Middle ear infections may continue to be frequent while using CPAP.

6.5 DISCUSSION

This study has shown that CPAP can be used as the primary long term therapy in a large proportion of children who present with clinically significant sleep apnoea. The success rate is greater than 75% of patients. With appropriate equipment and careful preparation of the child and their family, CPAP is a practical and useful form of therapy in children. The demand for this type of treatment has increased and is continuing to increase, as our capacity for managing these children has expanded. It is clear to us, that our capacity to deal with such referrals is the rate limiting factor in diagnosing and treating children with OSA.

The children in this study were treated on the basis of overnight diagnostic sleep studies in combination with clinical assessment. The history of snoring and upper airway obstruction is integral to the disorder of OSA in children. Where children are concerned it has become very clear to us that the history is subject to parents interpretation and is not a reliable indicator of the severity of obstruction. Where children have had lifelong, or long term problems, the symptoms are very likely to be interpreted as characteristics of the child's personality, rather than an indicator of an underlying problem. In these cases the identification of symptoms often occurs only in retrospect. As a group, problems of right heart failure, and failure to thrive have been uncommon presentations. Children with underlying syndromes or malformations are more likely to have obstructive apnoea and more likely to have ongoing obstruction following adenotonsillectomy (Brouillette 17).

There are a diversity of circumstances where CPAP is an appropriate treatment option (Table 2). Increased use has been largely attributable to our widely applicable system of therapy. While tracheostomy continues to be a treatment option, it is associated with its own morbidity and mortality (Prescott 118) and it is likely that effective use of CPAP will reduce the need for this surgery. Certainly in cases of OSA it is now rarely recommended. Our experience has been that, given the choice of CPAP or tracheostomy, the family have invariably chosen CPAP.

A three year old who had experienced CPAP preoperatively did not settle when a naso-pharyngeal tube had been left in place post-operatively for airway splinting. This child clearly indicated a request for CPAP instead of the naso-pharyngeal tube, and settled within minutes of the CPAP being in place.

6.5.1 Nasal CPAP methods

As with the diagnosis of OSA in children (Carroll 23), we have found that effective use of CPAP in children requires a different approach to that used in adults. We have presented the results of the use of nasal CPAP therapy within a sleep unit established for the purpose of studying children. The staff of the unit are from a paediatric background and have contributed significantly to the adaptation of previously successful treatment (Sullivan 140) to a new situation.

The first major advance leading to our successful use of CPAP therapy in children is the use of a behavioural program to introduce the therapy to children and their families. Young children often require a lot of patience on the parts of both the therapist and the parents. A gradual introduction to this form of treatment (which can at times be very demanding of the parents) increases the likelihood of continuing use. This gradual introduction is useful for both the parents and the children. Education of the practical aspects of CPAP for the carers is an extremely important component of this process, and a major factor in their subsequent acceptance of the treatment.

While it may be preferable to commence effective therapy immediately, we have had to consider the long term benefits our priority. This slow introduction is essential in order to achieve successful maintenance of CPAP for a number of children. In cases of urgency it has been necessary to bypass this slow introductory process.

6.5.2 Nasal CPAP equipment

The second major change that our unit has been able to introduce, is the manufacture of widely applicable infant and paediatric masks which are acceptable to a wide range of patients. The equipment described here is also new. One of the features has been the use of "bubble" masks, which are used in both adult and paediatric settings.

The CPAP equipment described here includes specific children's masks for a number of reasons. The clear manifold is an important feature which allows the carer to

easily see that the nostrils are not occluded (Figure 5). Smaller masks reduce the child's apprehension, as they allow other activities to continue while awake. The use of a feeding bottle or pacifier should be able to continue unhindered, as we have found this is to be an excellent way of settling a child while the CPAP is active.

6.5.3 Complications and side effects of treatment.

Nasal CPAP therapy has been used for many years in adult populations. The therapy has been shown to be widely acceptable and associated with very few complications. Marked sleep rebound, particularly REM rebound, is sometimes associated with hypoventilation in patients with severe obstructive apnoea (Kreiger 78). Depressed cardiac function may occur with the introduction of CPAP (Cournand 26). The worst reported complication was an incidence of pneumocephaly, in association with a patent fistula connecting the nasal passages to the central nervous system (Jarjour 71).

In considering the use of CPAP treatment in infants and children, many of the practical challenges during the early stages of treatment are similar to those seen in the adult population. The complications and side effects of CPAP in children are often common to the adult population. In particular, the nasal effects are similar where treatment is also easily transferred between the two patient populations. In our group, patient or parent intolerance of this therapy was the most common cause of failing to successfully establish treatment. These two categories accounted for 70% of

those failing to establish or maintain treatment. This may well be the case in adult populations (Kribbs 80).

Hypoventilation and CO_2 retention at high CPAP pressures has not been observed in adult populations. Potential mechanisms include upper airway loading compromising respiration, diaphragm depression opposing abdominal muscle respiratory activity and/or increased activity of stretch receptor (or other) reflexes initiating apnoea. Cardiac efficiency may also be affected, with altered circulatory dynamics contributing to this problem.

Children frequently have CO_2 retention in association with their initial presentation of OSA. At present we are unable to identify which children will be affected in this way either secondary to their OSA or subsequent CPAP treatment. It is likely that it indicates a depressed ventilatory response to this obstruction, and therefore accurate testing of ventilatory responses would assist in this identification. All children should have CO_2 monitoring during both their diagnostic and CPAP pressure determination studies.

The CPAP pressure levels required were generally less than those in the adult population. However, we have had to use pressures of up to 18 cm H_2O to overcome upper airway obstruction in children as young as 12 months of age. There is no correlation between the age of the patient and the CPAP pressure required. The important point is the finding that a ceiling pressure exists for a number of children,

and above this ceiling pressure adverse responses of CO_2 retention, increased frequency or duration of central apnoea, or treatment induced arousals may occur. These problems are not commonly found in an adult population.

Children have different symptoms as a result of their obstruction and not surprisingly have different response to successful treatment. We have seen a number of unusual presentations of children with upper airway obstruction, and their symptom resolution has been dramatic once the upper airway obstruction was diagnosed and treated. In some cases, the use of CPAP has provided a diagnostic test, regarding symptoms such as cyclic vomiting requiring repeated hospital admissions.

6.5.4 Long term therapy.

Nasal CPAP therapy has been used for up to 12.6 years in patients commenced on treatment as young children. We have also used CPAP in a number of cases where tracheostomy would previously have been considered the next appropriate treatment. For this reason, we have seen, and will continue to see the use of CPAP in a number of situations where tracheostomy was previously the first line of treatment.

The potential for children to improve and no longer require CPAP is a very positive aspect of this group. Adenotonsillectomy has seen a number of children recover from the initial problem; in these cases, the primary purpose of CPAP treatment was peri-operative stabilisation. Urgent surgical intervention, with the potential for post-

operative pulmonary oedema and other complications, was thus converted to a semi-elective procedure. Three children have improvement through growth or other medical therapies, which saw a reduction in the severity of the airway obstruction. For example, there are now two children treated predominantly for tracheobronchomalacia. There was significant improvement with growth, allowing cessation of this therapy. While obesity is potentially treatable, only one of seven children has achieved sufficient weight loss to allow the discontinuation of treatment.

Because the patients and parents don't know the realities of alternative treatments (particularly tracheostomy) they sometimes discount the importance of CPAP treatment. Those parents who have experienced the alternatives are often highly motivated and very accepting of the task of CPAP. Compliance becomes a problem where there is no basis for comparison. Because the daytime symptoms are often minimal, there is not the same incentive for ensuring success, even if the child's general and respiratory health is substantially improved over a time course of weeks. The threshold of tolerance differs markedly between families.

Changes in daytime function are not always marked in the patient or obvious to the parent. The evolution of symptoms may also be slow. It has taken up to 6-10 weeks after suspending treatment for symptoms to recur. Whether this means that it is appropriate to have an occasional night off treatment remains uncertain, but it is inevitable that children will do so for social reasons if others are able to tolerate the

snoring! As with other chronic conditions, adolescents are likely to be at risk. Alcohol is a compounding factor in this disorder (Issa 69), and in adolescence is likely to be socially associated with the same reasons for having a night off treatment.

6.5.5 CONCLUSION

Life threatening complications of sleep apnoea are still seen in children with obstructive sleep apnoea at the time of presentation. A practical and widely available treatment is needed for those children with OSA where adenotonsillectomy is either not successful or not a practical treatment option. We have been able to achieve an 86% successful use of this therapy. The criteria for deciding to treat less severely affected children, and the duration of therapy used, varies markedly between patients. Increased experience with the use of CPAP therapy in children has provided us with a much better understanding of the requirements for successful introduction of this treatment with the paediatric population. Use of CPAP in children with obstructive apnoea is both possible and practical if the correct methods and means are used.

TABLE 1. Summary data of children studied for obstructive sleep apnoea (OSA), and children treated with nasal mask CPAP (CPAP). The male predominance is highly significant in both of these groups. p values are shown for the results of the chi-squared test for goodness of fit.

	Studied for OSA n=252	**Treated with CPAP** n=80 (31.7%)
Mean age	5.8 years	5.7 years
Sex		
Male	154 (61%)	57 (71%)
Female	98 (39%)	23 (29%)
	$p < 0.001$	$p < 0.001$
Syndrome or Malformation	80 (32%)	32 (40%) 10 (11%) = 42 (51%)

TABLE 2. Situations where nasal mask continuous positive airway pressure (CPAP) has been used in children. CNLD = chronic neonatal lung disease. CF = cystic fibrosis.

SITUATIONS WHERE CPAP THERAPY HAS BEEN USED IN THIS GROUP
OSA persisting post adenotonsillectomy
adenotonsillectomy contraindicated
upper airway structurally abnormal
lower airway structurally abnormal (tracheo / broncho malacia)
upper airway functional abnormalities (palatal, laryngeal etc.)
chronic lung disease (CNLD, CF, bronchiectasis)
respiratory dysrhythmias
peri-operative stabilisation in severe OSA
treatment trial
management of OSA in palliative care

TABLE 3. Syndromes and malformations which have been present in children treated with nasal mask continuous positive airway pressure (CPAP). VSD = ventricular septal defect. Tetralogy = tetralogy of Fallot.

SYNDROMES	MALFORMATIONS
Skeletal dysplasias	Upper airway
Achondroplasia	Choanal stenosis
Albright	Cleft lip &/or palate
Desbuquois	Congenital vocal cord palsy
Osteogenesis Imperfecta	
Connective tissue	Cardio-Respiratory
Hurler	VSD
Morquio	Tetralogy
Marfan	Mitral valve stenosis
Craniosynostoses	Laryngomalacia
Apert	Bronchomalacia
Crouzon	Tracheomalacia
Chromosomal	Kyphoscoliosis
Down (trisomy 21)	
Trisomy 18	Neurologic
Fragile X	Myelomeningocoele
Respiratory	Arnold-chiari
Cystic fibrosis	Hydrocephalus
Endocrine	
DIDMODE (Wolfram)	
Pseudohypoparathyroid	
Airway	
Foetal dilantin	
Goldenhar	
Neurofibromatosis	
Shprintzen	
Others	
Noonan	
Sotos	
Rhinotricheophalyngeal	

TABLE 4. Children treated with nasal CPAP therapy who have subsequently died.

Subject	Age at presentation	Diagnosis	Duration of CPAP
SC	2.4 months	Hydrops	3 months
PP	6 months	Chronic neonatal lung disease	1 week
CJ	7 months	Trisomy 18	8 months
SC	4 years 4 months	Cerebral palsy	6 months
GH	12 years	Osteogenesis Imperfecta	2 weeks
DS	12 years 2 months	Morquio	3 years 11 months
JL	14 years 6 months	Cystic Fibrosis	1 year 11 months
DW	14 years 11 months	Cystic Fibrosis	4 months

TABLE 5. Problems experienced with the use of nasal mask continuous positive airway pressure (CPAP) in children. These are subdivided into those which have been able to be overcome, and those which have led to the discontinuation of this treatment.

Problems experienced with CPAP therapy
1. Adults
A. Therapy continued
increased duration / frequency of central apnoea
REM rebound associated with hypoventilation
induced nasal obstruction
vasomotor rhinitis / drying
facial pressure areas
doctor / staff ignorance and non-acceptance
b. Therapy discontinued
patient mask / therapy intolerance
patient non-acceptance of therapy
doctor / staff ignorance and non-acceptance
pneumoencephaly
depression of cardiac function
2. Children
A. Therapy continued
increased duration / frequency of central apnoea
mask / CPAP pressure induced arousals
induced nasal obstruction
vasomotor rhinitis / drying
facial pressure areas
hypoventilation at high pressures
doctor / staff ignorance and non-acceptance
b. Therapy discontinued
infant mask / therapy intolerance
parental non-acceptance of therapy
inadvertent high pressures / abreaction
induced breathing rhythm disturbance (? underlying control defect)
doctor / staff ignorance and non-acceptance

Figure 1.

Age of children at onset of nasal CPAP treatment. Clearly this distribution is skewed with a heavy predominance in the one and two year old age group.

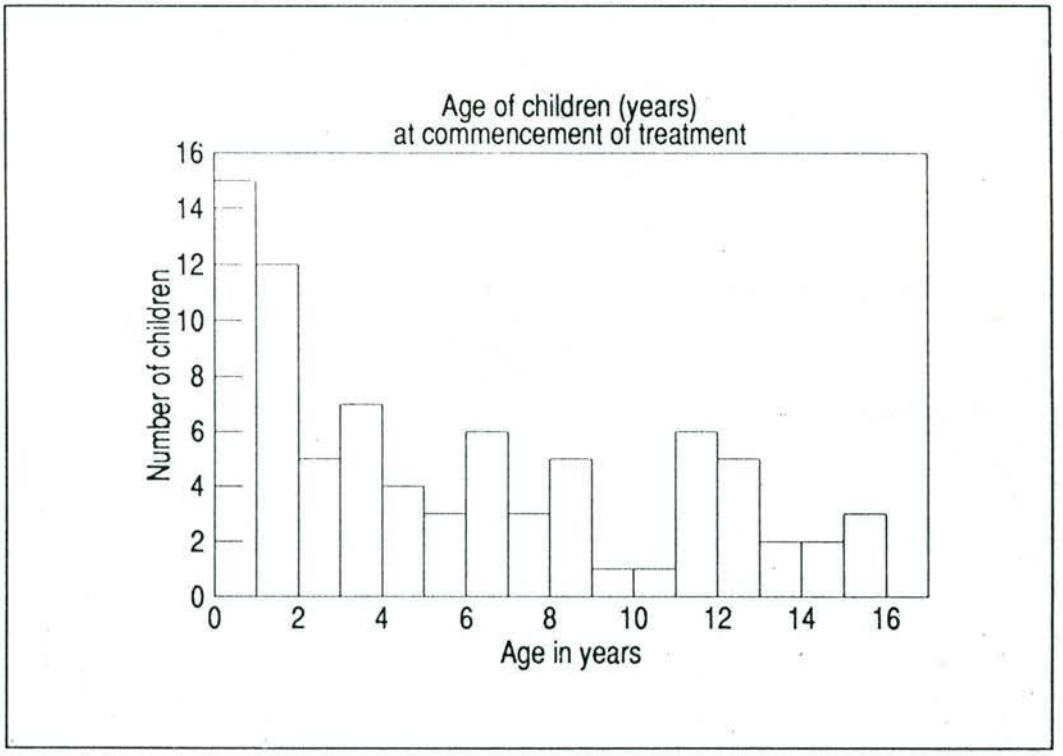
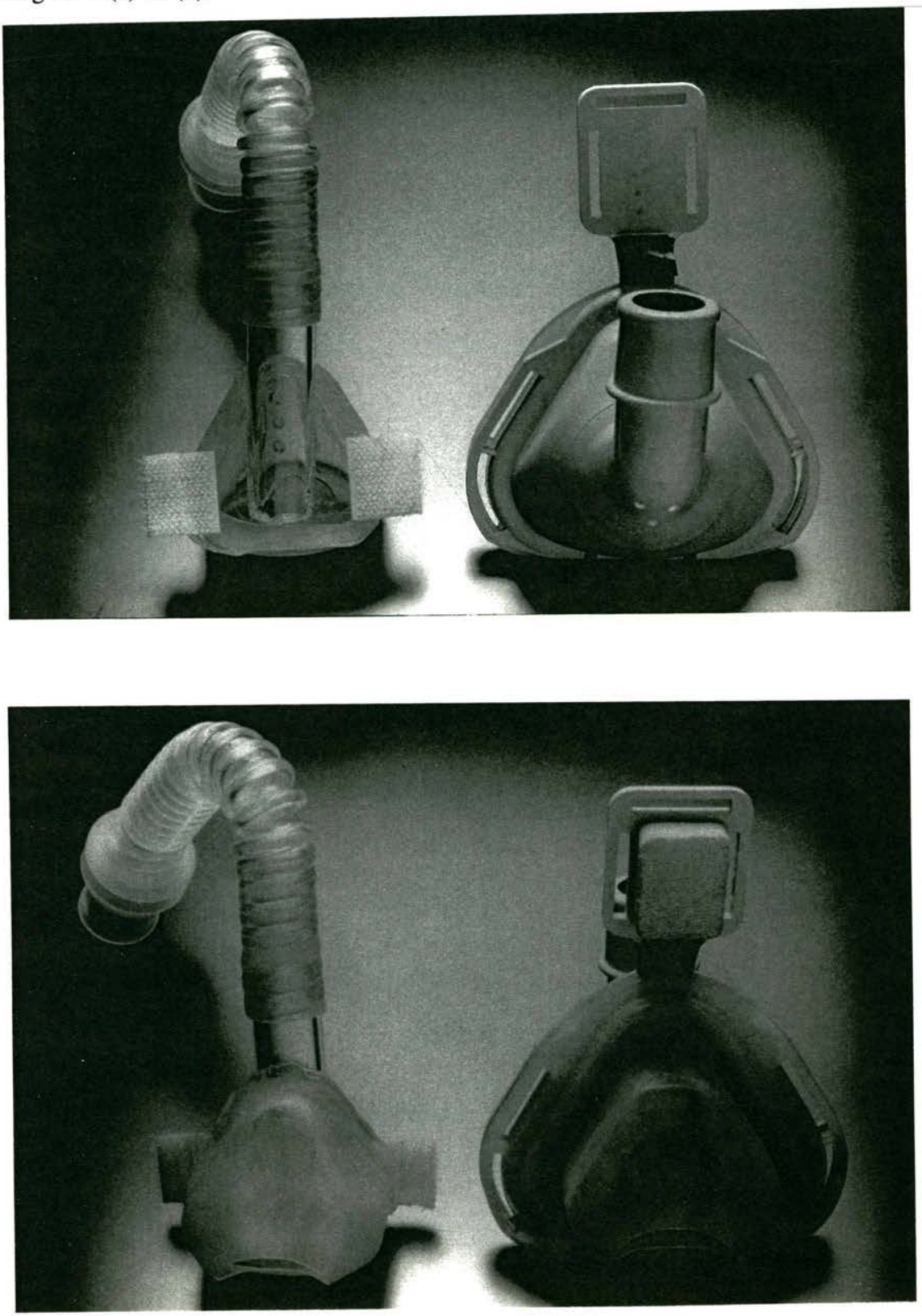


Figure 2 (a) & (b). Pediatric masks. The manifolds of the masks used vary in size. These pictures show the comparative sizes of the masks used. Figure 2 (b) shows the "bubble" component of the nose masks.

Figure 2 (a) & (b).



Pediatric masks. The manifolds of the masks used vary in size. These pictures show the comparative sizes of the masks used. Figure 2 (b) shows the "bubble" component of the nose masks.

Figure 3.

Pressure of nasal CPAP (centimetres of water) used to treat upper airway obstruction in this group of children. Fifty-eight children (83%) have a pressure setting at or below 10 cmH_2O, and 35 (50%) at or below 6.0 cm H_2O.

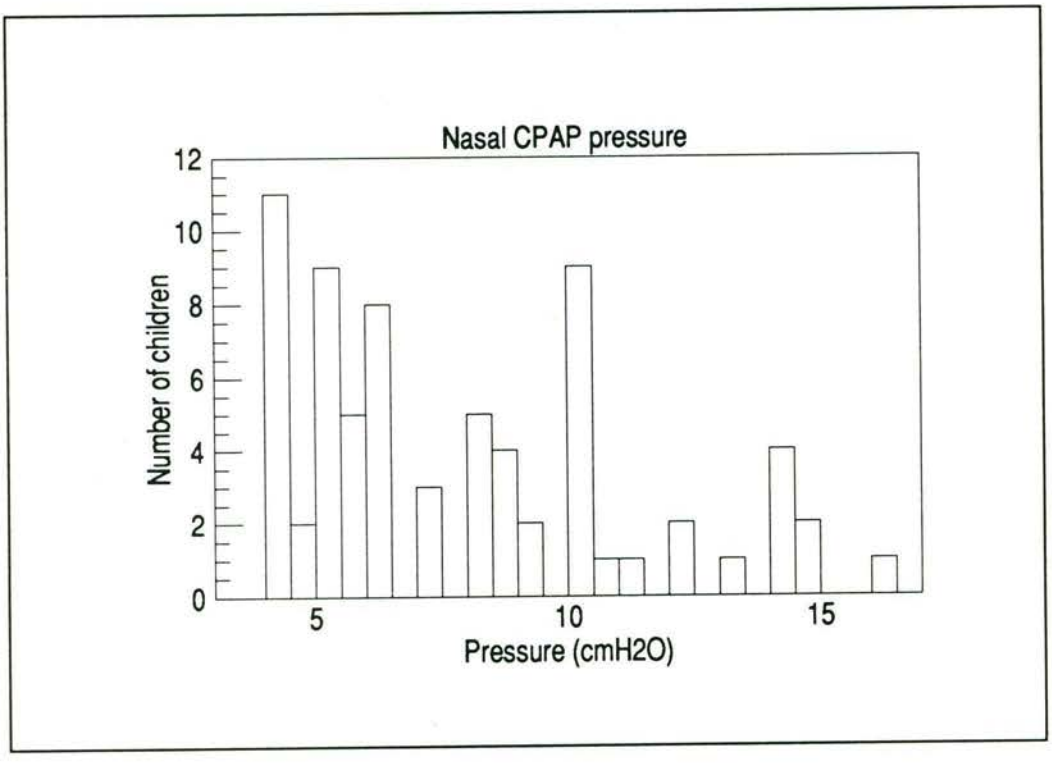


Figure 4.

Duration (years) of continuous nasal CPAP therapy in 68 children. Fifty percent of these children have been introduced to nasal CPAP therapy during the last 6 months.

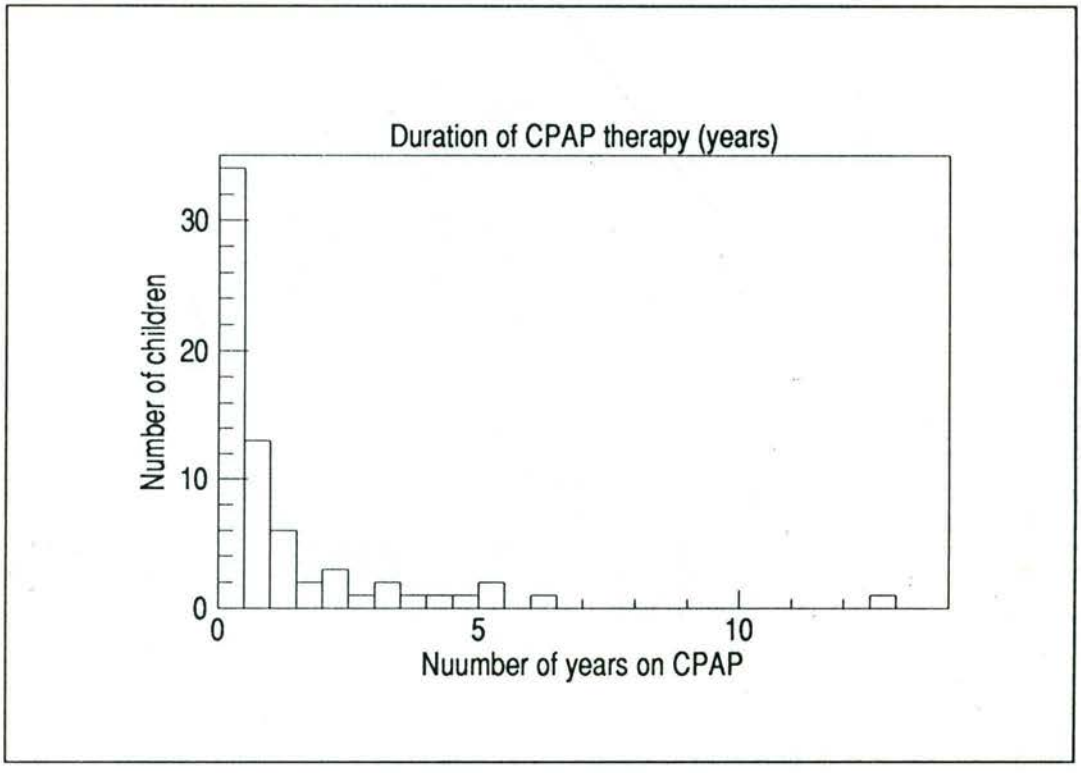
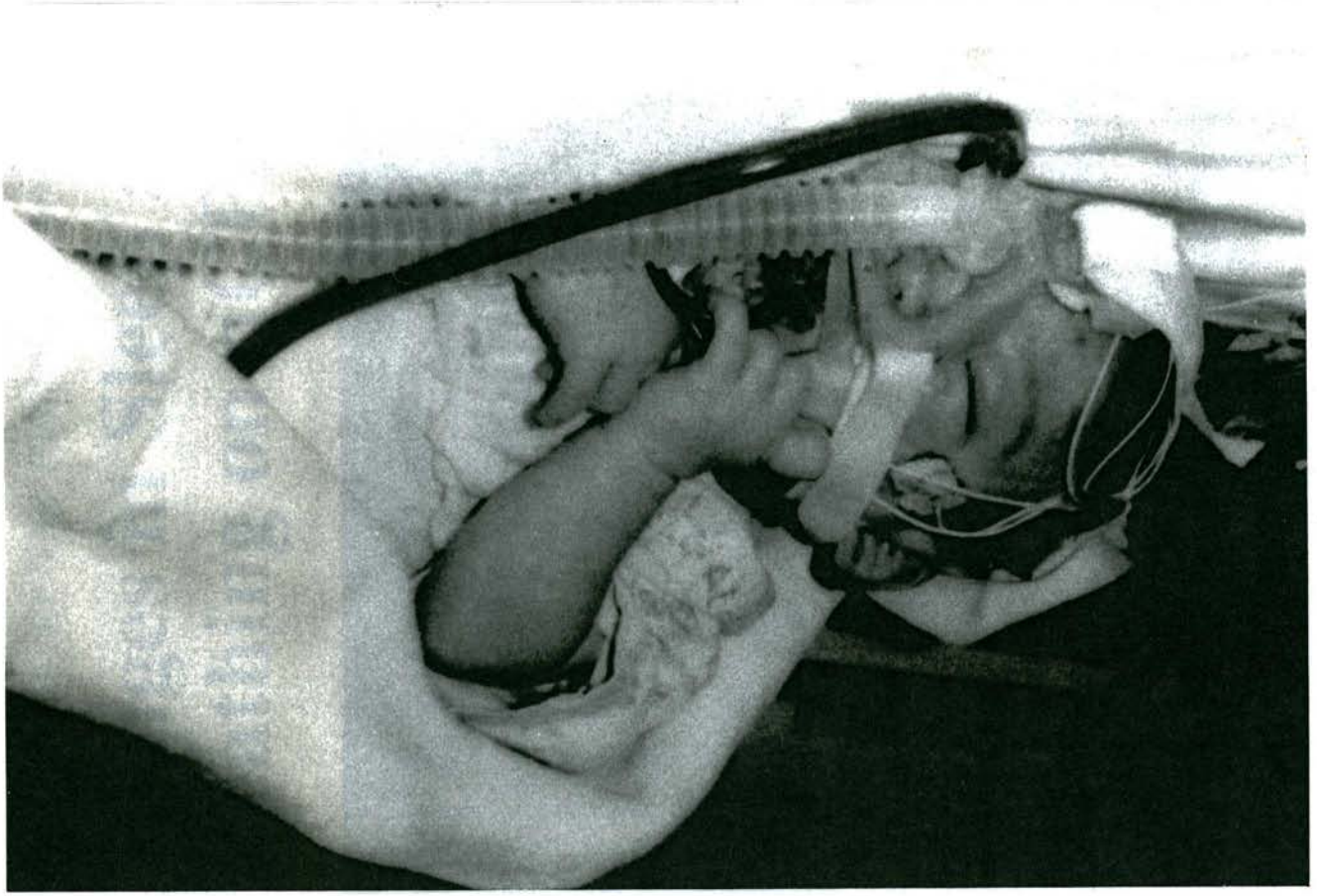


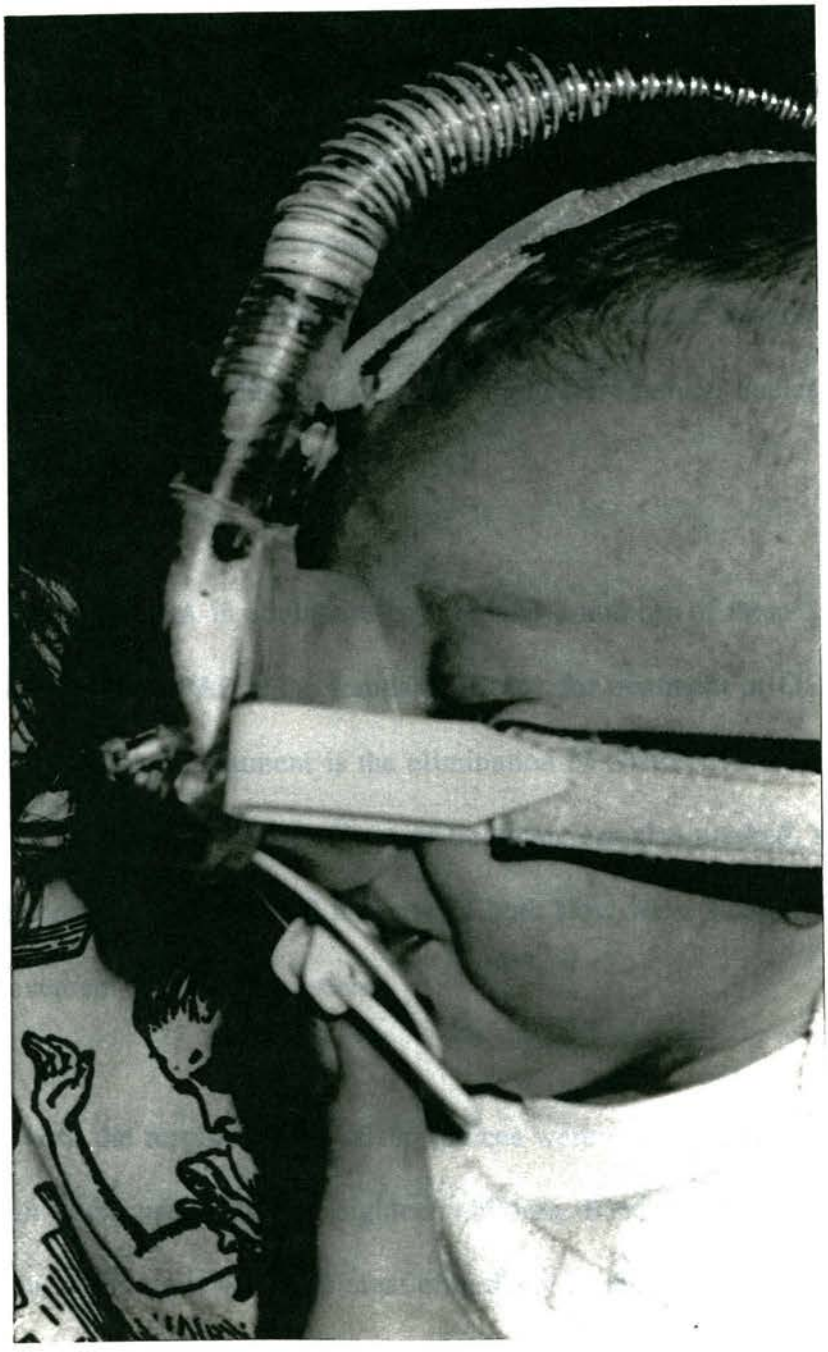
Figure 5.

The nasal mask in place on a young infant (age 2months). The clear manifold, allowing easy view of the patency of the nares, is demonstrated.



Chapter 7.

Changes in Sleep and Breathing on nCPAP



7 CHANGES IN SLEEP AND BREATHING ON CPAP

7.1 INTRODUCTION

Obstructive sleep apnoea (OSA) is diagnosed on the basis of the respiratory disturbance in sleep. Criteria have been established for a positive diagnosis to be made in adults (Definition of apnoea 53). The sleep consequences of the disorder in adults are also unmistakable since apnoea are terminated by arousal and sleep is disrupted as a consequence (Phillipson 114). Both the criteria for diagnosing OSA and the consequences of the disorder on sleep architecture remain unclear in children (Carroll 23).

The consequences of OSA in adults are striking and a number of them have been identified. Nasal mask CPAP is the standard therapy for treatment of OSA in adults and the primary effect of treatment is the elimination of obstructive respiratory events. When this is achieved, the effects of treatment are also marked; sleep is also consolidated and there is a rebound increase of both slow wave sleep (SWS) and rapid eye movement (REM) sleep seen.

In this study both the respiratory and sleep indices were evaluated before and after treatment with nasal mask CPAP in eighteen children. Because the introduction of CPAP to young children is achieved most effectively in their home environment (Chapter 6), they could not be restudied in our standard manner at the time of their

initial treatment. This has allowed us to evaluate the immediate and the sustained effects of CPAP treatment on both the respiratory and the sleep parameters of sleep studies in children with OSA.

7.2 PATIENTS

The mean age of the whole patient group was 9.0 +/-0.67 years (0.8-15.1). The group who were studied on their first night of treatment were older at 12.1 +/-0.85 years (6.7-15.1) than those who were gradually introduced to CPAP at 7.4 +/-0.7 years (0.9-14.4).

The proportion of he different sexes showed a predominance of males consistent with the overall study of children on CPAP (Chapter 6). There were 13 males (72%) and 5 females (27.8%) overall. There were six children studied on their first night of treatment including 5 males (83.3%) and one female (16.7%). Twelve children were studied after establishing CPAP at home including 8 boys (66.7%) and four girls (33.3%). The mean duration to the second study was 7.2 +/-2.4 months (1 week to 2.2 years). The longest delay occurred in a child who had had previous incomplete CPAP studies.

7.3 METHODS

All of the children in this study had overnight sleep studies to diagnose obstructive sleep apnoea in our unit. Follow-up studies were then performed to set the pressure required for CPAP treatment in each child. All studies were scored according to standard methods (Chapter 3) for both sleep stage and respiratory indices by the same person.

This study retrospectively reviews two groups of children who were treated and studied while using nasal mask CPAP. Study patients were selected if they had a full night diagnostic and full night treatment study available to be examined. The groups were separated after the studies were retrieved and scored according to the information available in the patient notes.

The first group the children were commenced on CPAP at the time that their pressure determination study was performed. These children were old enough to understand when the procedure was explained to them. In the majority of these cases the CPAP study was performed on the night subsequent to their diagnostic study.

The second group of children had a pressure determination study performed some time after CPAP was first used. These children were commenced on nasal CPAP therapy at home, according to our standard behavioural methods. This entails a period of gradual introduction to the components of CPAP. Initially the mask itself is introduced, and then subsequently CPAP is introduced at low pressures to allow for a period of adaptation. This is explained in detail in Chapter 6. Undergoing this process means that children have worn nasal CPAP at night for some period before they attend the unit for a pressure determination study.

Paired t-tests were performed between parameters of the first and second sleep studies performed. For the purpose of evaluation the groups were kept separate. Respiratory events are presented as number of events per hour unless otherwise

specified. Sleep stages are evaluated as percent of total sleep time. For the purposes of this study slow wave sleep (SWS) refers to total time in both stage 3 and stage 4 sleep. Light sleep (S1-2) refers to total time in stages one and two sleep. Total sleep time is presented in minutes. Comparison was made between the distribution and progression of sleep between the diagnostic and treatment study nights. Results are presented as mean +/-SEM (range), or as mean1, mean2 +/-SEM (p value / NS).

7.4 RESULTS

This is a sub-population of all of those children treated and studied with nasal mask CPAP. The decision to introduce CPAP treatment was made by paediatricians within the sleep unit on clinical grounds using information provided by a combination of history, physical examination, and overnight sleep studies. Where possible, children who have OSA have adenotonsillectomy performed as their first line of treatment. Children who had adenotonsillectomy had a repeat evaluation after this surgery to confirm the need for ongoing treatment.

Criteria for ongoing CPAP treatment then include repetitive complete obstruction resulting in oxygen desaturation (usually most severe in REM sleep) or partial obstruction resulting in CO2 retention greater than 12-15 mmHg (usually worst in SWS). Treatment was also recommended in those children with sleep fragmentation, secondary to respiratory events, usually worst at sleep onset, or in light sleep stages (including REM). The indications for commencing nasal CPAP treatment are detailed in Chapter 6.

All of the children in both treatment groups had a significant improvement in the respiratory indices of their study. These results are summarised in Table 1. The predominant improvement was in the number of obstructive apnoea and hypopnoea. Respiratory rates tended to decrease on CPAP, but this change was not significant. The range in both CO2 and oxygen saturation decreased. CO2 range fell from 16.9 to

12.0 +/-1.8 ($p < 0.08$) and peak CO2 fell from 56.6 to 50.7 +/- 1.8 ($p < 0.04$). Range of oxygen saturation fell from 47.9 to 7.9 +/-2 ($p < 0.001$) and baseline saturation increased from 96.3 to 97.2 +/-0.5 (NS). Central events showed a tendency to increase from 3.7 to 5.9 +/-1.2 (NS) but remained lower than the number seen in association with adenotonsillectomy 8.6 to 6.7 +/-2.3 (NS).

There was no significant change in total sleep time from 477 to 451 +/-19.3 mins (NS). Although the tendency for reduced sleep time was predominant in the second group this was not significant. The changes in sleep parameters were not universal. There was a significant increase in the percentage of SWS in the first group from 29.3 to 39.3 +/-2.7% ($p < 0.05$). Along with this S1-2 sleep tended to decrease from 57.1 to 45.6 +/-3.9% ($p < 0.09$). These changes also occurred in the second group, but were less marked. Percentage of SWS increased from 27.1 to 33.2 +/-2.4% ($p < 0.1$) while percent S1-2 decreased from 54.2 to 47.1 +/-3.6% ($p < 0.2$). When the two groups were combined, both of these changes became significant. SWS increased from 27.8 to 35.2 +/-1.8% ($p < 0.02$). (See Figure 1). and S1-2 decreased from 55.2 to 46.6 +/-2.2% ($p < 0.02$). There was a non-significant increase in the percentage of REM sleep for the groups. (See Figure 2). Combined values showed an increase from 17.1 to 18.5 +/-1.4% (NS).

7.5 DISCUSSION

The purpose of this study was to assess the consequences of effective treatment of OSA on sleep architecture in children. It is clear, but not extensively documented, that CPAP reduces the number of sleep associated obstructive apnoea and hypopnoea in children (Guilleminault 50, Tibballs 145). Any secondary effects on sleep architecture are not immediately apparent and are not well documented in children.

In adults, OSA is associated with marked sleep fragmentation as apnoea (and hypopnoea) are terminated by arousal (Phillipson 114). There is a marked increase in SWS and REM sleep when effective treatment is instituted (Issa 68). Children do not show the same arousal response to upper airway obstruction in sleep and there is no apparent alteration in sleep architecture because of this (Chapter 4). The documented sequelae of untreated apnoea in children include growth failure, right ventricular hypertrophy, and cardiac and respiratory failure (Brouillette 17, Guilleminault 54, Levy 84). There is, however, no explanation for the associated growth failure apart from the anecdotal report of reduced growth hormone secretion in a child who had loss of sleep architecture in a similar pattern to adult OSA (Goldstein 46). Similarly, children do not suffer excessive daytime sleepiness, consistent with the observation of preserved sleep architecture and failure to arouse.

In this study it has been clearly demonstrated that the introduction of CPAP results in improved respiratory status in sleep both initially and in a persistent fashion. This is

predominantly in the number of obstructive respiratory events which occur. Central events remained stable at around 5 per hour before and after treatment, consistent with other groups studied in our unit. There was a marked reduction in the range of variability of both CO2 and oxygen saturation after treatment, which indicates both that this group had severe OSA before treatment and that the treatment was effective.

There was a clear and dramatic effect of CPAP on the obstructive respiratory indices. This study has been beneficial in evaluating paediatric scoring criteria. In adults, an apnoea index of five per hour is normal (53). Using respiratory criteria that vary with age, by utilising the duration of the respiratory cycle, a normal value can be derived from this study by assuming that respiratory indices on CPAP are normal. After treatment the respiratory disturbance indices in this group were 5.7 obstructive events per hour, and 5.9 central events per hour.

This study confirms that major changes occur in the proportions of SWS and S1-2 sleep seen after treatment of upper airway obstruction in children (Frank 39, Guilleminault 56). These were most marked on the first night of treatment but were still present in those children treated for longer periods. It is possible that this was also an age related effect, and the effects are most marked only in older children. However, the trends were still present throughout the whole group, and the effect on percentage of S1-2 sleep only became significant in the group as a whole.

There was no change in REM sleep demonstrable in this group. It has been suggested, that like adults, the proportion of REM may be reduced in children in the presence of obstruction and that compared to normal controls, children with obstructive apnoea have 8.7 vs 10.2 hours of night sleep (Guilleminault 56). None of these effects were confirmed in this current study. The children here showed no change in total sleep time, and a slight decrease in sleep efficiency. There was also no change in movement indices.

This may imply that REM sleep is maintained despite obstruction in children, or that the apnoea is not so severe or prolonged in children. As a result there is no need to recover this sleep when obstruction is treated. However, the percentage of REM sleep seen in these children both before and after treatment is reduced compared to studies of normal children. It is possible that the mechanisms underlying OSA also affect the quantity of REM sleep that these children are able to achieve, or that a pattern of sleep is established during development (in the presence of OSA) that is not altered with relief of that obstruction.

The changes in SWS may well be significant to the growth of children with OSA and have effects even before there is complete loss of sleep architecture or absence of SWS. One clear effect of upper airway obstruction in adults is a reduction in Growth hormone (GH) secretion (Grunstein 49). It is possible that there are more subtle effects on SWS than absolute duration, which cannot be evaluated in the current study. The effects of obstructive sleep apnoea on hormonal and growth

mechanisms of children are still being evaluated. That these changes persisted after some time on treatment implies that the effects are dramatic and long lasting in the presence of obstruction.

In conclusion, this study has demonstrated the clear effectiveness of CPAP in the treatment of OSA in children. Apnoea indices fall and oxygen saturation and CO2 are stabilised both in the short term, and on long-term follow-up. There is also a clear effect on sleep architecture demonstrable with an increase in SWS and a comparable reduction in the proportion of S1-2 sleep seen. The effects on sleep architecture are most marked on the first night of treatment.

Table 1. Summary of sleep parameters in two groups of children treated with nasal CPAP. Group 1 consisted of six children who were studied on their first night of treatment with nasal CPAP. Group 2 consisted of twelve children who were commenced on nasal CPAP at home, and studied one week or more after their first night of treatment.

Parameter	Group 1 N=6	Group 2 N=12	Total N=18
Age (years)	12.1 (0.9) 6.7 to 15.1	7.4 (0.7) 0.9 to 14.4	9.0 (0.7) 0.8 to 15.1
Sex	5 M (83.3%) : 1 F (16.7%)	8 M (66.7%) : 4 F (33.3%)	13 M(72%) : 5 F (27.8%)
Diagnostic study			
TST	425 (15.3)	502 (18.0)	477 (19.3)
S1-2%	57.1 (3.9)	54.2 (3.6)	55.2 (2.2)
SWS%	29.3 (2.7)	27.1 (2.4)	27.8 (1.8)
REM%	13.6 (1.7)	18.8 (2.3)	17.2 (1.4)
Efficiency	89.8 (2.2)	91.9 (2.9)	91.2 (1.9)
Moves	4.6 (2.2)	5.8 (1.1)	5.4 (1.4)
Arousal	9.0 (1.7)	6.0 (0.9)	7.0 (0.8)
Treatment study			
TST	423	465	451
S1-2%	45.6 ($p = 0.09$)	47.1	46.6 ($p < 0.02$)
SWS%	39.3 ($p < 0.05$)	33.2	35.2 ($p < 0.02$)
REM%	15.8	19.8	18.5
Efficiency	89.0	85.8	86.9
Moves	1.6	2.9	2.5
Arousal	4.5 ($p < 0.08$ rank)	6.3	5.7

Table 2. Summary of changes in respiratory parameters with CPAP treatment. The groups are subdivided to those studied on the their first night of treatment and those studied after one week or more of treatment. Because these are non-parametric tests, the transformation is listed after the p value. "log" = log transformed data and "rank" = rank transformed data.

Parameter	Group 1 N=6	Group 2 N=12	Total N=18
Diagnostic study			
RDI	64 (7.6)	99 (11.0)	87.5 (5.3)
Obstructive	173 (47.6)	110 (17.2)	131 (20.9)
Central	1.7 (1.0)	4.7 (0.8)	3.7 (5.9)
CO2 -Range	19.1 (2.5)	16.4 (2.4)	16.9 (1.8)
High	56.9 (2.5)	57.0 (2.7)	56.6 (1.8)
SaO2 -Range	14 (1.2)	64.8 (35.7)	47.8 (2.0)
Baseline	96.2 (0.4)	96.8 (0.6)	96.3 (0.5)
Treatment night			
RDI	21.6 ($p < 0.01$)log	34 ($p < 0.01$)log	30 ($p < 0.01$)log
Obstructive	4.5 ($p < 0.01$)log	6.3 ($p < 0.001$)log	5.7 ($p < 0.01$)log
Central	3.1 NS	7.3 NS	5.9 NS
CO2 -Range	10.1 ($p < 0.05$)log	12.2 NS	12.0 ($p<0.05$)log
High	49.1 NS	50.8 NS	50.7 ($p<0.05$)
SaO2 -Range	8.2 ($p< 0.02$)rank	7.8 ($p<0.01$)rank	7.9 ($p<0.01$)rank
Baseline	96.2 NS	97.8 NS	97.2 NS

Figure 1.

Change in percent of Slow wave sleep (SWS) seen from diagnostic study to study night on CPAP. There was a significant increase in the percentage of SWS seen in those children restudied on their first night of treatment, but not in children studied on their second or subsequent night. Night 1 = those children studied on their first night of treatment. Stable = those children stabilised on CPAP at home prior to this study.

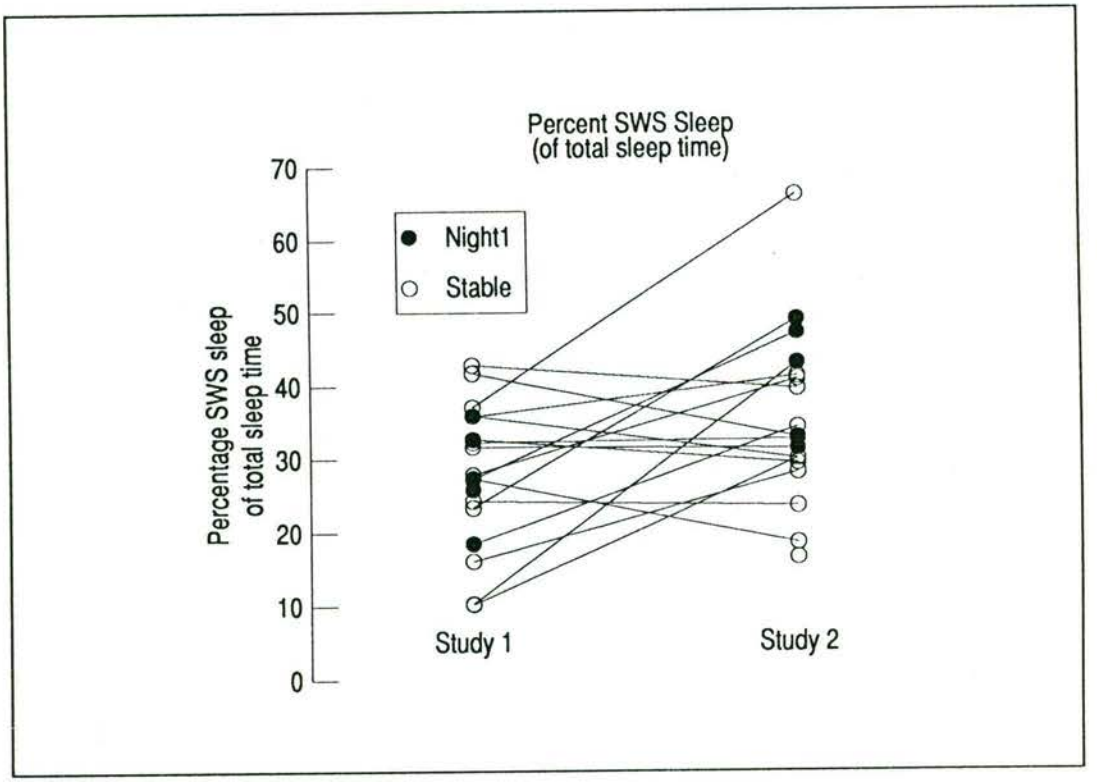
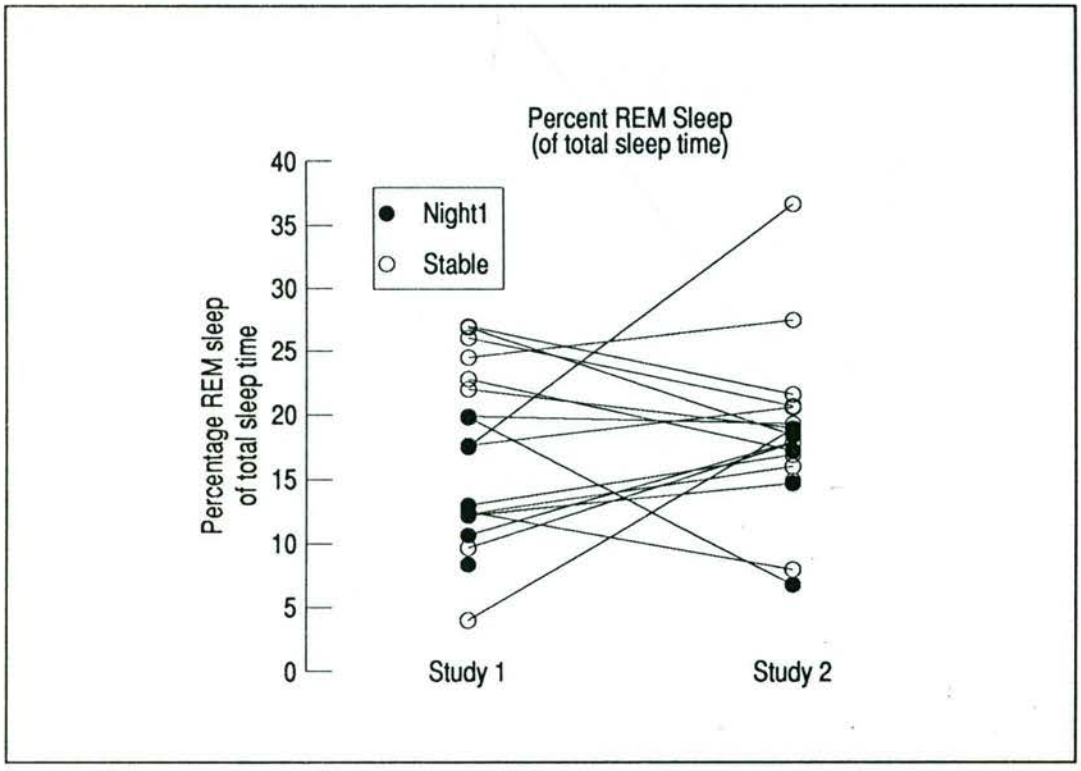
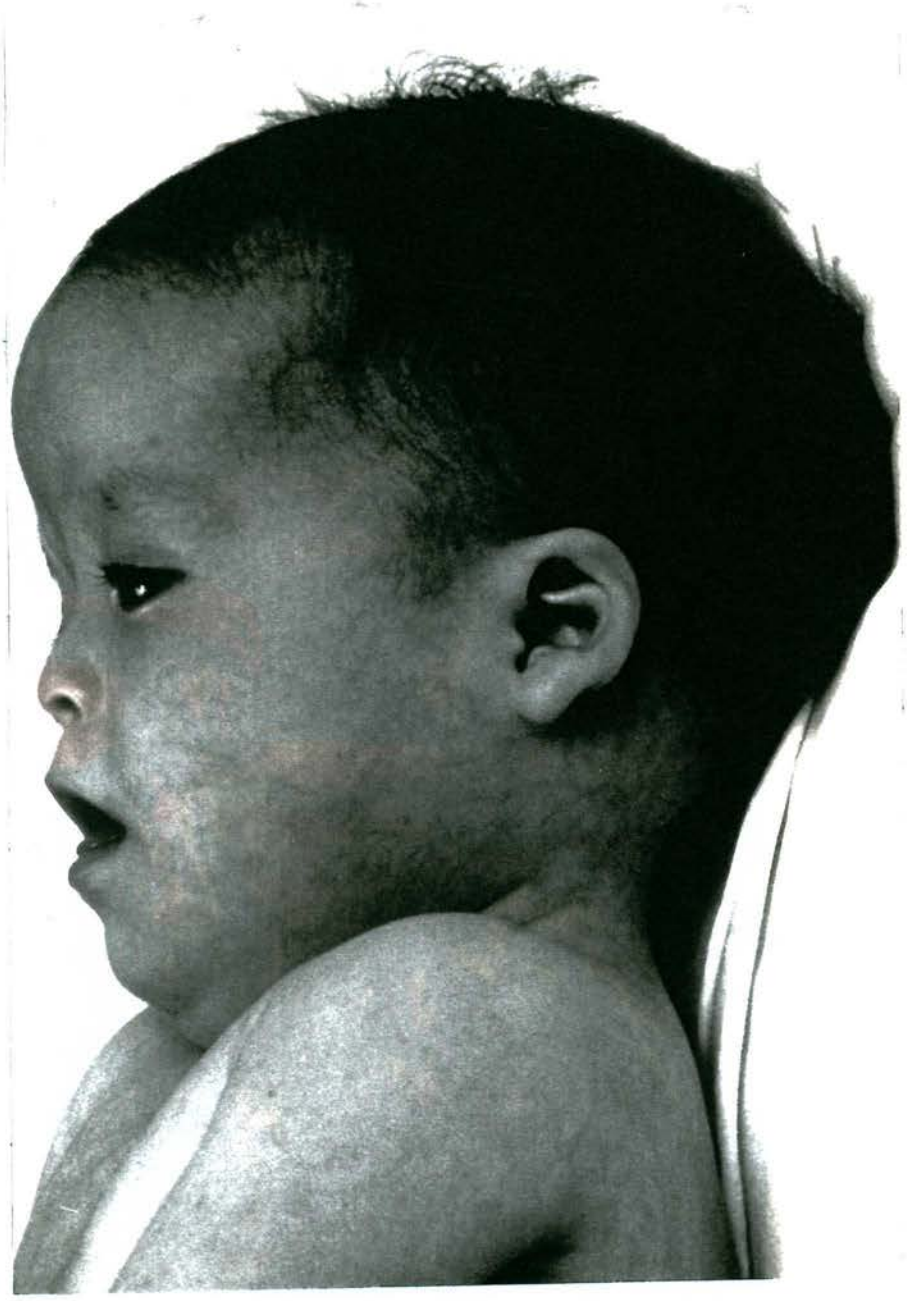


Figure 2.

Change in percent of REM sleep between diagnostic and treatment nights for the whole group. There was no significant change in either group. The first group did show a tendency to increased amount of REM sleep although this did not reach statistical significance.





Chapter 8.

Spina Bifida

8 SPINA BIFIDA

8.1 INTRODUCTION

Spina bifida, or myelomeningocoele, is a malformation of the central nervous system. The dominant lesion is incomplete closure of the spinal canal, leaving the spinal cord exposed, without skin covering. In around 90 percent of cases there is an association with the Arnold Chiari Malformation (ACM) causing disruption of the brain stem nuclei in some cases (Holschneider 64, Oakes 106). Symptoms of cranial nerve dysfunction, relating to the ACM occur in 13 - 33% of patients. Lung disease in older children is associated with a history of recurrent aspiration in infancy leading to permanent lung damage, and restrictive lung disease occurs in association with kyphoscoliosis which is also common in this disorder. The number with symptoms may increase with age, as adolescents and young adults have a propensity to develop clinical progression often attributable to the ACM (Oakes 106).

Abnormal ventilatory patterns have been observed in asymptomatic infants with myelomeningocoele (Davidson-Ward 27). Raised intracranial pressure has been associated with OSA (Pasterkamp 111). Hydrocephalus and the ACM may also be associated with bilateral abductor vocal cord paralysis which may result in obstruction not responsive to tracheostomy (Holinger 63). Stridor in the presence of myelomeningocoele is an early indicator of malfunction of the vagus nerve. The chiari II malformation is the principle cause of mortality, and posterior fossa / or

cervical decompression is of questionable value in the treatment of patients with symptoms attributed to hindbrain compression (McLone 94).

The respiratory complications associated with the ACM include abnormal control of breathing, upper airway dysfunction, aspiration pneumonia, and cor pulmonale. Use of early ventilatory support has resulted in favourable outcome (Oren 108). These patients demonstrate the characteristic abnormalities of beaking of the midbrain, caudal elongation of the fourth ventricle and cerebellar vermis to the cervical level, and hydromyelia. These patients lack sleeping and waking ventilatory responsiveness to hypoxemia and hypercarbia. Occasional patients have significant alveolar hypoventilation caused by bradypnea in the presence of normal or even increased tidal volume (Weese-Mayer 148).

Apnoea may be central and occur in acute response to acute hydrocephalus (Nickerson 105). The abnormal respiration in sleep may be a function of blunted arousal responses, as well as respiratory control dysfunction. Sleep studies are required to detect, and differentiate central apnoea, obstructive apnoea, ventilatory response to carbon dioxide, and arousal responses (Nickerson 105).

Maturation of brainstem auditory evoked potentials has been demonstrated in normal infants. Brainstem immaturity is indicated by delay in the brainstem component of the potentials. Improvement in the number of spontaneous apnoeic events has been associated with improved brainstem conductivity. Hypoxia is also associated with

abnormalities in these studies, and treatment of obstructive apnoea has also been associated with improved function.

This study describes the sleep associated respiratory abnormalities in eight of the children from the spina bifida clinic at The Children's Hospital (TCH) who had a history of early bulbar symptoms. Two other children without bulbar symptoms, who were to undertake decompressive surgery were also studied to check for alterations in respiratory patterns before and after surgery. Three children with spina bifida and marked sleep related respiratory disturbances have been successfully treated with nasal mask CPAP. Evoked potential studies were performed in these three children, before and after treatment.

8.2 PATIENTS

A total of ten children with spina bifida were studied. The mean age of the group was 2.4 years +/- 0.9 years (9 days - 8.4 years). There were six female and four males in the group. Eight had clinical symptoms of bulbar dysfunction including three infants in the first week of life. Four infants were first studied between 9 and 32 days of age, and six children with a history of bulbar symptoms in infancy, were studied between the ages of 1.0 and 8.4 years.

Two children were studied prior to cerebral decompressive surgery. One boy had a VP shunt inserted as an infant and a girl of 15 months underwent posterior fossa decompression.

8.3 METHODS

History and clinical examination were performed at the time of admission for the overnight sleep studies. All of the children with clinical symptoms of bulbar dysfunction had a history of snoring; the two children undergoing decompressive surgery were asymptomatic.

Full overnight sleep studies were performed according to the standard methods described in chapter 3. Two infants had oesophageal pressure monitoring during their follow-up study at three months of age. Oesophageal pressure was measured via a

fluid filled feeding catheter, connected to a pressure transducer (HS-9). Pressure recordings were calibrated to plus or minus 10 cmH_2O. These studies were used to confirm the nature of the obstructive apnoeic events seen on earlier studies.

The three children who were treated with nasal CPAP therapy had overnight sleep studies before and after treatment. Brainstem auditory evoked potentials (BAEPs), visual evoked potentials (VEPs), and somatosensory evoked potentials (SEPs) were also recorded before and after treatment.

Statistical analysis was not performed on any of these results because of the small numbers of subjects who underwent follow-up studies.

8.4 RESULTS

Two children, aged two weeks and fifteen months respectively, had decompressive surgery. These two children were asymptomatic despite increased intracranial or posterior fossa pressure. Neither of these children had symptoms of bulbar dysfunction. Total respiratory disturbance index (RDI) before the surgery was 17.9 hr^{-1}, with a slight increase after surgery when it was 21.9 hr^{-1}. There was an increase in the number of both obstructive and central events. Obstructive events (apnoeas and hypopnoeas) rose from 7.2 hr^{-1} to 9.6 hr^{-1}, and central events from 10.7 hr^{-1} to 12.4 hr^{-1}. None of these incidences of respiratory events was considered severe enough to warrant treatment in these two children.

All of the children with a history of bulbar dysfunction had obstructive sleep apnoea. A summary of their sleep study results is presented in Table 1. The mean age of this group of children was 2.9 years. The respiratory indices indicated that as a group, these children had significant respiratory disturbance from a combination of obstructive and central events. Mean RDI for the group was 46.8 events hr^{-1}. Only one child had an RDI less than 20. RDI for obstructive events was greater than 10 hr^{-1} in all of these children and greater than 20 hr^{-1} in three of eight (37%). RDI of central events was greater than 10 hr^{-1} in five of eight children (63%).

Sleep architecture in this group with bulbar symptoms showed a higher than expected percentage of slow wave sleep (SWS) at 30.9%, for the group. Percentage of rapid

eye movement (REM) and stage one and two (S1-2) sleep were at normal levels in this group at 29.1 +/- 5 and 48.0 +/- 3.0% respectively. Arousal, movement and sigh indices were 3.0 +/- 0.9, 7.6 +/- 7.6% and 8.6 +/- 2.6% per hour respectively.

Three children were established on CPAP therapy in the home. Follow-up sleep studies were performed to determine appropriate CPAP pressures and confirm an improvement in respiratory indices. The results of the sleep indices are in Table 2. Respiratory indices of this group studies are presented in Table 3. The eight year old child showed a reduction in respiratory disturbance indices, with a reduction in total RDI, particularly obstructive events. There was a marked increase in baseline saturation in this child from 92 to 97% for the night. The range of CO2 increase was greater on the second night as this child developed acute CO2 retention at CPAP pressures greater than 8.5 cmH2O. Final pressure was set lower than this level.

A unique effect of CPAP was observed in this 8.4 year old child. Her spinal lesion is at the level T8. On CPAP there was measurable recruitment of abdominal muscles during REM sleep. This child had active sternomastoid muscle activity in non-REM sleep but not REM sleep when breathing spontaneously. There was a nadir observed on CPAP therapy, where this activity was reduced to a minimum, only to increase at higher CPAP pressures. During this nadir period, on CPAP, it was noted that abdominal muscles were active in REM sleep, despite the lack of innervation to these muscles in this child (Figure 1).

The infants had a high frequency of respiratory events. In the initial diagnostic studies there was a high index of obstructive events in these two children who were 3 weeks old at the time. Follow-up studies were performed within five days of the diagnostic study in both cases. There was an improvement in respiratory indices (RDI fell from 81.3 to 54 events per hour) due to a decrease in the frequency of obstructive events (39.1 to 10.1). Central RDI did not change (42.2 to 43.9 hr^{-1}) when averaged, but one infant did have a big increase in the number of central events from 1.5 hr^{-1} to 31.1 hr^{-1} on CPAP. Sleep architecture also changed with the introduction of CPAP, and within the time frame of three days. Quiet sleep increased from 52.3% to 64.6% and active sleep decreased from 47.8% to 35.4% during the study on CPAP. Total sleep time decreased from 556 to 460 minutes, and sleep efficiency decreased from 90.2 to 76.7%.

While respiratory dysrhythmia settled markedly it was also possible to document the change in respiratory effort which occurred when these infants were treated with CPAP. This was documented using an oesophageal pressure transducer. Pressure swings in quiet sleep fell from +/- 10 cm of water to +/- 5 cm H2O (Figure 2a, and 2b).

SEP studies are shown in Table 4. These studies were normal in all three children studied. There were no consistent changes in these parameters following treatment with CPAP.

8.5 DISCUSSION

Spina bifida is not a localised disorder, and the neurologic abnormalities extend throughout the central nervous system. The arnold-chiari II malformation occurs in 85% of cases. There is an uncommon association with clinical dysfunction due to the arnold chiari malformation which is expressed as cranial nerve, and particularly bulbar, dysfunction. When this malformation is symptomatic it is a major cause of mortality in these children, with reports of up to 50% death rates. Increased intracranial pressure may also be associated with deterioration in respiratory status during sleep periods. The ACM may be associated with central disturbance of respiratory control. This may be expressed as central hypoventilation requiring ventilatory support (Weese-Mayer 148). Asymptomatic infants have also been shown to have respiratory abnormalities (Davidson-Ward 27).

The primary aim of this study was to investigate the possibility of obstructive sleep apnoea in children with myelomeningocoele. There were three categories of children in this current study. Of those with symptomatic ACM the older children had symptomatic bulbar dysfunction in infancy. These children had not had specific treatment at the time and in all cases their parents felt that the bulbar dysfunction had improved with age. These children were asked to return for overnight sleep studies. The three infants in this study had symptoms of bulbar dysfunction in the perinatal period and had sleep studies as one of the investigations undertaken because of these symptoms. Two children who were to undergo decompressive surgery were

investigated before and after surgery to look for associated changes in respiratory status.

Two children had decompressive surgery on clinical grounds. One infant had raised intracranial pressure and had a VP shunt inserted. Another child had a mid-thoracic lesion with minimal lower limb dysfunction. Investigations had revealed an associated ACM and posterior fossa decompression was undertaken to try and minimise any progression of symptoms because of this. Although these two children had some obstructive events in their diagnostic sleep studies, they were not symptomatic and the abnormalities did not warrant intervention. There was no indication on these two studies that the increased intracranial pressure had affected respiration in sleep.

In the group with symptomatic bulbar dysfunction there was a significant incidence of respiratory disturbance in sleep. A high proportion of these children had obstructive apnoea, and three of them were established successfully on nasal CPAP therapy. This treatment resulted in significant reduction in obstructive events. Sleep architecture was consistent with previous studies of children who had this level of obstruction (Frank 39, Chapter 5).

Potential mechanisms of the obstruction include weak or dysfunctional muscles in the oropharynx. Because these are normally responsible for maintaining airway patency, this results in passive obstruction in response to normal negative inspiratory pressure.

The presence of central apnoea, suggests that there may also be loss of normal cortical inhibition, of some reflex apnoeic responses. When the upper airway is stimulated, rather than reflex airway dilatation, these children show central apnoea.

In older children upper airway dysfunction was associated with, and complicated by, lower respiratory tract disease. Studies in two of these children showed a complex picture of obstructive apnoea associated with REM hypoventilation. Obstructive events were associated with severe desaturation, presumably secondary to respiratory insufficiency. REM hypoventilation is most likely due to loss of accessory muscle activity in this sleep state (Piper 115). Accompanying the presence of a high neurologic lesion, intercostal and abdominal muscle weakness may be long standing and detract from the normal compensatory mechanisms. It became apparent that another secondary effect was hypoventilation at high CPAP pressures producing acute CO2 retention.

The three children who were to undertake nasal CPAP therapy had brainstem auditory evoked potentials, visual evoked potentials, and somatosensory evoked potentials recorded before and after treatment. There were no significant abnormalities in these studies before or after treatment. It is possible that in a larger group these studies would be helpful in screening for bulbar dysfunction.

The children in our clinic who have symptoms of bulbar dysfunction all have a history of snoring and evidence of obstructive sleep apnoea on overnight sleep

studies. In older children this is associated with, and complicated by, lower respiratory tract disease. Nasal CPAP has been successful in the treatment of children with respiratory disturbance associated with spina bifida, in these studies. Central hypoventilation requiring ventilation has not been seen in association with the ACM in this group of ten children.

Table 1. Sleep study characteristics of ten children with spina bifida. Respiratory indices are given as number of events per hour of sleep time. Sleep indices are subdivided for the infants and older children. Ranges are give for the whole group. TST is in minutes and all other sleep indices are as percentages of total sleep time.

Characteristics	Respiratory Indices	Sleep Indices
N = 10	RDI 41.0 +/-9.1 (9.2-104)	TST older 483 +/-38.0 infant 489 +/-39.5 (385.0-623.2)
Age 2.4 years+/- 0.9 (9days - 8.4years)	ORDI 19.0 +/-4.8 (1.4-56.8)	Efficiency 84.2 +/-3.2 (66.4-98.7)
6 Female 4 Male	CRDI 22.1 +/-8.1 (1.1-82.8)	REM% older 21.2 +/-2.7 infant 46.5 +/-4.0 (13.8-54.6)
Infants <3weeks = 4 2 Female 2 Male	Arousals 2.9 +/-0.7 (0.5-8.3)	SWS% older 28.1 +/-4.4 infant 36.4 +/-9.0 (14.9-46.6)
	Moves 7.1 +/-2.5 (0.7-23.1)	S1-2% older 49.3 +/-2.8 (40.7-61.0)
	Sighs 7.7 +/-2.2 (0.8-24.1)	

Table 2. Sleep architecture of three children with spina bifida, treated with nasal mask CPAP. Subjects MM and BT are infants studied at 3 weeks of age. NREM in these children refers to both quiet and indeterminate sleep and REM refers to active sleep. Subject CF is an 8.4 year old girl in whom all sleep stages were able to be scored. TST = total sleep time, and is given in minutes. CO2-R is the range of transcutaneous CO2 during the overnight study. All other figure are percentages. Efficiency is the percentage of study time spent in sleep. SaO2-B = baseline oxygen saturation.

Subject	TST	Efficiency	NREM%	REM%	SaO2-B	CO2-R
CF - diag	385	66.4	82.6	17.4	92	10
- CPAP	453	77.0	84.6	15.4	97	21
MM - diag	562	93.2	59.1	40.9	97	20
- CPAP	503	75.6	76.9	23.1	98	8
BT - diag	551	87.2	54.6	54.6	98	25
- CPAP	416	77.8	47.6	47.6	98	7

Table 3. Respiratory Indices of three children with spina bifida, treated with nasal mask CPAP. RDI = Respiratory disturbance index, ORDI = obstructive respiratory events index, CRDI = central respiratory events index. Arousals, movements and sighs are all provided as indices of events per hour as well.

Subject	RDI	ORDI	CRDI	AROUSALS	SIGHS	MOVES
CF - diag	14.0	12.9	1.1	8.3	5.0	2.6
- CPAP	8.5	0.8	7.7	3.6	7.1	0
MM - diag	58.3	56.8	1.5	4.2	4.2	18.9
- CPAP	38.8	7.6	31.1	9.1	5.4	16.9
BT - diag	104.3	21.3	83.0	3.4	12.9	8.1
- CPAP	69.2	12.6	56.7	3.6	5.6	8.1

Table 4. Evoked potential results of three children before and after treatment with CPAP for sleep disordered breathing. SEP = Somatosensory evoked potentials recorded from stimulation of the median nerve at the wrist and reported as clinical grades (see methods) 1=normal, 2=low amplitude, 3=delayed, 4=absent. VEP = visual evoked potentials and BAEP = brainstem auditory evoked potentials, both of these are reported as time (msec). RIP and LIP are first, second and third interpeak latencies of right and left sides respectively. Subject JP was studied before and after insertion of a ventriculoperitoneal shunt. The other three subjects were studied before (Bef) and after (Aft) treatment with CPAP. BAEP results were abnormal in subjects JP and BT both before and after treatment. Visual evoked responses were indefinite in subjects MM and BT both before and after treatment with CPAP.

Subject (age)	SEP	VEP		BAEP	
	(graded 1-4)	R	L	RIP 1,2,3,	LIP 1,2,3
CF - Bef (8.4 yrs)	1	96	98.5	4.64,2.30,2.34	4.66,2.26,2.40
- Aft	2	103.5	105.5	4.46,2.10,2.36	4.82,2.40,2.42
MM - Bef (5 weeks)	1	130	-	4.26,2.68,1.58	4.56,2.82,1.74
- Aft	4	94.5	88.0	4.3,1.38,2.92	4.50,3.02,1.48
JP - Bef (3 weeks)	4	113.5	107.5	4.54,2.34,2.2	4.64,2.30,2.34
- Aft	4	105.5	104.5	4.64,2.48,2.16	4.92,2.46,2.46
BT - Bef (2 weeks)	4	-	94.5	-,-,-	-,3.02,-
- Aft	1	-	-	4.82,2.66,2.16	5.42,2.86,2.84

Figure 1. Activation of the abdominal muscles (surface EMG) in a child with a high lesion and lower motor neuron lesion at the level of the electrodes. This activation occurred while on CPAP and suggests the activation of some local spinal reflexes. This may be through increased abdominal distension or lung inflation.

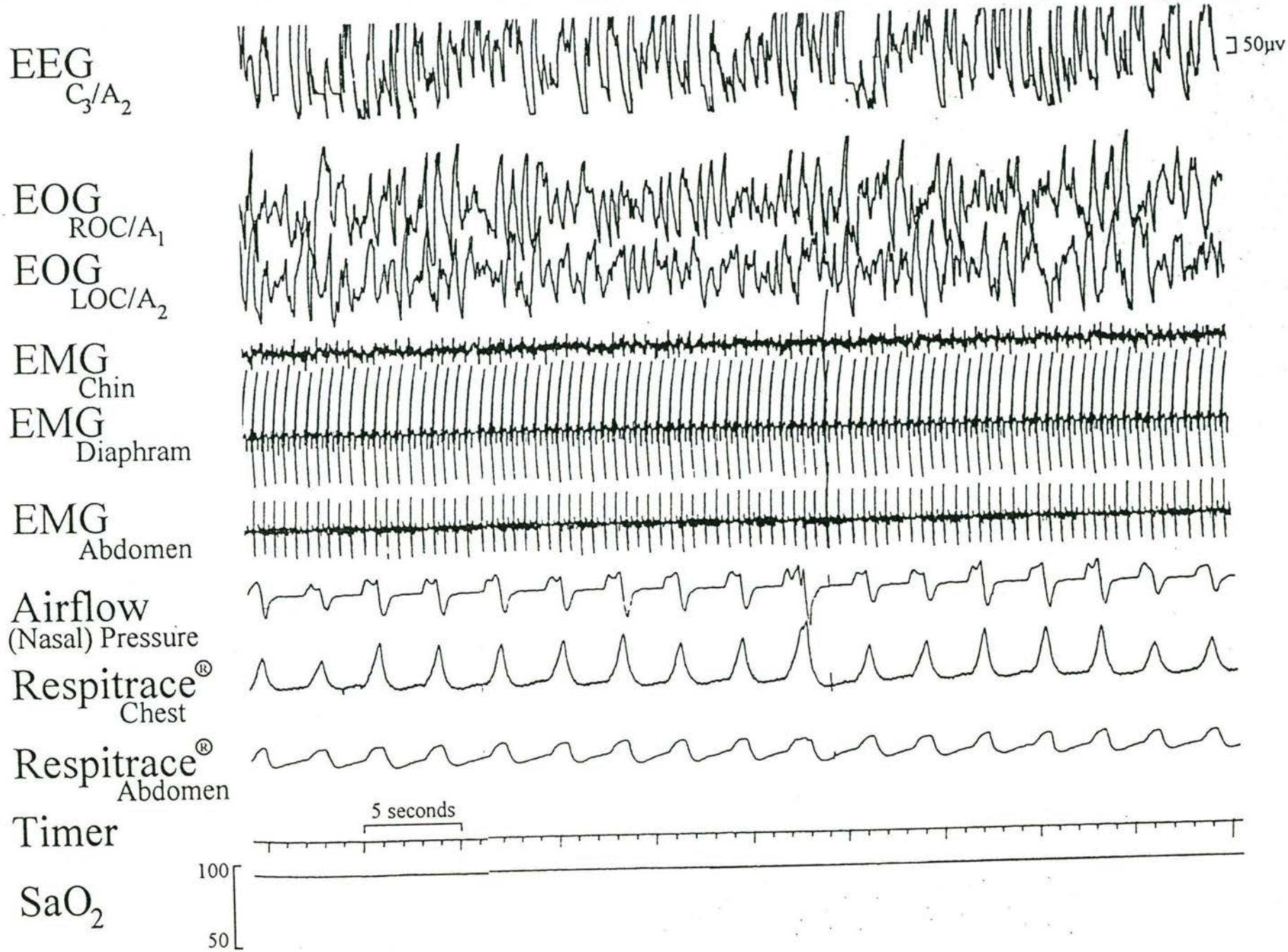

EEG
C3/A2
50µv
EOG
ROC/A1
EOG
LOC/A2
EMG
Chin
EMG
Diaphram
EMG
Abdomen
Airflow
(Nasal) Pressure
Respitrace®
Chest
Respitrace®
Abdomen
Timer
5 seconds
SaO2
100
50

Figure 2a. Study of an infant at age 10 days with spina bifida and symptoms of upper airway obstruction and bulbar dysfunction. An oesophageal pressure monitor is in place. The continued respiratory effort is demonstrated, with pressure swings to greater than -10 cmH_2O^{-1}.

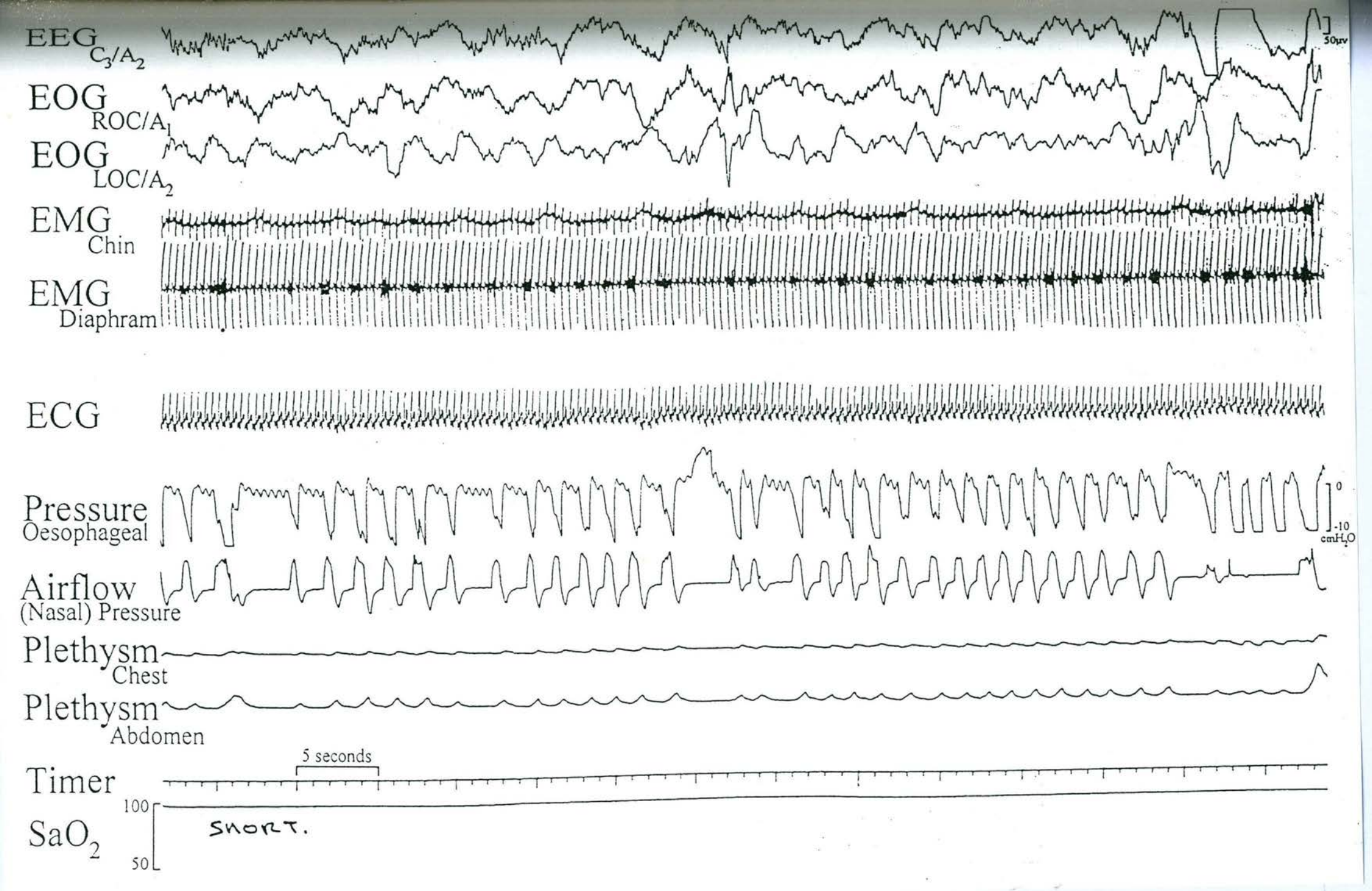
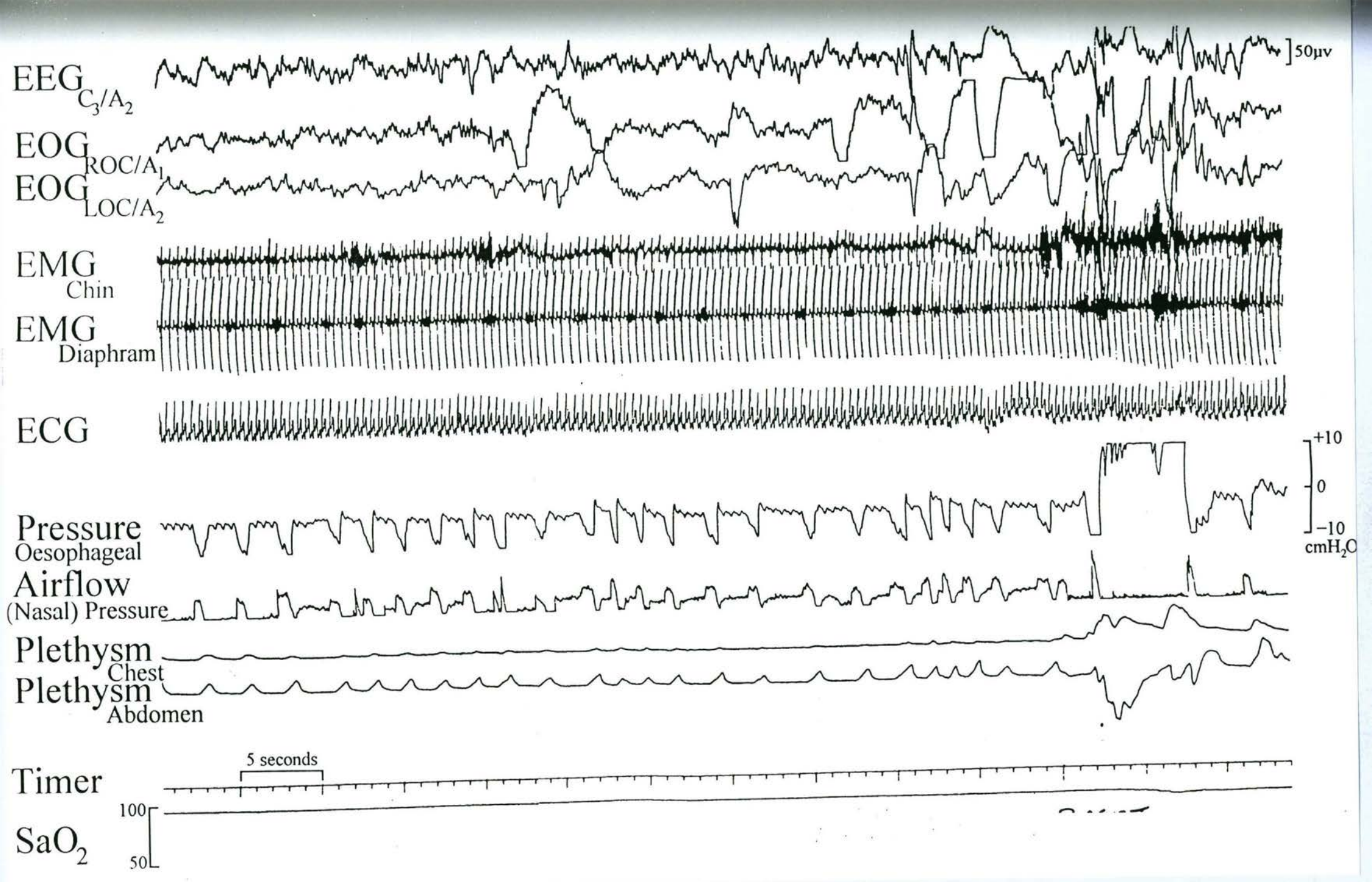
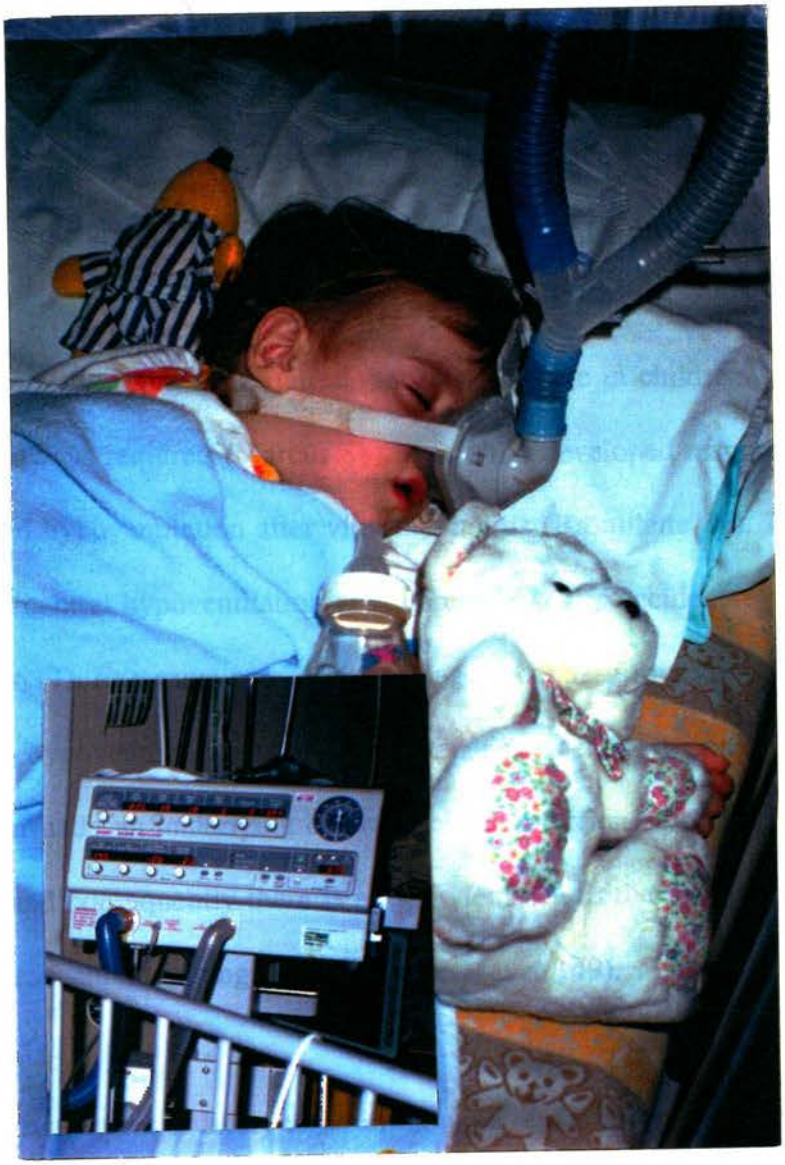

EEG C3/A2
50µv
EOG ROC/A1
EOG LOC/A2
EMG Chin
EMG Diaphram
ECG
Pressure Oesophageal
0
-10
cmH2O
Airflow (Nasal) Pressure
Plethysm Chest
Plethysm Abdomen
5 seconds
Timer
100
50
SaO2
SNORT.

Figure 2b. Study of the same infant as in Figure 2a, on the same night, but with nasal CPAP in place. There is reduced respiratory effort, with reduced activity of accessory muscles of respiration. The oesophageal pressure swings during quiet respiration are reduced to between -10 and -5 cmH_2O^{-1}.


EEG C3/A2
EOG ROC/A1
EOG LOC/A2
EMG Chin
EMG Diaphram
ECG
50µv
Pressure Oesophageal
+10
0
−10
cmH2O
Airflow (Nasal) Pressure
Plethysm Chest
Plethysm Abdomen
5 seconds
Timer
100
50
SaO2

Chapter 9.

Central Hypoventilation



9 ACQUIRED CENTRAL HYPOVENTILATION

9.1 INTRODUCTION

Central hypoventilation was described in 1970 by Mellins (Mellins 97). There has been increasing recognition and treatment of the disorder since then (Guilleminault 57, Weese-Mayer 150), particularly in neonates. The most recent review of central hypoventilation in children describes 32 cases with congenital hypoventilation presentating at a mean age of 3 months (0.2 - 56 months) (Weese-Mayer 150).

Central hypoventilation may be acquired, but this is is rare in children. Ventilatory support is not always required (Marcus 88). One child developed respiratory dysrhythmia and hypoventilation after viral meningitis (Brouillette 16). Two elderly men developed central hypoventilation after cerebrovascular accidents (Bogousslavsky 12). Extensive neurologic damage secondary to trauma, has also been associated with hypoventilation due to severe repetitive central apnoea (Quera-Salva 119). There is usually an underlying disorder, either infection or Chiari II malformation, and consequently there is a high yield of positive pathologic findings on Magnetic Resonance Imaging (MRI) (Weese-Mayer 149).

The primary derangement is likely to be in the area of the central chemoreceptor apparatus. MRI results in acquired central hypoventilation support this hypothesis with abnormalities demonstrable in this region of the brainstem. The congenital

syndrome has been associated with Hirschsprungs disease, lack of heart rate variability, congenital neuroblastoma, and ganglioneuroblastoma, suggesting either a primary defect of the stem cells of serotonergic nerves or a neural crest migrational abnormality. Hypothalamic dysfunction has also been associated (Weese-Mayer 149). Some older children presenting with central hypoventilation, may simply be a late presentation of a mild, congenital form of the disorder (Weese-Mayer 150).

Treatment is by nocturnal ventilation. Tracheostomy and positive pressure ventilation is the most common form but cuirass ventilation has been used. CPAP therapy may need to be combined with cuirass ventilation because of associated upper airway dysfunction (Ellis 34, Quera-Salva 119). Ventilation via a nose mask was introduced at the Royal Prince Alfred Hospital and described in 1988 (Ellis 35). It has been extensively used in adults where hypoventilation is usually secondary to pulmonary insufficiency. In these cases, loss of intercostal muscle activity in REM sleep results in hypoventilation based on end organ (neural, muscular, or lung) inadequacy rather than failure of ventilatory drive (Piper 115).

9.2 CASE REPORTS

There have been eight cases of acquired central hypoventilation diagnosed at the David Read Sleep Disorders Unit. Each of these patients presented after the first year of life. All of those who required respiratory support are established on nasal mask ventilation. These cases and their features of interest are presented. The average age at presentation was 11.4 years (1.33 to 38.67 years) for this group. Excluding the one adult in this group, the average age of the children was 7.5 years (1.33 to 14.42 years). Not all cases have an associated pathology identified. All but one of these individuals have had normal daytime intellectual function during the period of treatment. All of these patients are still alive and six are currently using nocturnal nasal mask ventilation. The cases are presented in ascending order of age at presentation.

9.2.1 CASE 1 (KM). Age of presentation 16 months.

This girl presented at a peripheral hospital, aged 15 months, with a history of recent cyanosis and apnoea. She had a respiratory illness at the time, apparently acquired from other family members in the preceding three weeks. The predominant symptom was cough, but this young girl had become increasingly unwell during the week prior to presentation.

The history was suggestive of previous abnormalities. The child was born at 36 weeks gestation with a birth weight of 2480 gm, following an uncomplicated pregnancy. Delivery was complicated by foetal distress with meconium stained liquor. The apgar scores were three at one minute and seven at five minutes. In the immediate postnatal period the child was well, but at 48 hours, she had apnoeic episodes with cyanosis, and was placed in oxygen. Ventilation was not required. Treatment with theophylline was commenced and ceased at four months of age, and respiratory monitoring continued up to the age of six months. During that period, there were three episodes of apnoea which caused concern to the parents, but none which required active intervention. The episodes were typically associated with feeds, but did occur in both wakefulness and sleep; these events had ceased by six months of age. Because of the history of apnoeic events, only one pertussis immunisation was given.

At the age of eleven months, there were three further episodes of cyanosis and apparent apnoea. The first occurred during a feed, the others occurred while awake and walking about with no apparent precipitant. None of these triggered any further intervention.

The child remained well until she was fifteen months old, three weeks prior to presentation. At that time she developed her first upper respiratory tract infection. During this acute illness, the child was extremely lethargic, and was noted to have intermittent cyanosis. There was no improvement with amoxycillin. When the child

presented to the local hospital, she was cyanosed and therefore placed in oxygen. Frequent apnoeic episodes occurred. Electrolytes showed a bicarbonate level of 40 millimol per litre (mmol/l), with low chloride, but were otherwise normal. On the third day, two seizures occurred. Phenobarbitone was commenced and a lumbar puncture was performed. Two hours later, the child deteriorated and had a respiratory arrest. A blood gas taken at this time showed a pCO_2 of 59 mmHg. The child was intubated, ventilated and transferred to intensive care.

At the time of admission a long history of frequent night waking was obtained, with an average of six to seven arousals per night. The child had a regular daytime sleep of two hours without disruption. Both parents smoked, but neither had a history of snoring or apparent sleep related respiratory disturbance. One older sibling had a combination of snoring, obesity and lethargy, and subsequent sleep study showed mild obstructive apnoea. There was a maternal family history of febrile convulsions, but no other significant history.

In intensive care, normal gases were secured through intubation and artificial ventilation. Bilateral consolidation was seen on chest x-ray, and sputum was positive for pertussis on immunoflourescence, although bacterial culture was negative. EEG showed generalised slowing, consistent with the recent history of seizures. CT scan, CSF, immunoglobulins, and pertussis serology were normal. Treatment, and clinical course over the following ten days were consistent with pertussis pneumonia.

However, despite clinical and chest x-ray (CXR) evidence of recovery the child was unable to be weaned from the ventilator.

A trial of extubation was unsuccessful, and resulted in significant CO_2 retention (to greater than 60 mmHg). Stridor, copious thick secretions and subglottic trauma associated with endotracheal intubation all contributed to significant respiratory compromise. The child was re-intubated for a further seven days and was able to maintain normal blood gases with spontaneous ventilation when awake on endotracheal CPAP at 5 - 8 cmH2O. Normal blood gases were maintained only with CPAP, and hypoventilation developed when a swedish nose was applied. Respiratory stimulation was attempted using an aminophylline infusion but without effect. Arterial pCO_2 rose to 100 mmHg when the child was breathing spontaneously in sleep. A further trial of extubation was successful during wakefulness, but hypoventilation recurred in sleep.

Treatment for persistent sleep associated hypoventilation included extubation, followed by CPAP via a nasopharyngeal tube for two days. In wakefulness, the child maintained normal oxygen saturation but this fell to 80 percent soon after sleep onset, and was initially treated with nasal oxygen supplementation. During this period, several episodes of altered consciousness occurred from the awake state. Initially these were thought to be due to hypoventilation but there were no associated blood gas changes. They were also documented with EEG and were not seizures.

An overnight sleep study, while breathing spontaneously, showed no evidence of upper airway obstruction, but hypoventilation was clearly present. This was most severe in SWS and REM sleep periods. CO_2 retention of 30 mmHg occurred quickly after sleep onset. Transcutaneous CO_2 levels reached a maximum of 83 mmHg in sleep, and oxygen saturation dropped to a minimum of 80%. Blood gases on waking revealed an arterial pCO_2 of 57 mmHg, and pH of 7.2.

Nasal mask ventilation was established over the following ten days in hospital. Daytime function improved markedly, with increased daytime activity and improved appetite. Sleep behaviour also improved, and both initial settling and subsequent night wakenings were more easily managed than any time previously in the child's life. In contrast to the history of taking 30 minutes or longer to settle to sleep, sleep onset now occurred within five minutes of commencing nasal mask ventilation in the evenings. Night wakenings remained frequent, but brief and the child required minimal attention at these times.

9.2.1.1 Important features of this case:

- this child was not identified as having abnormal respiratory control prior to her acute presentation
- in retrospect, historical features may imply abnormal respiratory control from the perinatal period
- the child was assessed as normal between the ages of 6 months and 15 months by her parents and her medical attendants

- there is a family history of other sleep associated respiratory disturbances
- presumed pertussis pneumonia in this child required treatment with intubation and ventilation which is unusual at this age
- the child presented acutely with cyanosis and apnoea, and pCO_2 levels of up to 100 mmHg following administration of oxygen
- during the recovery period there were episodes of altered consciousness, which initially seemed to be associated with hypoventilation, but no clear explanation was found. With continued adequate ventilation, these episodes ceased spontaneously.
- extubation was associated with the recovery of adequate, spontaneous ventilation in the awake state
- mask ventilation was successfully established in this child at 16 months of age

9.2.2 CASE 2 (TG). Age of presentation 5 years 7 months.

The perinatal history of this male child was of a normal vaginal delivery at term. No resuscitation was necessary, but phototherapy was required for three days to treat neonatal jaundice. He had two older siblings, one male and one female, who were well. A third sibling died at four hours of age, severely dysmorphic, but without a specific diagnosis.

This child presented at 5 years 8 months, with a history of apnoea associated with upper respiratory tract infections. This was associated with snoring and witnessed apnoea. The parents sat by his bed at night, and waking him when he stopped breathing. A diagnosis of obstructive sleep apnoea was made, and because of the clear history of apnoeic events requiring arousal, he was admitted to his local hospital for observation during his next upper respiratory infection.

During the initial period of observation, there were three episodes of desaturation to the 80's lasting 1-2 minutes, recovering spontaneously. Nasal oxygen was used following an episode of desaturation to 55% for a period of around 10 minutes. There were no attempts to arouse the child. During a subsequent prolonged apnoea, there was cyanosis despite oxygen supplementation, and the child was not able to be roused. A blood gas at this time showed pH 7.1, with pCO_2 89 mmHg. Intubation and ventilation followed. Three generalised seizures were treated with valium and

phenobarbitone. The child showed rapid recovery from this incident, and was awake, sitting up, and trying to pull out his endotracheal tube (ETT) 6 hours later.

Transfer to TCH was arranged for further investigation. The child remained intubated, and was sedated for transfer. Sinus bradycardia was noted. Hypoventilation was noted prior to anaesthetic for adenotonsillectomy. A blood gas during spontaneous ventilation with the ETT in place, showed pCO_2 to 72 mmHg, and pH 7.18. Halothane anaesthetic was used for the adenotonsillectomy. He was extremely sensitive to the halothane, and stopped breathing as this was introduced in theatre. The surgery was otherwise uncomplicated. The adenoids were felt to be very enlarged, with moderate size tonsils. Histopathology of these tissues was unremarkable.

Two days after presentation it became clear that the child was hypoventilating, both awake and asleep. A past history of cyanotic breatholding spells was elicited, and the unusual history of this boy being able to swim underwater for surprising duration. His "party trick" was to dive underwater and retrieve objects repeatedly.

Investigations were undertaken to look for causes of brainstem encephalopathy. Hypoventilation in both awake and asleep states, continued for 15 days. A trial of Doxapram was unsuccessful. Several acute episodes of apparent loss of consciousness and acute hypoventilation were precipitated by procedures in the unit. These episodes were shown not to be seizures. Later episodes were associated with an altered state

of consciousness, but normal ventilation. Tracheostomy was planned because of the prolonged intubation and failure to recover adequate automatic ventilation. A trial of extubation showed normal spontaneous ventilation in the awake state. Within 30 minutes of extubation spontaneous improvement had occurred and pCO_2 fell from 52 mmHg, to 35 mmHg.

Sleep associated hypoventilation persisted and ventilation via a nasal mask was commenced in sleep the following night. Sleep study confirmed severe, sleep associated, hypoventilation within 50 minutes of sleep onset. SaO_2 fell to 60 percent, $TcCO_2$ rose to 65 mmHg, and pH was 7.17. This was associated with marked slowing on the EEG, and no arousal response was seen. Nasal ventilation was recommenced. The child was discharged to his home, continuing on nocturnal nasal mask ventilation, six weeks after his initial presentation.

Investigations during the admission were extensive. They included routine biochemical and blood count evaluations. The biochemistry initially showed a high bicarbonate; changes attributed to intra-venous therapy and ventilation. A drug screen was clear of substances other than those administered in hospital. Metabolic screen revealed reduced glycine, alanine, and a mild ketosis. Lactic and pyruvic acids were not increased, either in blood or cerebrospinal fluid (CSF). CSF protein and glucose levels were normal. Liver and thyroid function tests were normal. Visual evoked potential studies showed clearly defined and reproducible results.

Abnormal results included brainstem auditory evoked potentials which recorded a prolonged latency on the left side, normal on the right. EEG initially showed moderate generalised excess slowing, suggesting encephalopathy, with some right sided preponderance. This improved progressively over the following six weeks. Serological studies demonstrated seroconversion to infectious mononucleosis, with positive IgM studies to this same virus. MRI scan demonstrated two lucent areas in the anterior and posterior regions of the brainstem (Figure 1).

Subsequently there have been two further inpatient admissions, and six repeat overnight sleep studies. Ulceration occurred on the nasal bridge, secondary to pressure from the nasal mask used for ventilation. Nasal prongs have been used successfully since that time. A follow-up MRI scan twelve months after initial presentation was normal.

Sleep studies have demonstrated persistence of nocturnal hypoventilation most marked in slow wave sleep. There has been significant recovery of arousal responses to the spontaneously developing hypoxia and hypercapnia in sleep. Arousal did not occur on initial studies, despite oxygen saturation levels of 60%. On the most recent study, spontaneous arousal occurred at saturation of 78%. pCO_2 was set at a lower level, but still ranged over 34 mmHg during the night's sleep (Figure 2). Nasal mask ventilation in sleep has continued for 21 months in the home environment for this child. The family has declined nursing or respite care for this child, who attends a normal school, and is progressing without difficulty in his education.

9.2.2.1 Important features of this case:

- this child did not present until the age of 5 years 8 months,
- the previous history could support the presence of a pre-existing respiratory control abnormality; this includes cyanotic breathholding attacks and the ability to spend prolonged periods swimming underwater without distress
- administration of oxygen was associated with CO_2 retention to levels of 90 mmHg
- endotracheal intubation was associated with a strong depressant effect on awake ventilation
- extubation was associated with immediate recovery to normal awake ventilation
- nasal mask ventilation was introduced effectively from the time of ETT extubation, when the diagnosis of central hypoventilation was made
- pressure effects of the nasal mask caused ulceration of the nasal bridge and required transfer to a system of nasal prong ventilation which has been successful for over two years now
- seroconversion to infectious mononucleosis occurred during the acute presenting illness. Associated EEG and evoked potential abnormalities may have been due to acute hypoxic encephalopathy, or a more diffuse infectious encephalitic process, but CSF studies did not support the latter.
- MRI scan findings initially showed small areas of lucency in both the anterior and posterior aspects of the brainstem. These disappeared on subsequent study 12 months later. They also correspond anatomically to areas directly responsible for respiratory control.

- arousal responses to spontaneous hypoxic hypercapnia have shown both recovery and plasticity in the two years since initial presentation. Hypoventilation persists in slow wave sleep while ventilation in REM sleep is well maintained; predisposing to hyperventilation in this sleep state

- after a period of regular hyperventilation the child was able to breath spontaneously throughout a whole night, without significant hypoxia, but the CO_2 continued to vary by more than 30 mmHg

- use of nasal mask ventilation has probably been part of the reason this family has apparently failed to grasp the significance of their child's respiratory abnormality. On return to school after his acute illness his parents did not provide any explanation of their child's condition to the school. There were no identifiable abnormalities as far as the school administration were concerned. The school only found out about the use of nocturnal ventilation for this child when our community nurse contacted them to advise on emergency care.

9.2.3 CASE 3 (KC). Age of presentation 5 years 9 months.

This female child was born at 37 weeks gestation, after an uncomplicated pregnancy, weighing 2.6 kg. The perinatal history was consistent with a significant hypoxic insult. Foetal distress during labour precipitated an emergency caesarean section, and the apgar scores were one at one minute, and four at five minutes. Severe foeto-placental transfusion had occurred and the initial haemoglobin of the infant was 5 gm%, requiring transfusion soon after birth. Complications included early hypoglycaemia, and ventilatory support was required for five days, partly because of hypoventilation with CO_2 retention.

Cerebral ultrasound showed bilateral intraventricular haemorrhages, dilatation of the ventricular system, with increased echogenicity in the right parietal region.

Generalised seizures on Day 1 were treated with phenobarbitone and phenytoin.

There was slow initial improvement with persisting hypotension, but the infant was discharged from hospital, on oral feeds, at three weeks of age. Anticonvulsants were discontinued prior to discharge from hospital. At 12 month review, there was mild developmental delay and signs of lower limb cerebral palsy. Sitting was achieved at six to seven months, standing at 11 months, walking at sixteen months, and speaking in sentences at two years.

After this difficult neonatal period the child remained well. Her first hospital admission was at the age of two and a half years following a prolonged, afebrile, focal (left facial) convulsion lasting 45 minutes. This seizure began during sleep. The

seizure was controlled with rectal diazepam, and the child was drowsy for a one hour period post-ictally. Biochemistry, including calcium and magnesium levels, and full blood count were normal at this time. EEG showed right parietal spikes consistent with an epileptic focus. A CT scan was arranged one month later, to investigate these focal findings.

Administration of thiopentone for the CT scan, resulted in apnoea, and the child was paralysed with alcuronium, intubated and ventilated. The procedure itself was uneventful. Post-anaesthetic cyanosis and hypoventilation responded to naloxone in the recovery ward. However, cyanosis and hypoventilation recurred in the general ward, and the response to naloxone was partial and brief on this occasion. A blood gas taken when the child was receiving mask oxygen, but hypotonic and unresponsive, showed pH 6.9, pCO_2 146 mmHg and O_2 466 mmHg. The child was intubated, ventilated and transferred to the intensive care ward.

A further three seizure episodes occurred over the subsequent 24 hours, including one twenty minute grand-mal seizure. Seizures continued to occur during the following week, and were treated with phenobarbitone. Although the child woke and became responsive, hypoventilation persisted for five days; well beyond the period of drug clearance of the anaesthetic or benzodiazepines. Atropine and neostigmine were administered but had no effect on spontaneous respiratory state.

The CT scan had shown mild ventricular dilatation with an old infarct in the right parietal region. Subsequent investigations showed clear CSF with normal protein and glucose levels. Fever was associated with right upper lobe collapse, and streptococcus pneumoniae was cultured from endotracheal aspirate. EEG showed diffuse slowing consistent with a post-ictal state, not indicative of an encephalopathy.

Hypoventilation was more severe in sleep, with improved ventilatory effort when awake. Supportive ventilation was progressively weaned, with CO_2 maintained at 60-64 mmHg, and SaO_2 at around 90%, during the period of intubation. The child was extubated twelve days after the initial anaesthetic. Spontaneous ventilation improved further following extubation and the child was discharged home. At review one month later the parents felt that the child had returned to her normal behaviour and sleep patterns, with normal mood, memory and speech. They specifically felt that there were no sleep related problems, and so no further investigations were undertaken at that time. The family were advised that this girl's ventilatory responses were still likely to be abnormal, and there was a high risk of similar problems should another general anaesthetic be required.

A second anaesthetic was required two and a half years later, for dental extractions. Because of this girls past history, overnight observation was arranged in intensive care following the anaesthetic. Desaturation occurred post-anaesthetic and was partly corrected by face mask oxygen. More severe desaturation and hypoventilation occurred in sleep, and formal overnight sleep studies were arranged.

At the time of admission for sleep study, history revealed that the child had continued to suffer grand mal seizures in sleep, despite continued epilim anticonvulsant therapy. There were four night time events in the two year period preceding the first sleep study. In the twelve months preceding the study, she had also begun to have daytime partial seizures. Seven to twelve of these brief episodes were observed. For three months she had also complained of headaches following these seizure episodes, lasting around thirty minutes and resolving spontaneously. Three headache episodes had been associated with vomiting. There was a lifelong history of behavioural problems, poor concentration, and hyperactivity, making her very difficult to discipline. Neurology review and MRI scan were also arranged.

The overnight study confirmed sleep associated hypoventilation, with desaturation to 60%, and $TcCO_2$ rose to a maximum of 80 mmHg. The daytime episodes were diagnosed as absence seizures. Endocrine investigations (LP, FSH, testosterone, oestradiol, dihydroepiandrosterone (DHAS), and pelvic ultrasound) were undertaken because of premature thelarche. All were normal prepubertal results. MRI demonstrated normal brainstem and hypothalamus and confirmed signs of an old infarct in the right parieto-occipital area.

It was not possible to provide a ventilator for the child at this time, and a regime of third hourly waking during sleep periods was commenced. The parents were able to see a significant behavioural improvement once this regime had been instituted. However, three weeks after this was commenced, a prolonged seizure episode

occurred, starting in sleep. Ambulance officers called to attend to the child, administered lignocaine, glucose and phenytoin. In the post-ictal period there was persistent hypoventilation which necessitated endotracheal intubation despite all attempts to avoid this. Flumazenil was given to counter diazepam and positive pressure ventilation was given by face mask. At the time of intubation pCO_2 was 123.7 mmHg. Following intubation the child was again transferred to TCH.

Because of this child's past history of documented hypoventilation no further sedation was given, she was extubated 24 hours later, and nasal mask ventilation was commenced during all sleep periods. Nasal mask ventilation was established during the subsequent 10 days hospital admission, and the child was discharged home at the end of this time.

There was significant improvement in the child's daytime attention span and behaviour, with no generalised fits observed for a period of three months. Charcoal tablets were given to treat the flatulence caused by air swallowing during nasal ventilation. Generalised seizures recurred after this due to absorption of anticonvulsant medications. There has been one further inpatient admission to our hospital, for ventilation review. A second admission was required to the local hospital because of a purulent nasal discharge, which was secondary to an intranasal foreign body.

9.2.3.1 Important features of this case:

- hypoventilation in this child may have been secondary to perinatal asphyxia
- some degree of central hypoventilation may have been present since the neonatal period in this child
- hypoventilation may have caused and exacerbated the perinatal hypoxia
- from the age of two and a half to four years, nocturnal seizures were the only clear symptoms suggesting sleep associated central hypoventilation
- at presentation there was a history of headaches and seizures related to sleep periods
- progression of symptoms may have been related to deterioration in respiratory control, or of cumulative effects of the sleep related disorder
- hypoventilation initially became clinically significant after receiving drugs with a respiratory depressant effect
- this child and others have shown inordinate sensitivity to drugs which are known to have any respiratory depressant effect
- when a ventilator was not immediately available a regime of third hourly waking did result in clinical improvement
- it is impossible to distinguish how much perinatal asphyxia or subsequent hypoxia in sleep have contributed to the long term problems of seizures and behavioural difficulties
- ventilation via nasal mask was able to be introduced from the time of endotracheal extubation
- the child was discharged home 10 days after commencing nasal mask ventilation

- current home management requires nursing support on four nights per week
- clinical improvement involved increase in daytime attention span, and responsiveness, and a marked reduction in the frequency of both daytime and sleep associated seizures
- headaches previously diagnosed as migraine have resolved since the introduction of nocturnal ventilation
- an intranasal foreign body (introduced by the child) complicated the early period of nasal mask ventilation
- arm splints and a dummy were practical necessities in order to maintain adequate nocturnal ventilation in this child; loss of the two front (baby) teeth have been associated with significant mouth leak.
- charcoal tablets were administered because of flatulence caused by air swallowing during ventilation, and caused a secondary exacerbation of seizure activity

9.2.4 CASE 4 (EKB). Age of presentation 6 years 1 month.

This female child was born at 42 weeks gestation. The delivery was complicated by a concurrent, maternal, flu-like illness and the child was born with pneumonia. Treatment consisted of intra-venous antibiotics for two weeks in Intensive Care. Recovery was apparently complete.

There was a subsequent history of recurrent wheeze from the age of three months, without other features of atopy. The wheezing episodes were frequent and severe. After a failed trial of sodium chromoglycate therapy, oral prednisolone was instituted at 14 months of age. Doses of up to 15 milligram (mg) daily were required by 18 months of age. Frequent admissions to the local hospital were required during acute episodes, which were slow to respond to bronchodilators. The first admission to our hospital was at the age of five years. There was some delay in acquisition of motor milestones, and the child did not walk until 20 months of age.

Oral steroids had been replaced with the inhaled form at four years of age. At 4 years and 2 months of age, she began to have recurrent episodes of oedema of the face, hands, and feet. This initially settled spontaneously, but subsequently became associated with acute dyspnoea wheeze, cough, cyanosis and intermittent syncope. The episodes were treated as a concurrent allergic reaction associated with asthma. At 4 years 6 months, an acute episode of cardiac failure occurred, with no known

precipitant. There was good clinical response to treatment with frusemide and antibiotics (Erythromycin).

Admission to The Children's Hospital (TCH) followed eight months later, with a history of recurrent nocturnal respiratory distress and cough, associated with cyanosis around the eyes and of the hands. The acute respiratory distress and cyanosis woke this girl, but tended to settle within half an hour. Physical examination on admission, revealed an obese child with widespread crackles and wheeze throughout the chest. Generalised oedema was present at the time of admission. The symptoms and signs settled with bronchodilator therapy, and she was discharged with a diagnosis of angiooedema and asthma.

The episodes of asthma subsequently became less frequent, occurring only two to three times per year. However there was a history of increasing baseline respiratory difficulty. The child experienced marked dyspnoea on exercise, slept propped up on two pillows, and had increasingly frequent episodes of observed cyanosis, usually precipitated by crying or exertion. An admission at 6 years and one month was precipitated by increasingly frequent episodes of fainting which occurred, on average, once per week. They were usually associated with cyanosis and occurred in the morning soon after sleep, or with exercise. The child was always very sweaty afterwards. They occurred more often when the child was physically tired, but were not associated with crying or trauma.

There was a history of increased daytime sleepiness. Observation of the child in sleep revealed snoring, apnoeic periods and very shallow respirations. Studies showed that she desaturated to the 80's in sleep, and a blood gas, taken during sleep (on O_2), showed a CO_2 of 122.6 mmHg, with pO_2 72.6. This precipitated acute intubation and ventilation in intensive care. Adenotonsillectomy was performed.

In intensive care the child had persistent respiratory depression, failing to breath spontaneously despite pCO_2 levels as high as 90 mmHg. Investigations confirmed central hypoventilation without revealing an underlying cause or acute precipitating factor.

Bronchoscopy showed changes consistent with asthma only. Muscle biopsy was normal, with low glycogen, but mitochondrial studies were normal. An overnight sleep study confirmed episodes of desaturation associated with CO_2 retention, which were self limiting, and not associated with upper airway obstruction. Ventilatory responses revealed absent hypoxic response, and depressed CO_2 responses. Computerised tomography (CT) scan, thyroid function tests (TFT's), and hypothalamic studies were normal including follicle stimulating hormone (FSH), growth hormone (GH), Cortisol, and Prolactin levels. Measles serology, and Respiratory Syncitial Virus immuno-fluorescence were negative. Lumbar puncture was normal. The EEG was initially consistent with a diffuse encephalopathy, but returned to normal within three months.

Nocturnal ventilation via a nasal mask was commenced during this admission and continued subsequently with intermittent monitoring in the sleep unit. Hypernasal speech was apparent following adenotonsillectomy. A chin strap was required because of a mouth leak during nasal ventilation. Exacerbations of asthma continued to precipitate hospital admission over the following four years. These episodes tended to present with acute cyanosis and syncope. Nocturnal ventilation was stable, and there were no signs of cardiac dysfunction or cor pulmonale. There were no further episodes of acute oedema.

At the age of 11 years and six months palatoplasty was undertaken because of persistent difficulty with hypernasal speech which was making communication very difficult for this girl. Her asthma was felt to be well controlled on treatment of ventolin, ipatropium bromide, sodium chromoglycate and beclamethasone 200 microgram twice daily. At review six months later, the child's speech and palatal function had again deteriorated despite the recent surgery. Examination now revealed other signs of brainstem dysfunction. MRI scan now demonstrated a huge exophytic brainstem lesion, infiltrating and expanding the brainstem from the level of the fourth ventricle to the medulla (Figure 3). An open biopsy of the lesion was attempted but the pathology was inconclusive. This surgery was associated with significant depression of multiple brainstem functions post-operatively, but there was return to pre-operative levels of function within two weeks. The lesion was diagnosed as a low grade astrocytoma, and after extensive discussions with the family and the child a course of chemotherapy was undertaken.

There has been progressive deterioration of brainstem function in this child over the subsequent two years, particularly bulbar function. The deterioration has been slow, and nocturnal nasal ventilation has continued throughout that time. A decision has been made by the child and her family, not to undertake any more aggressive intervention, particularly tracheostomy or gastrostomy.

9.2.4.1 Important features of this case:

- this child had a long history of respiratory illness, but her history did not distinguish her as having respiratory control abnormalities
- the presentation of respiratory failure in this child was of gradual onset
- the absence of hypoxic (and hypercapnic) responses in this child meant that her asthma presented without apparent respiratory distress. Asthma in this child presented with cyanosis and loss of consciousness
- initial investigations did not reveal any brainstem lesion. The only sign of brainstem dysfunction was a unilateral abnormal auditory evoked potential
- hypoxic ventilatory responses showed initial recovery
- secondary loss of hypoxic ventilatory responses occurred
- one major difficulty of managing home ventilation in this family was their tendancy to constantly re-adjust the ventilator settings.
- this family used "nights off" the ventilator as a reward for the child
- clinical symptoms of brainstem dysfunction were very slow to evolve, and were not identified by the family

- a brainstem tumour was diagnosed six years after her presentation with sleep associated central hypoventilation, and six years after nocturnal nasal ventilation was commenced
- identification of the brainstem lesion does not appear to have altered the course of the disease, which continues to progress slowly
- the use of nasal mask ventilation has allowed this family to limit the level of medical intervention without the development of symptomatic respiratory failure
- nasal mask ventilation allows for easy withdrawal of therapy if, and when, this becomes appropriate.

9.2.5 CASE 5 (JK). Age of presentation 9 years 3 months.

This boy initially presented with apnoea at 3 weeks of age. He was born at term, with no problems during either the pregnancy or delivery. He had subsequent diagnoses of mild asthma, chronic rhinitis and sinusitis, and attention deficit disorder. Past surgery includes adenotonsillectomy, septoplasty and sinus washout. His father has obstructive apnoea, treated with nasal CPAP therapy. His mother has Sjoegren's syndrome, and mild arthritis. Both he and his younger sister were on apnoea monitors to the age of four years because of continuing apnoeic events.

Overnight sleep studies were initially undertaken because of symptoms suggesting obstructive sleep apnoea. These symptoms improved following adenotonsillectomy. The symptom of daytime tiredness then increased progressively and a repeat overnight study was performed. At the time of his overnight study, he was on beclamethasone nasal spray for rhinitis, sodium chromoglycate for asthma, and imipramine for attention deficit disorder.

An initial sleep study at the age of 8 years and 8 months, prior to adenotonsillectomy and sinus surgery, showed mild obstruction with apnoeas and hypopnoeas. Respiratory disturbance index was 11 per hour in non-REM (NREM) sleep and 17 per hour in REM, with a minimum oxygen saturation 89%. There were also periods of a coupled cardiac dysrhythmia. CO_2 varied from 42 mmHg when awake to a peak CO_2 of 53 mmHg in slow wave sleep (SWS). REM was associated with a fall in CO_2

to 44 mmHg. Entering REM from the awake state was associated with an increase of 4 mmHg CO_2. SaO_2 in SWS sat at 93-95%, and in light sleep or REM 96-98%.

A repeat study was performed following ear nose and throat (ENT) surgery because of increasing symptoms of daytime lethargy and sleepiness at the age of 9 years 6 months. This study showed CO_2 retention of 15 mmHg during the period of the study with acute rises of 3-5 mmHg during periods of SWS and REM, and a steady increase in the baseline CO_2 during the night. The only respiratory events consisted of brief central apnoeas in REM sleep. A further repeat study off Imipramine at age 10 years 2 months, showed normal CO_2 variation of 7 (45-52) mmHg during the night. SaO_2 during this study was stable at 95-98% throughout the night.

9.2.5.1 Important features of this case:

- there is a strong (but complicated) family history of respiratory "control" dysfunction
- there is a history of apnoea in infancy which started at 3 weeks and settled by 6 months of age
- a complicated history has led to marked difficulty in identifying the impact of the documented respiratory abnormalities
- this child's father is not obese and has documented OSA at the age of 36 years requiring treatment with nasal CPAP.
- the obstructive sleep apnoea identified initially in this child was not severe

- obstructive sleep apnoea in this child was associated with CO_2 retention of 11 mmHg during the night

- surgery which corrected the upper airway obstruction did not alter the degree of CO_2 retention

- anaesthetic was not associated with failure of respiratory drive in this child

- the most likely causative factor identified is imipramine supported by increased CO_2 retention when the dosage was increased and resolution of the hypoventilation when the medication was removed

- the pharmacology of imipramine does not explain how it could cause this child's central hypoventilation

9.2.6 CASE 6 (TG). Age of presentation 9 years 10 months.

This girl presented at 9 years and 11 months, with a head injury following a fall from a horse. She had been previously well, with no significant illnesses.

The child and was born by forceps assisted vaginal delivery, with no perinatal problems. She was the first of two children with a history of asthma affecting the mother and sibling, and multiple family members suffering arthritis. The father has a history of occasional snoring, only after drinking alcohol. The maternal grandfather had a history strongly suggesting obstructive sleep apnoea (OSA), and died at the age of 70 years from a cerebro-vascular accident. There was no history of obstructive breathing, snoring or morning drowsiness at any time in the past in this child.

The acute history was that the child had been riding a horse following her father and had fallen off. The fall was not witnessed. The child was found lying unconscious on the ground by her father, who performed mouth to mouth resuscitation and noted that she was very stiff with three episodes of clonic jerking each lasting less than one minute during the following two hour period. She was incontinent of urine and unconscious for at least 5 minutes. On arrival at casualty, she was crying, but obeying commands, and irritable. Neurologic examination showed no focal signs, but she was tender over the left shoulder, head and neck. She was admitted for observation, after x-rays of the skull and cervical spine were found to be normal. No precipitating event could be determined for the fall.

At the time of admission, the child was difficult to rouse and her oxygen saturation fell briefly to 51%. Blood pressure was 140/60 and there were no focal neurologic signs. During the following night several further episodes of desaturation were noted. Some of these were associated with obvious cyanosis, but there were no signs of respiratory distress and these episodes were treated with face mask oxygen. The child aroused and became distressed when blood gases were taken. pH was 7.4, pCO_2 37 and pO_2 346.

Overnight studies demonstrated sleep associated CO_2 retention. Blood gases on arousal showed pH 7.39, pCO_2 46 mmHg, and pO_2 of 98.9 in air. Other investigations during the admission included ECG, echocardiogram, and CT scan. There were no epileptic phenomena witnessed clinically or on EEG. There was focal slowing posteriorly on the EEG consistent with cerebral contusion. The CT scan excluded subarachnoid and subdural haemorrhage, but the posterior fossa was not seen well. Full blood count showed Hb 13.5, platelets were normal, the white cell count was 5.5 with a normal differential and the ESR was 9 mm/Hour. The overnight saturation levels improved prior to hospital discharge, but CO_2 monitoring was not able to be repeated.

Overnight sleep studies were arranged. This revealed central hypoventilation with pCO_2 rising to 64 mmHg (19 mmHg above baseline levels). Morning blood gas analysis showed pH 7.18, pCO_2 49 mmHg, and pO_2 of 55 mmHg in air. This pCO_2 corresponded precisely to the transcutaneous CO_2 recording at the time. There were

frequent central apnoeas in REM sleep with a maximum duration of 20 seconds, and desaturation to 90%. No treatment was undertaken.

Two months later the child had a second unwitnessed fall. The child fell off a swing, could not remember the event, and sustained a supracondylar fracture of the left humerus. Blood pressure was now normal at 100/60, and detailed neurologic examination remained normal.

At this time a history was obtained of the child feeling that she needed to take a deep breath intermittently when awake, since the first accident. This was occurring less frequently now than initially. One episode of loss of colour had been noted around 7 pm in the evening, at home. The parents had witnessed shallow breathing in sleep, but no other sleep associated problems, in particular, no symptoms of obstructed respiration in sleep. Although there was a long history of daytime headaches, these had not changed in association with recent events, and there was no past or recent history of morning headaches. There were no changes in daytime behaviour, memory or sleepiness, either preceding or following the accidents.

A second sleep study, four months after the original incident showed CO_2 retention of 16 mmHg on transcutaneous recording, and minimum oxygen saturation 85%. REM was disrupted by frequent arousals, but there were no significant central apnoeas. A blood gas on wakening showed pCO_2 of 46 mmHg pH 7.37, and pO_2 100

mmHg. Ventilatory responses performed at this time showed a hypoxic response slope of 0.13, and CO_2 response slope of 1.02 (N= 1.5 to 4.0).

On review 7 months after the initial fall, the child was maintaining her usual grades at school with no further episodes. No further follow-up studies have been performed.

9.2.6.1 Important features of this case:

- hypoventilation was first noted following a traumatic head injury
- it remains speculative whether the fall was the primary or secondary event
- hypoventilation was documented and appears to be improving with time
- the pattern of hypoventilation is consistent with the other cases, being worst in slow wave sleep
- ventilatory response testing confirmed depressed responses at the time of diagnosis
- there are no historical features to suggest a pre-existing respiratory control abnormality

9.2.7 CASE 7 (KL). Age of presentation 14 years 5 months.

Prior to her first presentation this girl had been entirely well. At the age of seven years, while on holidays with her family in Ireland, she developed an illness with malaise, sore throat, urticaria, profound lethargy and generalised lymphadenopathy. This was diagnosed clinically as glandular fever.

At 14 years of age, following a second severe viral illness, she developed symptomatic bulbar dysfunction with swallowing difficulties, regurgitation of food through the nose and abnormal speech. Examination confirmed bulbar palsy. Investigations at that time were consistent with infectious mononucleosis, with mononuclear cells on blood count and conversion from a negative to a positive monospot. Other investigations were normal. These included serum biochemistry, TFT's, skull x-ray, CT scan of head, lumbar puncture (pressure 10 cm CSF), tensilon test, brucella titres, brainstem auditory evoked potentials (BAEP's) and four vessel cerebral angiography.

A pneumoencephalogram was subsequently arranged. This was performed under general anaesthetic, complicated by subsequent persisting hypoventilation. The aftermath of this, was an eight week period of treatment with ventilation, and tracheostomy, in intensive care. Treatment during that time also included ventricular puncture, steroids, and mannitol. The pneumoencephalogram suggested a diagnosis of medullary tumour, and a course of radiotherapy was undertaken.

The bulbar symptoms improved during the next three years, although there was residual dysarthia and dysphagia. During this time however, symptoms of increasing daytime sleepiness developed to a level which interfered with school progress. During the third year following radiotherapy, cyanosis was noted during sleep periods. The progression of symptoms then included development of sleep fragmentation with cyanosis and choking on waking from sleep. Re-admission to hospital was arranged five years after the initial illness, for observation in intensive care, because of worsening bulbar symptoms, mild gait ataxia, decreased hearing in the right ear, and cyanosis in sleep.

Cyanosis in sleep was confirmed and blood gases on waking showed a chronically compensated respiratory acidosis, with pH 7.22, pCO_2 87 mmHg, pO_2 40 mmHg, HCO3 34 and BE +4. When fully awake, CO_2 retention persisted, with pH 7.35, pCO_2 68 mmHg, pO_2 83 mmHg, HCO3 38, and BE +10. Medroxyprogesterone did not produce respiratory stimulation. Repeat CT scan of the head at this time was normal. Transfer was arranged for further investigation and management of central hypoventilation in sleep.

On admission at the age of 18 years, this young woman was very unwell. Signs of Cushings syndrome were associated with multiple cranial nerve abnormalities. These included bilateral horizontal nystagmus, bilateral ptosis, reduced hearing in the right ear, nasal speech, palatal weakness, bilateral 4/5 sternomastoid weakness, occasional tongue fasciculations and weak tongue protrusion. There was mild generalised

weakness, bilateral cerebellar signs and impaired tandem gait. Diaphragmatic palsy and mitral valve prolapse were diagnosed.

Studies demonstrated profound central hypoventilation in sleep, with oxygen saturation ranging from 0 to 40% in sleep, and $TcCO_2$ rising from a baseline of 50 mmHg to greater than 100 mmHg. Oxygen saturation rose to 95% at times of arousal. There was very little heart rate variability in response to these changes, and respiratory rate remained around 60 to 80 breaths per minute throughout sleep. Nasal oxygen at 2 litres per minute corrected the poor saturations, but CO_2 retention to levels of 130 mmHg persisted.

Cuirass ventilation was commenced with nasal oxygen. After stabilisation on this therapy, repeat study off the cuirass ventilator showed improvement in the patients ability to maintain gas exchange in sleep. Saturation now remained above 80%, and $TcCO_2$ reached 80 mmHg. However, no REM sleep occurred. Studies on the cuirass ventilator showed oxygen saturation maintained between 89 and 97% without additional nasal oxygen, CO_2 levels in sleep were maintained between 50 and 70 mmHg and REM sleep was achieved. This was associated with marked symptomatic improvement and markedly improved sleep quality subjectively. After waking feeling refreshed with no morning headaches there was also less daytime sleepiness. Neurologic symptoms and signs also improved, and both dexamethasone and thiamine were ceased. Extensive pulmonary function testing showed normal volumes, normal carbon monoxide diffusion of the lungs (DLCO), normal nasal resistance, and

improved muscle strength after one month. There was progression of the right sided deafness following discharge. The association with general improvement of all other neurologic signs raised the possibility of a brainstem demyelinating disorder.

Cuirass ventilation in sleep was associated with upper airway obstruction particularly in REM sleep. 15 months after commencing cuirass ventilation nasal CPAP was combined with cuirass ventilation with good effect. Two weeks after this trial, positive pressure ventilation was commenced using the same nasal mask. Studies using nasal mask ventilation have confirmed saturation levels of 97-99% throughout the night, with CO_2 ranging between 38 and 45 mmHg.

Studies while breathing spontaneously in sleep show SaO_2 and CO_2 now maintained at relatively stable levels, but hypoventilation persists. When breathing spontaneously in sleep, after six years of nocturnal ventilation, oxygen saturations fell to 81% and $TcCO_2$ rose to 54 mmHg, Respiratory rhythm, oxygen saturation, and CO_2 levels were most unstable during REM sleep, which was now achieved even while breathing spontaneously. Respiratory rates in sleep are 40-45 breaths per minute (bpm), compared to an awake rate of 22 bpm.

MRI studies were undertaken when these became available in 1986. The brainstem, pons, and medulla were seen clearly and were normal. Small plaques in the cerebral hemispheres were felt to possibly represent demyelination, but there has been no subsequent clinical deterioration and further MRI studies have been normal.

Currently, symptoms during physical exertion and emotional disturbance are consistent with poor ventilatory response to these physiologic states. There are residual cranial nerve abnormalities, but no progression of these. Repeat MRI scans have remained unchanged. Cardiac evaluation confirms resolution of pulmonary hypertension, and pulmonary function testing and lung volumes remain normal. The diagnosis of brainstem tumour has been revised in view of subsequent clinical course and investigative results. The initial illness is now considered to have been a localised brainstem encephalitis. Nocturnal nasal mask ventilation continues to be effective therapy in this young woman, eight years after it was first commenced. She has completed a university degree in agriculture, and is currently in her second year of training as an occupational therapist. She leads a normal, active life.

9.2.7.1 Important features of this case:

- there was an initial viral illness at seven years of age associated with profound lethargy but no medical reports of this illness are available to us and respiration in sleep was not investigated at that time
- an acute illness at age 14 years was associated with seroconversion (monospot) to epstein barr virus (EBV).
- seroconversion to EBV and hypoventilation preceded brainstem irradiation
- hypoventilation was acutely precipitated with the administration of a general anaesthetic leading to inpatient treatment in the intensive care unit (ICU) for a period of eight weeks

- symptoms of other cranial nerve abnormalities have been present since the initial presentation
- MRI scans of the brainstem remain normal despite the early abnormalities suggesting demyelination
- sleep related symptoms progressed over a four year period before precipitating further medical investigation
- deterioration in nocturnal respiratory function was associated with deterioration in brainstem functional abnormalities
- treatment with cuirass ventilation did result in symptomatic improvement
- schooling and academic performance were seriously affected by the respiratory abnormalities
- nocturnal ventilation has been continued while a university degree was succesfully completed
- hypoventilation has persisted for 7 years since commencing nocturnal ventilation, and 11 years since the first illness when this was documented
- cuirass ventilation was associated with upper airway obstruction, which was overcome by the implementation of nasal mask ventilation
- no upper respiratory tract infection has prevented the use of the nocturnal nasal mask ventilation in six years
- failure of ventilatory response to exercise and emotion has been symptomatic
- repeat studies after being stabilised on nocturnal ventilation show recovery of arousal responses to hypercapnic hypoxia
- initial presentation was associated with inability to achieve or sustain REM sleep

- despite respiratory destabilisation in REM sleep, REM sleep is now achieved and sustained when breathing spontaneously

- persisting ventilatory control abnormalities have been documented

- the effects of the respiratory control abnormalities (both in consequence and tolerance) have changed with treatment

- the symptoms secondary to failure of adequate respiratory compensation in exercise have taken seven years to be recognised

9.2.8 CASE 8 (JR). Age of presentation 38 years 8 months.

This man presented at the age of 38 years in cardiorespiratory failure of unknown cause. He was admitted to his local hospital, treated for cardiac failure, and investigated for an underlying cardiac abnormality. No cardiac abnormality was found.

Further respiratory investigation were arranged, including overnight sleep studies. Sleep related hypoventilation was documented, associated with intermittent apnoea. A respiratory arrest occurred within one week of the sleep study, leading to intubation, ventilation, and admission to intensive care.

Nocturnal cuirass ventilation was commenced after extubation. This resulted in significant improvement in both daytime and night time symptoms. Daytime blood gases returned to normal. Daytime respiratory function also improved, following ventilation during all sleep periods, allowing return to normal daytime activities.

The man was stabilised on cuirass ventilation during sleep at home. Daytime proximal muscle weakness became apparent ten years later. A muscle biopsy was performed which demonstrated non-specific myopathic changes and electromyogram was diagnostic for myopathy. Nasal mask ventilation was commenced at the last review, producing improvement in daytime and night time blood gases. He has recently developed skeletal muscle weakness.

9.2.8.1 Important features of this case:

- nocturnal hypoventilation was the presenting symptom of a myopathy
- it took ten years for the myopathy to declare itself in any form other than sleep associated respiratory depression
- this man has been able to return to normal work with nocturnal ventilation
- cuirass ventilation was symptomatically effective but was complicated by upper airway obstruction
- nasal mask ventilation produced the most stable nocturnal ventilation
- ventilatory responses were initially depressed but showed improvement with treatment

9.3 SUMMARY FEATURES

All of these individuals have acquired central hypoventilation in sleep. Six of eight individuals required treatment with nocturnal ventilation, and all of those requiring ventilation have now been established on nasal mask ventilation. The potential causes of central hypoventilation here are listed in Table 1. Long term follow-up has seen the evolution of a brainstem tumour in one child, seven years after her initial diagnosis with central hypoventilation. In a second case, a myopathy has been diagnosed ten years after initial presentation. Two children have been observed to have mild central hypoventilation with no MRI abnormalities present. Hypoventilation in these children has not required treatment, and remained mild, or improved. Two cases sero-converted to the Epstein-Barr virus during the acute presenting illness. Two cases were initially treated with cuirass ventilation and subsequently transferred to nasal mask ventilation.

A potential causative mechanism has been identified in each of these cases. In two cases the primary pathology did not emerge until 7-10 years after central hypoventilation was identified. This clearly indicates the need for close review of both neurologic signs and investigations in those children and adults presenting with apparently primary central hypoventilation.

Despite the subsequent identification of a myopathy the patient described here had documented loss of both central and peripheral chemoreceptor responses at the time

of presentation. This chemoreceptor function recovered after effective night ventilation was established. Sleep associated hypoventilation has persisted when studied without respiratory support.

Two children presented acutely with symptoms of central hypoventilation. In these two cases, seroconversion to EBV occurred during the acute illness, without persisting identifiable structural brainstem pathology, but with persisting central hypoventilation. In one of these cases there are other cranial nerve deficits. This patient received brainstem irradiation during the initial illness.

Laryngeal reflexes can cause significant depression of ventilation in cases where there is chemoreceptor insensitivity. This relates to three cases of prolonged endotracheal intubation for persistent hypoventilation when awake with the endotracheal tube in place. There has been complete recovery of awake ventilation on extubation, despite persistence of nocturnal hypoventilation. In three recent cases, nasal mask ventilation was commenced immediately after extubation in children as young as sixteen months of age.

It is possible that abnormal respiratory drive is present without distinctive historical features. Events precipitating respiratory failure have occurred after hospital admission in a number of cases. These have included the routine administration of anaesthetic agents which resulted in acute deterioration of respiratory function in three of these cases. Two children had respiratory arrests precipitated by the

administration of oxygen during sleep associated periods of hypoventilation. Hypoxic respiratory drive appears to be important in maintaining whatever level of ventilation is achieved in sleep. The respiratory abnormality which is present is not responsive to "respiratory stimulant" medications and these have not been successful in any of these cases, even temporarily.

9.4 DISCUSSION

These eight cases of acquired central hypoventilation provide a profile of the syndrome of acquired central hypoventilation. In each of these cases, the disorder presented after the first year of life and is not apparently congenital in origin. It is possible that in three of the children the disorder was present at the time of birth, but did not cause clinically significant problems, until there was an additional precipitating incident. However, central hypoventilation was not documented in the perinatal period, and none had a clinical course warranting further investigation or intervention. Historical features had not distinguished these individuals, until the acute incident.

The pattern of hypoventilation has followed a consistent pattern in these children who also have normal pulmonary function. The degree of hypoventilation is at its worst in slow wave sleep, with relatively normal spontaneous ventilation in REM sleep. This is true even in those cases where a structural brainstem abnormality has been identified. This follows the same pattern described in children with congenital central hypoventilation, and contrasts with that seen in patients with other lung disease. Two adults have demonstrated deterioration in REM sleep.

Ventilatory and arousal responses, which were initially depressed, have shown improvement after a period of regular nocturnal ventilation, even where a structural abnormality has been subsequently identified. This may be due to acutely detrimental

effects of hypoxia and hypercarbia on ventilatory control. In contrast cases 1 and 7 appeared to have maintained their ventilatory arousal responses, and had marked sleep disruption at presentation because of this. Case 2 has helped shed further light on this phenomenon, through observation during periods of ventilation to different levels of CO_2. When relatively hyperventilated on a regular basis, his arousal responses were set at levels much closer to the normal range.

This was not a permanent recovery. When his regular ventilation was reduced to relative normocapnia, his arousal responses again became depressed to levels similar to those seen at his initial presentation.

These case studies profile different forms of central hypoventilation of variable severity. In the two cases with the most mild form, the causative mechanism is unusual, and not previously described. Presumably the minor head injury in case 6 has resulted in contusion in an area of the central nervous system vital to respiratory control, but this was not demonstrable on current imaging modalities of MRI scan. Case 5 has had a well documented respiratory disturbance in the presence of imipramine, although there is no clear pharmacologic mechanism for this effect.

Case 8 illustrates the limitations of ventilatory response testing. Central hypoventilation appears to have been the initial presentation of a myopathy, even though there was no clinically testable muscle weakness at that time. It is possible that central respiratory control is abnormal in this man. Alternatively, ventilatory

response testing has revealed the limitations of his respiratory muscle responses, and the abnormal respiratory response to chemical stimulation is entirely due to muscle weakness.

It is possible that EBV can cause an encephalopathy, including focal brainstem disease. As cases two and seven both seroconverted during their acute illness of presentation, and had no evidence of previous respiratory failure, it appears to have been the only identifiable agent. Alternatively, it is so ubiquitous that its occurrence in these two cases was incidental and bore no causal relationship to the syndrome of central hypoventilation.

None of these children has the Arnold-Chiari malformation, which has previously been the most commonly identified cause of acquired central hypoventilation. Three of these patients had cor pulmonale at the time or presentation, and in each of these cases, the progression of symptoms had apparently occurred over the course of some years. As in the case of childhood obstructive sleep apnoea, it is likely that there is individual variability in the level of pulmonary vascular reactivity and variation in the time course it will take for right heart disease to develop.

The variability of the preceding respiratory problems in these patients was broad. In cases 1, and 3 it is tempting to postulate that the respiratory control disorder has been present lifelong, but this remains speculative. It is possible that these children had mild, but persistent forms of the disorder with progressively compounding effects

of cumulative hypoxia. Alternatively, a second factor was required to produce a critical level of respiratory control failure. The frequency at which medications, usually anaesthetics, have led to critical hypoventilation suggests that this combined effect is important clinically, but the functional effect remains unknown at this time. Since imipramine is used frequently, without deleterious respiratory effects, even Case five would support this notion.

Where there has been prolonged follow up underlying causes have progressively emerged, highlighting the importance of continued vigilance when managing such individuals. In two cases (four and eight) it has taken more than six years, for this underlying pathology to declare itself in any other form than central hypoventilation. This supports the previously reported opinion that acquired central hypoventilation is associated with a high incidence of demonstrable underlying pathology on the MRI scan (149). These cases suggest that this notion is correct, but should be broadened. Pathologies other than those confined to the central nervous system may present in this form.

Two of these cases (two and three) and have presented acutely at the time of a general anaesthetic with failure to recover normal ventilation, even in the awake state, while intubated. Their recovery of normal ventilation in the awake state has repeatedly demonstrated the marked negative impact of an endotracheal tube in these individuals. Presumably inhibitory laryngeal reflexes are not able to be overcome in the absence of adequate chemoreceptor control. Without this knowledge, the period

of intubation may be so prolonged that secondary complications of subglottic stenosis can occur. Extubation in an individual with CO_2 levels of 60 to 70 mmHg when breathing spontaneously may seem heroic, but our access to nasal mask ventilation has certainly avoided the need for tracheostomy in three of these children. Case 4 demonstrates the need for follow-up investigations where such respiratory depression occurs, especially when there is apparent recovery.

These two children (case two and three) also had respiratory arrests following administration of oxygen when hypoxia was demonstrated. With the now ubiquitous use of oxygen saturation monitors it is imperative that medical staff become aware that depression of hypoxic respiratory drive can occur in the paediatric population. CO_2 monitoring, arterial blood gases, or more conservative use of oxygen would help to identify such children, and avoid recurrences of such events.

Six of these individuals have been established successfully on nocturnal nasal mask ventilation. All of the children have been introduced to this therapy from the time of presentation. The older adults presented prior to our regular use of this therapy, but have been subsequently successfully transferred. This has meant that none of these children has required a tracheostomy to in order to be ventilated. This is of great psychosocial benefit to these children, who are then able to attend daytime activities without the need for special care, allowing better integration into normal life. In case one this meant that the child's parents were able to withhold the information regarding his need for ventilatory support from his school. Because of the potential

danger of any period of loss of consciousness in this child the school administration has been fully informed of that child's needs.

One peculiar advantage of nasal ventilation has been that none of these individuals have ever had an upper respiratory tract infection causing nasal obstruction which could prohibit the use of this ventilatory support. Although there has been concern that this would cause significant management problems there has been no incident either in any of these children, or in the adult population treated with mask ventilation. The presence of an intranasal foreign body did interrupt ventilation in one child. This complication is almost certainly confined to the paediatric population!

All of these individuals are ventilated in their home environment, and in all cases this was possible within one month of establishing night time nasal ventilation. This has shortened the duration of the initial hospital admission. Young children do need close supervision however, and night time nursing support has still been required in most cases.

Some of the difficulties we have encountered with nasal ventilation in children are listed in Table 2. They include effects of the mask and ventilator and difficulties relating to the use of a portable ventilator in the home setting, particularly in children.

Volume cycle ventilation has been most effective in these cases, as it allows for the variation in muscle tone which occurs in different sleep states. To date the alarms which are incorporated into the ventilator itself have been adequate to alert to any ventilatory faults. The usual mode of ventilation has been assist-control. SIMV has had limited success, but was unsuccessful in one child who developed marked hypocapnia during REM sleep through hyperventilation on SIMV. We have used the ventilators inherent alarm system, but the need for monitoring in the home in association with this treatment is still debated. There is a fine balance between the need for close respiratory control, and the need to minimise technology in the home and encourage a normal lifestyle.

Most families have developed an astute awareness of the nuances of ventilation in their children. In combination with this parental supervision, regular overnight sleep studies have meant that none of these individuals has right ventricular hypertrophy. Each of the families that we have dealt with has had a unique response to their child's illness and the treatment required. All have seen nasal ventilation as a marked advantage over tracheostomy.

None of these cases have shown sufficient improvement to allow cessation of nocturnal ventilation once it was commenced. The families have been counselled that this is a very rare disorder, but there are none who have recovered sufficiently to discontinue nocturnal ventilation. In all cases where deterioration has occurred an underlying pathology has been identified. While two of these individuals were not

ventilated, their mild hypoventilation has persisted on subsequent studies. While medication may underlay the disorder in case 5, his mother is not prepared to stop treatment with imipramine because of the effects on daytime behaviour associated with this.

The initial treatment period is critical, as during this time, all of these individuals have had very depressed arousal responses. With regular adequate ventilation, the arousal responses have recovered in all cases. This process has consistently taken a period of several months. It is possible that a relationship exists before the integration of ventilation and arousal (Marcus 86). Alternatively the depressed arousal is the primary abnormality, but the fact that this response can show recovery does not support this. In obstructive sleep apnoea, sleep fragmentation has been demonstrated to depress arousal responses, and it is likely that this is the primary mechanism in cases with acquired central hypoventilation as well. In those cases where they have been measured, children have shown recovery of hypoxic responses which may well be a similar effect. Repeated exposure to hypoxia has been shown to blunt the hypoxic responses of young animals (Fewell 37). Tolerance of CO_2 variability may show some limited recovery. Implicit in the statement that the disorder does not resolve, this response does not recover to normal in these individuals. The mechanism is more likely to be a failure of carotid body interaction in the arousal (Grunstein 48).

While it is possible that the younger children here have mild central hypoventilation, the remainder appear to have truly acquired failure of respiratory drive. The pathology in these cases has been well documented now. Three cases fit into the picture of failure of respiratory drive rather than normal drive with end organ insufficiency.

Table 1. Summary Features of Seven Cases of Central Hypoventilation.

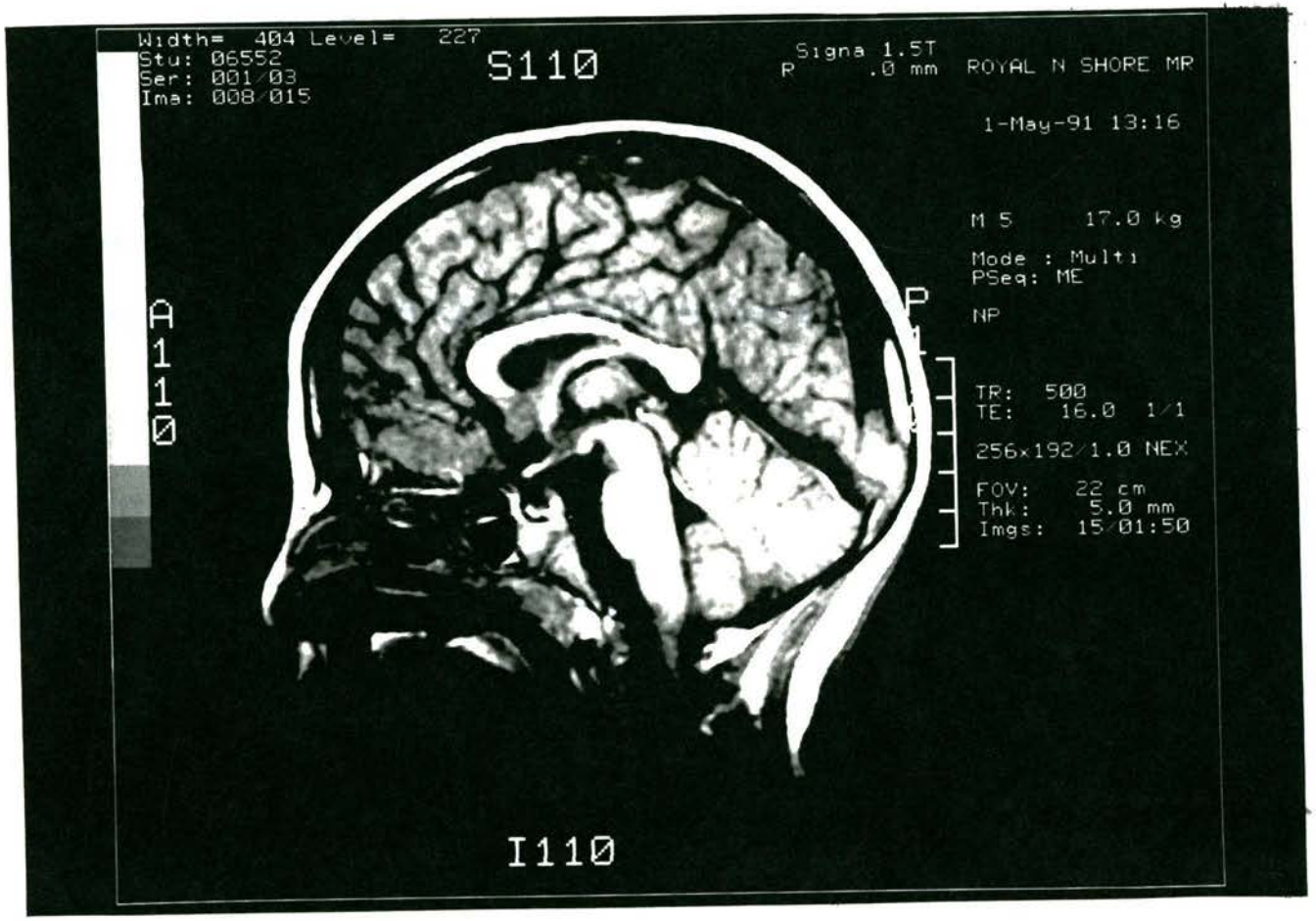
Subject (DOB)	Age (date) at presentation	Sex	Presentation	Ventilated (duration)	CO_2range (mmHg)	SaO_2 range(%)	Pathology
KM (27.11.91)	16 mths (16.3.93)	F	Cyanotic episodes	Y (3 months)	43-79	82-100	Pertussis
TG (30.8.85)	5 years 7 months (15.4.91)	M	Obstructive apnoea, respiratory arrest after O2	Y (26 months)	34-65	65-98	EBV
KC (24.7.86)	5 years 9 months (19.5.92)	F	Nocturnal seizure, anaesthetic complications	Y (13 months)	40-82	60-95	Perinatal asphyxia
EKB (12.6.79)	6 years 1 month (31.7.85)	F	Asthma, respiratory failure	Y (7.9 years)	51-75	70-99	Brainstem tumour
JK (28.2.83)	9 years 3 months (3.6.92)	M	Obstructive apnoea	N	38-54	85-100	Imipramine
TG (29.4.82)	9 years 10 months (12.3.92)	F	Head injury	N	42-58	90-100	Trauma
KL (28.6.65)	14 years 5 months (14.12.79)	F	Respiratory failure	Y (9.5 years)	48-110	0-94	EBV
JR (15.12.43)	38 years 8 months (9.9.82)	M	Cardio-respiratory failure	Y (10.8 years)	65-95	61-94	Myopathy

Table 2.

Problems associated with the use of nasal mask ventilation of children in the home environment.

Problems relating to the effects of the ventilator /tion	Problems relating to family management
-pressure effects of the mask -hyperventilation - solution has been increased initial rate (slow wave sleep), with reduction when parents go to bed. -mask leaks -prongs and loss of the nasal cushions used with nasal prongs (into the circuit) -nasal foreign body causing purulent discharge and smelly circuit which took a long time to identify - synchronised intermittent mandatory ventilation (SIMV) inspiratory sensitivity is very critical and may be associated with hyperventilation, or periodic breathing	-parental fiddling with the ventilator settings - use of "nights off" as rewards -high pressure alarms / disabling these because they are seen as "nuisance" alarms. -initial behavioural improvement in case three was not sustained -behaviour problems of difficult children in adapting to mask ventilation -need for intermittent nursing respite mainly because of behaviour / age - relative ease with which children can avoid or disconnect the ventilation with this method

Figure 1. MRI scan of TG at presentation. There are two lucent areas at the level of the medulla, one on the anterior aspect, and one on the posterior aspect. These are marked with arrows.


Width= 404 Level= 227
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Ser: 001/03
Ima: 008/015
S110
Signa 1.5T
P .0 mm ROYAL N SHORE MR
1-May-91 13:16
M 5 17.0 kg
Mode : Multi
PSeq: ME
NP
TR: 500
TE: 16.0 1/1
256x192/1.0 NEX
FOV: 22 cm
Thk: 5.0 mm
Imgs: 15/01:50
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Figure 2a. Oxygen saturation (SaO_2) and transcutaneous carbon dioxide ($TcCO_2$) trace of Case2 (TG).

After one week of ventilation

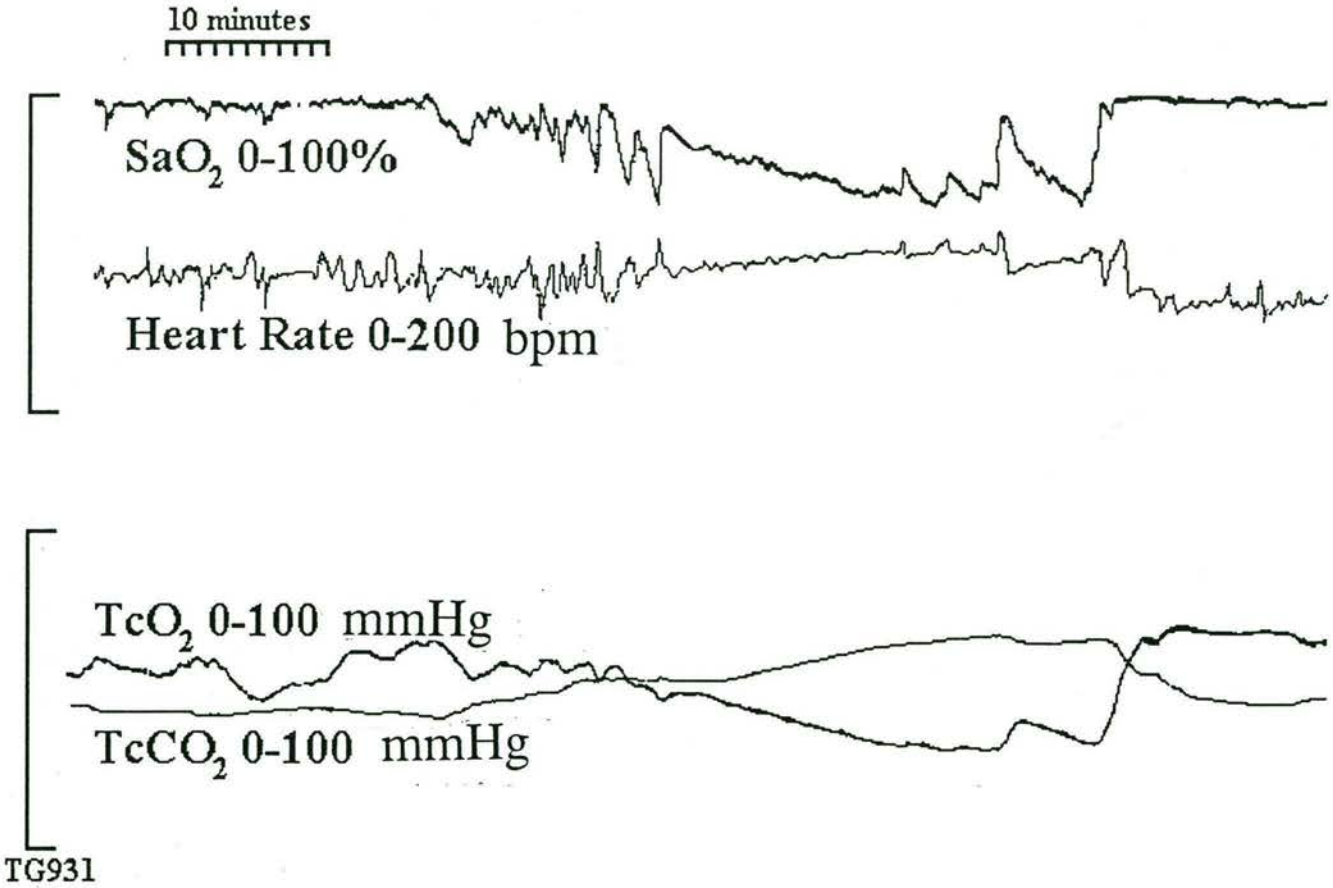
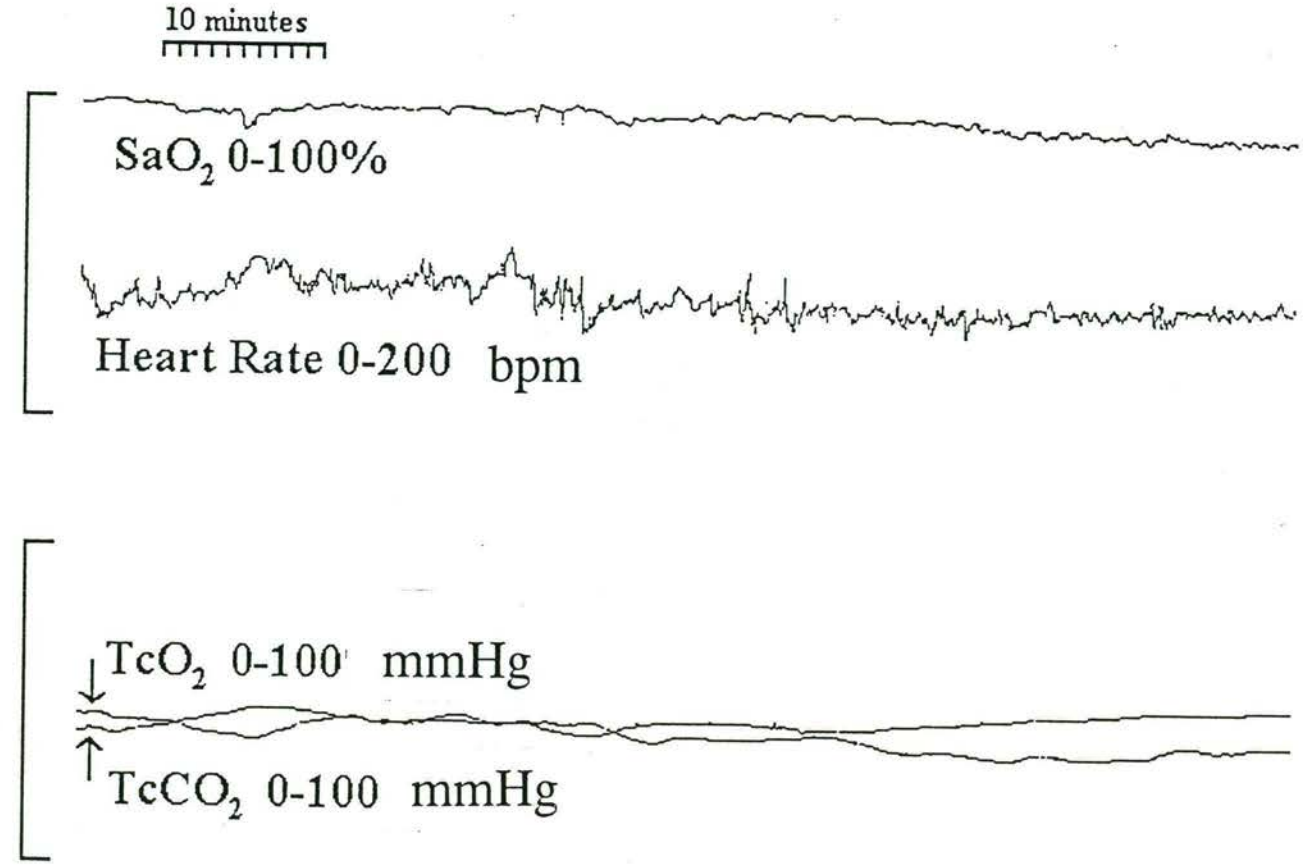

10 minutes
SaO2 0-100%
Heart Rate 0-200 bpm
TcO2 0-100 mmHg
TcCO2 0-100 mmHg
TG931

Figure 2b. Oxygen saturation (SaO_2) and transcutaneous carbon dioxide ($TcCO_2$) trace of Case2 (TG).

After relative hyperventilation

Figure 2c. Oxygen saturation (SaO_2) and transcutaneous carbon dioxide ($TcCO_2$) trace of Case2 (TG).

After ventilation to normal CO2 levels.

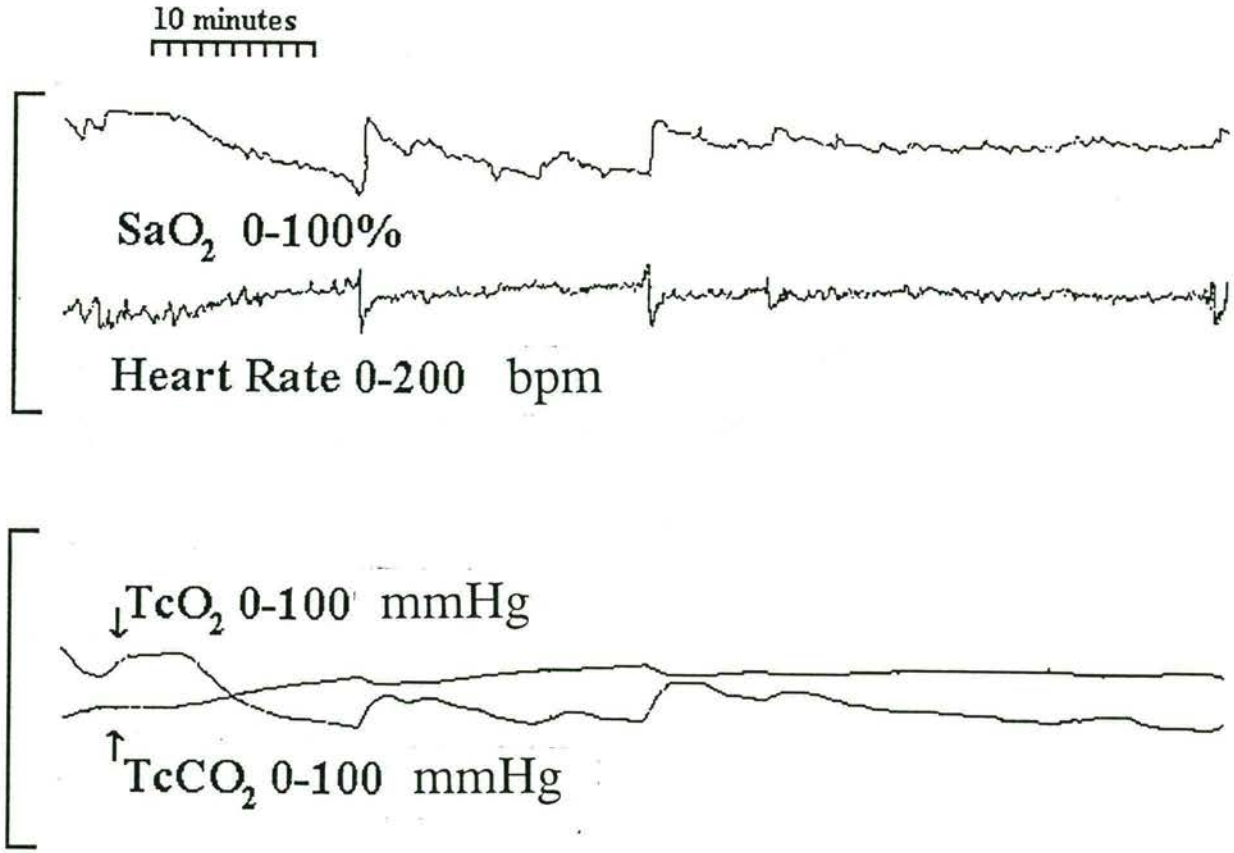

10 minutes
SaO2 0-100%
Heart Rate 0-200 bpm
TcO2 0-100 mmHg
TcCO2 0-100 mmHg

TG922

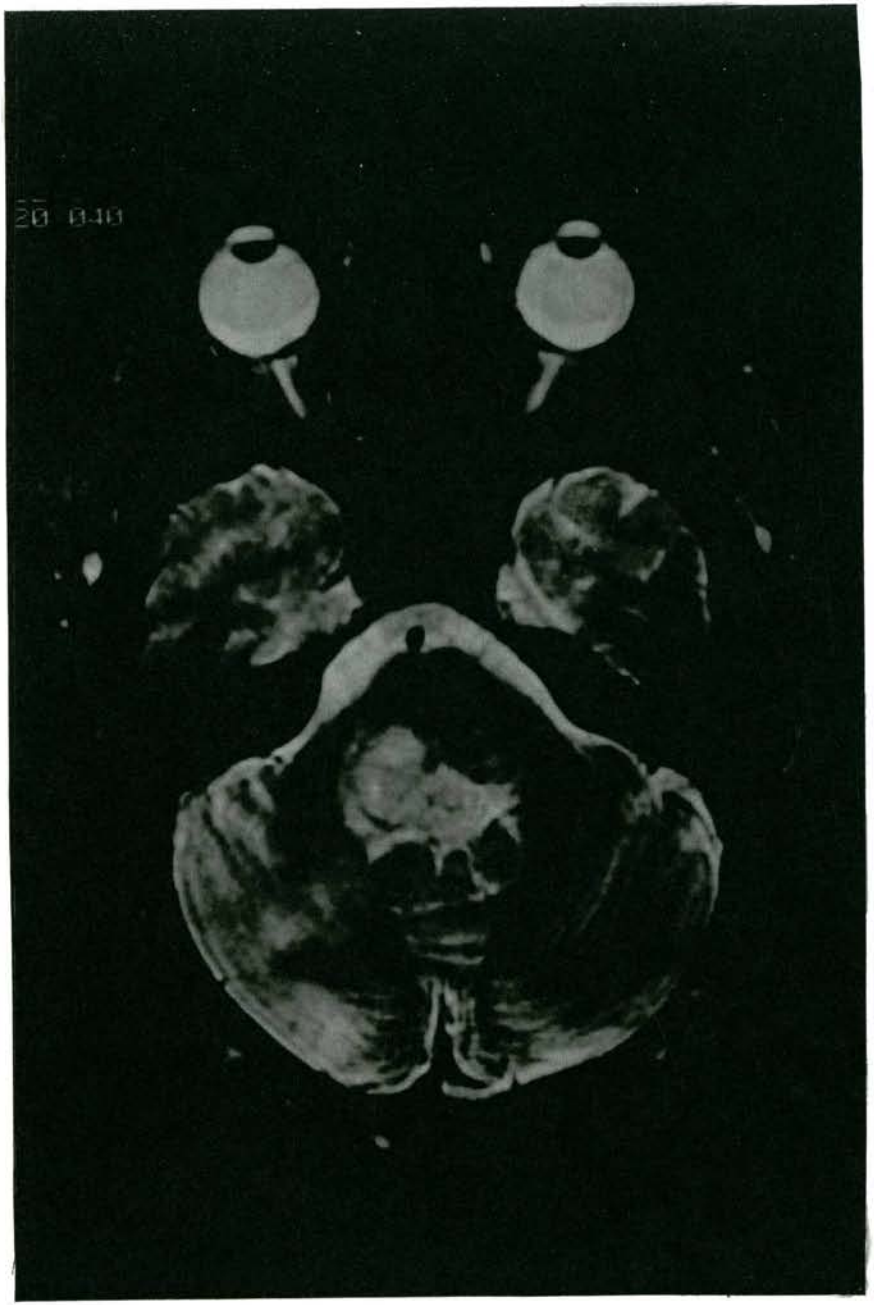
Figure 3.

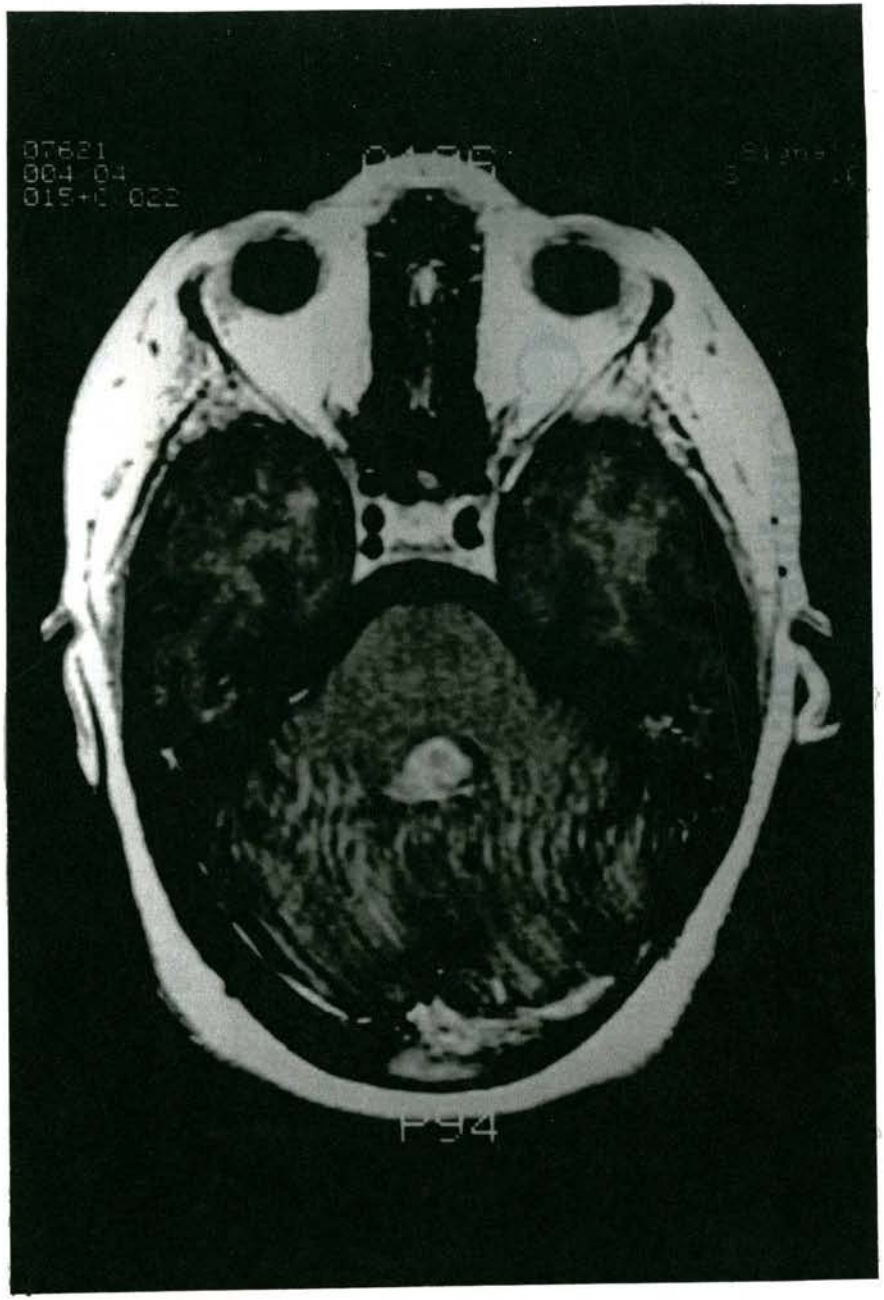
a). The MRI scan of patient EKB showing a brainstem tumour.

b). The CT scan at the time of first presentation. No brainstem architecture could be seen because of the scatter associated with CT scanning of the posterior fossa.


10 minutes
SaO2 0-100%
Heart Rate 0-200 bpm
↓TcO2 0-100 mmHg
↑TcCO2 0-100 mmHg

TG921

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P94

Chapter 10.

Conclusion

10 CONCLUSION

Sleep disordered breathing occurs commonly in children.

There is a male predominance in those children with sleep disordered breathing

There is a male predominance in those children who require treatment for sleep disordered breathing.

Adenotonsillectomy results in improvement, but not resolution of obstructive sleep apnoea in children.

Nasal CPAP is a practical and effective treatment option for children with OSA.

There is an increase in the proportion of SWS and a decrease in the proportion of stages one and two sleep in children, compared to their diagnostic studies, after effective treatment of OSA.

There is no change in the proportion of REM sleep in children with OSA after treatment.

Sleep disordered breathing is common in children with spina bifida who have a history of bulbar dysfunction.

Nasal mask CPAP can be used effectively to treat upper airway obstruction in infants and children with spina bifida and sleep disordered breathing.

Children who present with acquired central hypoventilation can be treated effectively with nasal mask ventilation.

Acquired central hypoventilation is commonly associated with an identifiable underlying pathology.

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Appendices I

APPENDICES I

a. SLEEP DISORDERED BREATHING IN CHILDREN

Sex	DOB	Study	HT	WT	HC	Studs	Diagnoses
F	12-Jun-1979	14-Aug-1987	?????	?????	?????	1	C HYPOVENT
?	13-Dec-1975	17-Aug-1987	?????	?????	?????	1	FITS
?	30-Aug-1974	24-Sep-1987	?????	?????	?????	1	OSA, CPAP
M	22-Aug-1986	21-Jan-1989	?????	?????	?????	1	APNEA
M	16-Jul-1987	01-Mar-1989	81.50	13.80	?????	1	FOETAL DILAN, OSA
F	18-Feb-1986	01-Mar-1989	80.50	11.00	?????	1	ACHONDROPLAS, OSA
M	22-Jun-1985	07-Mar-1989	100.0	15.50	?????	1	C HYPOVENT
F	02-Jan-1975	30-Mar-1989	?????	?????	?????	1	EDS, KLEIN LEVIN
F	23-Apr-1987	10-May-1989	80.00	12.10	?????	1	CONG VARICEL, CP
M	15-Oct-1974	16-May-1989	176.0	57.00	?????	1	SLEEP WALK, PARASOMNIA
M	10-Mar-1985	05-Jun-1989	103.0	17.50	?????	1	C HYPOVENT
M	16-Jul-1987	16-Jun-1989	88.00	15.00	?????	2	FOETAL DILAN, OSA
M	08-Feb-1984	29-Jun-1989	135.0	47.00	?????	1	GIGANTISM, OSA
M	10-Jan-1980	03-Jul-1989	128.0	25.00	?????	1	C HYPOVENT
?	25-Jun-1977	18-Jul-1989	?????	?????	?????	1	OSA
F	03-Dec-1987	03-Oct-1989	85.00	11.50	?????	1	APNEA
M	22-Aug-1986	03-Oct-1989	97.00	16.00	?????	2	APNEA
M	10-Mar-1985	09-Oct-1989	115.0	18.50	?????	3	C HYPOVENT, VENTILATED
M	16-Jul-1987	18-Oct-1989	87.00	16.50	?????	1	?
M	07-Dec-1974	23-Oct-1989	157.0	44.00	?????	1	NARCOLEPSY, EDS
F	28-Apr-1981	07-Nov-1989	128.0	42.00	?????	1	EDS
F	03-Aug-1975	10-Nov-1989	154.0	39.00	?????	1	CF
F	25-Feb-1984	08-Dec-1989	106.0	19.00	?????	2	OSA
F	03-Dec-1987	18-Dec-1989	87.50	13.50	?????	3	APNEA
M	22-Aug-1986	18-Dec-1989	98.00	16.00	?????	1	APNEA
M	13-May-1985	19-Dec-1989	99.00	15.00	?????	1	OSA, T&A
M	03-Sep-1974	11-Jan-1990	165.0	102.5	?????	1	OSA
M	01-Feb-1990	12-Feb-1990	?????	?????	?????	1	ACHONDROPLAS
M	14-Dec-1976	12-Feb-1990	113.3	36.50	?????	1	ACHONDROPLAS, OSA, DYSMORPHIC
F	15-Nov-1977	14-Feb-1990	121.5	42.00	?????	1	CYCLIC VOMIT, OSA
F	06-May-1989	16-Feb-1990	89.00	6.500	?????	4	APNEA, CYANOTIC APN, CPAP
M	16-Jul-1987	19-Feb-1990	?????	?????	?????	1	FOETAL DILAN, OSA
M	14-Jan-1976	20-Feb-1990	163.0	51.00	?????	1	HEAD BANG, PARASOMNIA
M	26-Aug-1987	01-Mar-1990	89.00	12.00	?????	1	OSA
M	20-Aug-1978	12-Mar-1990	133.0	32.00	?????	1	NARCOLEPSY, CATAPLEXY
M	16-Jun-1987	12-Mar-1990	80.00	14.75	?????	1	ACHONDROPLAS, OSA
F	13-Dec-1979	19-Mar-1990	104.0	22.00	?????	1	ACHONDROPLAS, OSA
M	31-Jan-1989	26-Mar-1990	65.00	7.300	?????	1	VSD, OSA
F	08-Jul-1986	28-Mar-1990	?????	?????	?????	1	OSA
F	16-Feb-1990	30-Mar-1990	?????	?????	?????	1	ARSIDS, SIBLING, TWIN
M	01-Feb-1990	04-Apr-1990	50.00	4.500	40.50	2	ACHONDROPLAS
F	15-Nov-1977	19-Apr-1990	123.0	42.75	?????	2	OSA, CPAP
F	03-Dec-1979	23-Apr-1990	145.0	52.00	?????	1	ASTHMA, OSA, EDS
M	25-Sep-1985	26-Apr-1990	121.0	51.00	?????	1	POST T&A, OSA, OBESE
F	18-Feb-1986	01-May-1990	86.50	14.00	?????	2	ACHONDROPLAS, OSA
F	04-Feb-1987	04-May-1990	86.00	42.00	?????	1	OBESE, OSA

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	06-Sep-1987	07-May-1990	92.00	18.00	?????	1	ACHONDROPLAS, OSA
F	28-Nov-1976	07-May-1990	125.0	56.00	?????	1	ACHONDROPLAS, OSA
M	19-Jan-1985	08-May-1990	122.0	23.50	?????	1	OSA
F	16-Feb-1990	09-May-1990	?????	5.330	?????	2	ARSIDS, SIBLING, APNEA
M	16-Jul-1987	09-May-1990	91.00	19.00	?????	5	FOETAL DILAN, OSA, CPAP
M	10-Mar-1978	10-May-1990	?????	?????	?????	1	C HYPOVENT
M	06-Nov-1984	11-May-1990	?????	?????	?????	1	OSA, VC PARESIS
M	08-Feb-1984	14-May-1990	140.0	52.00	?????	2	SOTOS, OSA
M	02-Jun-1975	15-May-1990	?????	?????	?????	1	DIDMOA, C HYPOVENT, VENTILATED
M	02-Jun-1975	16-May-1990	?????	?????	?????	2	DIDMOA, C HYPOVENT, CPAP
F	15-Nov-1977	12-Jun-1990	?????	?????	?????	3	OSA, DAY
M	31-Jan-1989	15-Jun-1990	?????	?????	?????	2	VSD, PULMNRY H/T, OSA
M	26-Jun-1983	15-Jun-1990	109.0	18.50	?????	1	C HYPOVENT
M	26-Jun-1983	19-Jun-1990	109.0	18.50	?????	2	C HYPOVENT, NIPPV
M	23-Jul-1988	20-Jun-1990	89.50	14.00	?????	1	ASTHMA, AC OBSTRUCTI
M	25-Sep-1985	21-Jun-1990	123.0	46.00	?????	2	OSA, POST T&A, OBESE
M	01-Feb-1990	26-Jun-1990	?????	?????	?????	3	ACHONDROPLAS, PNEUMONIA
M	30-Jul-1982	26-Jun-1990	129.0	32.00	?????	1	OSA
M	21-Feb-1990	02-Jul-1990	?????	?????	?????	1	ARSIDS, FHX, ALTE, OSA
F	30-Oct-1986	09-Jul-1990	102.0	16.00	?????	1	OSA, T&A
M	14-Dec-1976	09-Jul-1990	117.0	36.50	?????	2	ACHONDROPLAS, OSA
M	26-Aug-1985	11-Jul-1990	115.0	25.00	?????	1	OSA, T&A
F	12-Jun-1979	12-Jul-1990	141.5	53.00	?????	2	C HYPOVENT, ASTHMA
M	13-Dec-1987	18-Jul-1990	83.00	10.00	?????	1	CP, APNEA, NIGHT WAKING
F	16-May-1986	24-Jul-1990	110.0	19.50	?????	1	APNEA, ASTHMA, ATOPIC
M	07-Jul-1976	25-Jul-1990	182.0	104.0	?????	1	FITS, COMPLEX PART, REM FITS
M	26-Apr-1984	30-Jul-1990	92.00	17.00	?????	1	ACHONDROPLAS, OSA, T&A
M	11-Feb-1986	01-Aug-1990	108.5	28.70	?????	1	NORMAL, OSA
F	12-Jun-1976	09-Aug-1990	?????	?????	?????	1	NEUROMUSC, RESP FAILURE
M	30-Jul-1989	13-Aug-1990	80.00	12.00	?????	1	OSA, T&A
M	11-Apr-1982	13-Aug-1990	90.00	18.00	?????	1	ACHONDROPLAS, OSA
F	16-Feb-1990	15-Aug-1990	?????	?????	?????	3	ARSIDS, SIBLING
F	12-Jun-1979	16-Aug-1990	141.0	52.50	?????	3	C HYPOVENT, NIPPV
F	03-Sep-1987	20-Aug-1990	105.0	18.00	?????	1	OSA
F	02-Aug-1990	22-Aug-1990	?????	?????	?????	1	SNIFFS, APNEA
M	22-Oct-1987	23-Aug-1990	92.00	14.00	?????	1	CRI DU CHAT, DYSMORPHIC, OSA, TRACHEOSTOMY
M	01-Feb-1990	27-Aug-1990	89.00	5.000	?????	4	ACHONDROPLAS, APNEA
M	16-Jul-1987	27-Aug-1990	97.00	18.50	?????	6	FOETAL DILAN, OSA, CPAP
F	12-Jun-1976	29-Aug-1990	?????	13.00	?????	2	NEUROMUSC, RESP FAILURE, NIPPV
F	05-Feb-1987	03-Sep-1990	104.0	17.00	?????	1	NIGHT TERROR, BREATHOLD, CYANOSIS
F	22-Apr-1986	03-Sep-1990	81.00	13.80	?????	1	ACHONDROPLAS, OSA
M	06-Nov-1984	04-Sep-1990	115.0	17.00	?????	2	VC PARESIS
M	02-Apr-1990	04-Sep-1990	?????	2.920	?????	1	EX-PREM, CNLD
M	21-Jun-1985	10-Sep-1990	83.00	16.00	?????	1	ACHONDROPLAS, OSA, O2
M	02-May-1983	10-Sep-1990	122.5	25.00	?????	1	PSA
M	02-Aug-1990	19-Sep-1990	?????	?????	?????	2	SNIFF, INFANT
M	06-Feb-1985	21-Sep-1990	110.0	19.00	?????	1	POST T&A, OSA
M	26-Dec-1988	08-Oct-1990	83.00	9.500	?????	1	OSA, T&A
F	19-Aug-1984	08-Oct-1990	125.0	39.00	?????	1	OSA, EDS, HEADACHE

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
M	26-Jul-1990	10-Oct-1990	?????	3.360	?????	1	ARSIDS, EXPREM, TWIN, P BREATHING
M	24-May-1987	17-Oct-1990	99.00	14.70	?????	1	OSA, T&A
F	18-Feb-1986	22-Oct-1990	?????	?????	?????	3	ACHONDROPLAS, OSA
M	02-Apr-1990	25-Oct-1990	?????	?????	?????	2	ARSIDS
M	28-Jul-1986	26-Oct-1990	?????	?????	?????	1	CP, FITS
M	26-May-1977	29-Oct-1990	?????	?????	?????	1	FITS
M	04-Jul-1988	30-Oct-1990	?????	?????	?????	1	ACHONDROPLAS, OSA
M	08-Jun-1988	31-Oct-1990	88.00	11.70	?????	1	OSA, T&A
M	17-Feb-1987	02-Nov-1990	97.00	15.00	?????	1	OSA
M	29-Oct-1981	08-Nov-1990	130.0	43.00	?????	1	OSA, PSEUDOHYPOPA, CPAP
F	31-Aug-1988	09-Nov-1990	87.00	13.00	?????	1	OSA
M	20-Jun-1989	13-Nov-1990	76.00	8.800	?????	1	OSA, CPAP, T&A, VSD
M	05-Apr-1989	14-Nov-1990	80.00	9.800	?????	1	OSA, T&A
M	01-Jan-1980	16-Nov-1990	134.0	30.00	?????	1	OSA, POST T&A, ATOPY
F	01-Feb-1980	19-Nov-1990	?????	?????	?????	1	NIGHT TERROR PARASOMNIA
M	17-Dec-1989	19-Nov-1990	?????	7.450	?????	1	OSA, T&A, CPAP
F	06-Aug-1990	22-Nov-1990	?????	4.350	?????	1	DOWNS, OSA, CPAP, TB MALACIA
M	26-Jul-1990	22-Nov-1990	?????	?????	?????	2	ARSIDS, SIBLING, TWIN
F	06-Aug-1990	26-Nov-1990	?????	4.350	?????	2	DOWNS, OSA, CPAP, TB MALACIA
F	30-May-1986	26-Nov-1990	79.00	13.50	?????	1	ACHONDROPLAS, OSA
M	28-Dec-1988	28-Nov-1990	?????	10.50	?????	1	TETRALOGY, CNLD, O2
M	03-Jan-1985	03-Dec-1990	90.00	17.00	?????	1	ACHONDROPLAS, OSA
F	09-Aug-1975	03-Dec-1990	172.0	106.0	?????	1	OSA, EDS
F	24-Dec-1986	05-Dec-1990	108.0	19.00	?????	1	OSA
M	26-Jun-1975	05-Dec-1990	173.0	26.25	?????	2	OSA, MARFANS
F	26-Mar-1982	11-Dec-1990	?????	?????	?????	1	OSA, MPS, CPAP
F	26-Mar-1986	11-Dec-1990	92.00	15.25	?????	1	OSA, HUNTERS
M	25-Aug-1987	12-Dec-1990	88.30	13.00	?????	1	OSA, FOETAL CMV, APNEA
M	03-Jan-1985	13-Dec-1990	?????	12.00	?????	2	ACHONDROPLA, OSA, CPAP
M	28-Dec-1988	13-Dec-1990	?????	10.00	?????	2	TET OF FALLO, CNLD, CPAP, O2
F	14-Jun-1984	17-Dec-1990	116.0	19.00	?????	1	OSA
F	06-Aug-1990	18-Dec-1990	55.80	4.800	?????	3	DOWNS, OSA, CPAP, TB MALACIA
?	03-Aug-1984	19-Dec-1990	?????	?????	?????	1	OSA
M	06-Apr-1986	04-Jan-1991	108.5	19.00	?????	1	OSA
F	11-Mar-1976	07-Jan-1991	148.5	75.50	?????	1	OBESE, ASTHMA, OSA
M	06-Apr-1986	09-Jan-1991	?????	?????	?????	2	OSA
F	14-Sep-1988	09-Jan-1991	?????	?????	?????	1	OSA, T&A
M	22-Aug-1986	21-Jan-1991	105.0	18.00	?????	4	APNEA
F	03-Dec-1987	21-Jan-1991	98.00	15.50	?????	3	APNEA
M	17-Oct-1983	22-Jan-1991	117.0	23.00	?????	1	EDS, PARASOMNIA
M	01-Feb-1990	24-Jan-1991	?????	?????	?????	5	ACHONDROPLAS
M	26-Apr-1984	30-Jan-1991	91.00	15.00	?????	2	ACHONDROPLAS, POST T&A, OSA
F	03-May-1985	07-Feb-1991	123.0	26.00	?????	1	OSA, T&A
M	26-Aug-1990	11-Feb-1991	?????	?????	?????	1	AC OBSTRUCTI
M	21-Mar-1981	18-Feb-1991	129.0	20.00	?????	1	DUCHENNES
F	23-Nov-1986	19-Feb-1991	112.0	18.75	?????	1	OSA
M	28-Dec-1988	20-Feb-1991	81.00	11.00	?????	3	POST T&A, OSA, TET OF FALLO, CNLD
F	03-Mar-1987	27-Feb-1991	77.00	11.20	?????	1	ACHONDROPLAS, OSA

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
M	29-Oct-1981	28-Feb-1991	132.0	43.50	?????	2	OSA, PSEUDOHYPOPA, POST T&A
F	23-Jul-1977	01-Mar-1991	?????	?????	?????	1	OSA, T&A, DYSMORPHIC
M	16-Jul-1987	06-Mar-1991	102.0	19.50	?????	7	FOETAL DILAN, OSA, POST T&A, CPAP
F	13-Feb-1977	06-Mar-1991	153.0	68.00	?????	1	OSA, FHX, OBESE
F	08-Jan-1991	11-Mar-1991	48.60	2.700	?????	1	CNLD, EX-PREM, APNEA
M	26-Oct-1989	13-Mar-1991	75.00	9.500	?????	1	CNLD, O2
F	07-Feb-1987	25-Mar-1991	?????	?????	?????	1	OSA
M	16-Jul-1980	25-Mar-1991	120.0	20.00	?????	1	OSA, CPAP
F	14-Feb-1985	03-Apr-1991	119.0	23.10	?????	1	NIGHT TERROR, PARASOMNIA
M	02-Jun-1975	03-Apr-1991	?????	?????	?????	3	DIDMOA, C HYPOVENT, VENTILATED
M	29-Apr-1976	08-Apr-1991	166.0	61.50	?????	1	EDS, NARCOLEPSY
F	09-Jan-1987	17-Apr-1991	101.0	15.60	?????	1	OSA, T&A
F	14-Mar-1991	22-Apr-1991	?????	?????	?????	1	ARSIDS, TET OF FALLO
M	11-Apr-1982	24-Apr-1991	96.00	19.50	?????	2	ACHONDROPLAS, OSA, POST T&A
M	15-Oct-1976	24-Apr-1991	138.0	41.00	?????	1	CF, OSA, HYPOVENTILAT
M	13-Jun-1990	26-Apr-1991	?????	?????	?????	1	MARFANS, FAMILY HX
F	14-Mar-1991	26-Apr-1991	?????	?????	?????	2	ARSIDS, TET OF FALLO, CPAP
M	06-Nov-1984	26-Apr-1991	115.0	19.50	?????	3	OSA, VC PARESIS, CPAP
M	21-Jul-1989	01-May-1991	71.00	10.40	?????	1	ACHONDROPLAS, OSA
M	07-Mar-1991	02-May-1991	?????	?????	?????	1	ARSIDS, NEAR MISS, APNEA
F	14-Mar-1991	06-May-1991	?????	?????	?????	3	ARSIDS, TET OF FALLO, CPAP
M	07-Mar-1989	08-May-1991	94.00	13.90	?????	1	OSA, T&A
F	02-Jul-1990	12-May-1991	?????	?????	?????	1	OSA
M	29-Mar-1985	13-May-1991	?????	?????	?????	1	OSA
M	26-Jun-1975	14-May-1991	?????	?????	?????	1	OSA, CPAP
M	29-Mar-1985	15-May-1991	?????	?????	?????	2	OSA, CPAP
F	08-Nov-1987	16-May-1991	?????	?????	?????	1	OSA, T&A
F	28-May-1983	20-May-1991	?????	?????	?????	1	OSA
M	16-Jul-1987	22-May-1991	?????	?????	?????	8	OSA, FOETAL DILAN, CPAP
M	10-Jan-1980	28-May-1991	?????	?????	?????	2	C HYPOVENT, TRACHEOSTOMY
?	13-Mar-1989	29-May-1991	?????	?????	?????	1	APNEA, DISORGANISED
F	25-Oct-1990	30-May-1991	?????	?????	?????	1	OSA
M	14-Jul-1990	03-Jun-1991	?????	?????	?????	1	OSA, T/B MALACIA
?	27-Sep-1975	04-Jun-1991	?????	?????	?????	1	OSA
F	03-Mar-1987	05-Jun-1991	?????	?????	?????	2	ACHONDROPLAS, OSA
M	30-Aug-1985	06-Jun-1991	?????	?????	?????	1	VENTILATED, C HYPOVENT
M	31-Jan-1989	19-Jun-1991	?????	?????	?????	3	CNLD
M	03-Jan-1985	19-Jun-1991	?????	?????	?????	3	ACHONDROPLAS, OSA, CPAP
?	11-Jun-1990	24-Jun-1991	?????	?????	?????	1	OSA
M	04-Jul-1988	26-Jun-1991	?????	?????	?????	2	ACHONDROPLAS, OSA, POST T&A
F	09-Feb-1981	28-Jun-1991	?????	?????	?????	1	ACHONDROPLAS
?	09-Jun-1991	01-Jul-1991	?????	?????	?????	1	ARSIDS, APNEA
?	02-Feb-1977	02-Jul-1991	?????	?????	?????	1	OSA
M	14-Jul-1990	05-Jul-1991	?????	?????	?????	2	OSA, T/B MALACIA, CPAP
M	30-Aug-1985	09-Jul-1991	?????	?????	?????	2	C HYPOVENT, VENTILATED
F	12-Jun-1979	17-Jul-1991	?????	?????	?????	4	C HYPOVENT
M	28-Dec-1988	17-Jul-1991	?????	?????	?????	4	CNLD, TETRALOGY
M	10-Mar-1985	18-Jul-1991	?????	?????	?????	3	C HYPOVENT, VENTILATED

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
?	05-Mar-1988	23-Jul-1991	?????	?????	?????	1	OSA, OBESE
F	06-Aug-1990	24-Jul-1991	?????	?????	?????	4	DOWNS, OSA
F	12-Jun-1979	26-Jul-1991	?????	?????	?????	5	C HYPOVENT
F	26-Oct-1990	30-Jul-1991	?????	?????	?????	1	APNEA
?	29-Jun-1989	13-Aug-1991	?????	?????	?????	1	OSA
M	03-Jul-1978	13-Aug-1991	?????	?????	?????	1	MARFANS, CPAP, OSA
?	01-Oct-1990	21-Aug-1991	?????	?????	?????	1	NIGHT TERROR
?	19-Sep-1979	27-Aug-1991	?????	?????	?????	1	OSA, OBESE
F	31-Oct-1990	28-Aug-1991	?????	?????	?????	1	APNEA
F	10-Jul-1985	30-Aug-1991	?????	?????	?????	1	OSA
M	27-Aug-1991	03-Sep-1991	?????	?????	?????	1	ARSIDS, APNEA
?	16-Mar-1990	10-Sep-1991	?????	?????	?????	1	CENTRAL APNEA
M	27-Aug-1991	17-Sep-1991	?????	?????	?????	2	ARSIDS, APNEA
M	09-Jun-1988	02-Oct-1991	?????	?????	?????	1	ACHONDROPLAS, OSA
M	19-Jul-1991	08-Oct-1991	?????	?????	?????	1	APNEA
M	08-Sep-1987	09-Oct-1991	?????	?????	?????	1	OSA
M	10-Aug-1979	14-Oct-1991	?????	?????	?????	1	OSA, OBESE
M	28-Feb-1983	16-Oct-1991	?????	?????	?????	1	APNEA, OSA, BIGEMINY
?	01-Feb-1976	18-Oct-1991	?????	?????	?????	1	OSA, T&A
M	27-Aug-1991	29-Oct-1991	?????	?????	?????	3	ARSIDS, APNEA
M	10-Aug-1979	31-Oct-1991	?????	76.00	?????	2	OSA
M	26-Oct-1989	06-Nov-1991	?????	?????	?????	2	CNLD
F	21-Nov-1980	07-Nov-1991	153.0	43.00	?????	1	NARCOLEPSY, EDS
M	19-Sep-1988	07-Nov-1991	97.80	12.34	?????	1	OSA
?	03-Sep-1977	08-Nov-1991	?????	?????	?????	1	OSA
M	30-Aug-1985	11-Nov-1991	?????	?????	?????	3	C HYPOVENT,VENTILATED
F	26-Apr-1991	13-Nov-1991	?????	?????	?????	1	TRISOMY 18, PIERRE ROBIN, OSA
F	03-Mar-1987	13-Nov-1991	?????	?????	?????	3	ACHONDROPLAS, OSA
M	27-Aug-1991	14-Nov-1991	59.00	5.350	?????	4	ARSIDS
?	25-Nov-1989	18-Nov-1991	?????	?????	?????	1	STRIDOR, LARYNGOMALAC
M	25-Jun-1991	26-Nov-1991	68.00	7.895	?????	1	TRIGEMINAL
M	21-Jul-1989	27-Nov-1991	?????	?????	?????	2	ACHONDROPLAS
M	27-Aug-1991	27-Nov-1991	59.00	5.350	?????	5	ARSIDS
F	26-Mar-1990	27-Nov-1991	?????	?????	?????	1	OSA, T&A
M	27-Aug-1991	28-Nov-1991	59.00	5.350	?????	6	ARSIDS
M	26-Jan-1990	28-Nov-1991	?????	?????	?????	1	OSA, T&A
M	11-Mar-1978	28-Nov-1991	?????	?????	?????	1	CLEFT, PRE-ANAESTHE
M	27-Aug-1991	02-Dec-1991	?????	?????	?????	7	ARSIDS
M	07-May-1990	02-Dec-1991	?????	11.95	?????	1	OSA
M	27-Aug-1991	03-Dec-1991	?????	?????	?????	8	ARSIDS
M	23-Oct-1990	03-Dec-1991	?????	?????	?????	1	OSA, T&A
M	27-Aug-1991	05-Dec-1991	?????	?????	?????	9	ARSIDS
F	31-Oct-1983	05-Dec-1991	?????	?????	?????	1	HUNTERS
M	30-Sep-1991	10-Dec-1991	?????	?????	?????	1	C HYPOVENT
M	27-Aug-1991	10-Dec-1991	?????	?????	?????	10	ARSIDS
M	10-Aug-1979	11-Dec-1991	?????	?????	?????	3	OSA
M	03-Jul-1991	11-Dec-1991	?????	?????	?????	1	OSA, BREATHOLD
M	03-Jul-1991	12-Dec-1991	?????	?????	?????	2	OSA, BREATHOLD,CPAP
F	11-Apr-1988	12-Dec-1991	?????	?????	?????	1	OSA, T&A
M	27-Aug-1991	16-Dec-1991	60.70	?????	?????	11	ARSIDS
M	03-Nov-1980	16-Dec-1991	149.0	41.50	?????	1	OSA
M	27-Aug-1991	17-Dec-1991	?????	?????	?????	12	ARSIDS
M	09-Jun-1988	17-Dec-1991	?????	?????	?????	2	OSA, ACHONDROPLAS
M	22-Jan-1988	18-Dec-1991	100.0	15.20	?????	1	OSA

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
?	07-Jun-1978	08-Jan-1992	?????	?????	?????	1	POOR STUDY
?	07-Jun-1978	09-Jan-1992	?????	?????	?????	2	OSA
M	14-Aug-1990	15-Jan-1992	?????	?????	?????	1	OSA, ASTHMA
M	27-Aug-1991	16-Jan-1992	?????	?????	?????	13	ARSIDS, APNEA
M	27-Aug-1991	17-Jan-1992	?????	?????	?????	14	ARSIDS, APNEA, CPAP
M	16-Sep-1987	21-Jan-1992	?????	?????	?????	1	OSA, CPAP(1/2)
M	23-Jul-1983	28-Jan-1992	?????	?????	?????	1	MARFANS
F	16-Dec-1985	29-Jan-1992	?????	?????	?????	1	OSA, DYSMORPHIC
M	27-Aug-1991	03-Feb-1992	?????	?????	?????	15	ARSIDS
M	19-Jul-1991	03-Feb-1992	73.00	8.350	45.00	2	ARSIDS, ALTE
F	06-Aug-1990	04-Feb-1992	72.50	9.000	?????	5	OSA, DOWNS, TB MALACIA
M	03-Apr-1977	04-Feb-1992	?????	?????	?????	1	OSA, T&A
M	10-Mar-1990	05-Feb-1992	76.00	9.400	?????	1	CNLD
M	29-Apr-1991	06-Feb-1992	69.00	9.000	?????	1	CNLD
F	06-May-1986	06-Feb-1992	104.0	20.00	?????	1	OSA, DEVEL DELAY
F	27-Jan-1989	10-Feb-1992	85.00	11.00	?????	1	OSA, TURNERS, T&A
F	02-Jul-1990	10-Feb-1992	?????	?????	?????	2	OSA, DOWNS
F	17-Feb-1991	11-Feb-1992	?????	?????	?????	1	ARSIDS
F	06-Aug-1990	11-Feb-1992	72.50	9.000	?????	6	OSA, DOWNS, TB MALACIA
F	18-May-1988	12-Feb-1992	141.0	40.40	55.00	1	OSA, T&A
M	21-Aug-1986	12-Feb-1992	?????	?????	?????	1	OSA
M	29-Apr-1989	13-Feb-1992	?????	13.50	?????	1	OSA, CLEFT
M	27-Aug-1991	02-Mar-1992	?????	8.000	?????	16	ARSIDS
M	07-Feb-1989	02-Mar-1992	92.50	14.50	?????	1	NIGHT TERROR
F	26-Nov-1987	04-Mar-1992	94.00	14.20	48.00	1	OSA, CP, FITS, AC OBSTRUCTION
M	20-Apr-1982	04-Mar-1992	130.0	26.10	55.50	1	OSA, CROUZON
M	13-Jan-1982	05-Mar-1992	?????	27.80	?????	1	OSA, CP
F	26-Oct-1990	05-Mar-1992	?????	?????	?????	2	ARSIDS
M	10-Aug-1979	09-Mar-1992	158.0	63.20	55.00	4	OSA
M	29-May-1990	09-Mar-1992	86.00	12.50	46.50	2	OSA, T&A
F	25-Aug-1983	10-Mar-1992	137.0	35.90	?????	1	OSA, ASTHMA
F	24-Sep-1981	10-Mar-1992	139.0	31.50	?????	1	ARSIDS, OSA
M	27-Dec-1990	11-Mar-1992	78.00	11.90	47.00	1	OSA, POST A
F	26-Nov-1987	11-Mar-1992	94.00	13.75	48.00	2	CP, OSA, CPAP, AC OBSTRUCTION
F	29-Apr-1982	12-Mar-1992	141.0	40.40	55.00	1	C HYPOVENT, VENTILATED
M	17-Jul-1990	12-Mar-1992	70.00	7.520	?????	1	OSA, DOWNS, T&A
M	26-Oct-1989	16-Mar-1992	84.00	10.50	?????	3	OSA, CNLD
M	04-Jul-1988	17-Mar-1992	74.00	12.40	?????	3	OSA, ACHONDROPLAS
F	20-Oct-1982	17-Mar-1992	134.0	45.60	?????	1	OSA, DEVEL DELAY
M	16-Jul-1987	18-Mar-1992	108.0	24.50	?????	9	OSA, FOETAL DILAN
F	22-Oct-1985	18-Mar-1992	129.0	47.10	?????	1	OSA, OBESE, ANATHOSIS N
F	25-Oct-1990	19-Mar-1992	77.00	12.50	?????	2	OSA
F	25-Feb-1981	19-Mar-1992	?????	?????	?????	1	OSA
M	27-Aug-1991	23-Mar-1992	?????	?????	?????	17	ARSIDS
F	26-Sep-1984	23-Mar-1992	?????	22.00	?????	1	OSA, POST T&A
M	27-Aug-1991	24-Mar-1992	?????	?????	?????	18	ARSIDS
F	15-Nov-1977	24-Mar-1992	128.0	52.10	?????	4	OSA
M	21-Jan-1992	25-Mar-1992	57.50	4.400	?????	1	ARSIDS
M	03-Dec-1991	25-Mar-1992	41.80	2.115	?????	1	ARSIDS
F	16-May-1986	26-Mar-1992	116.5	22.90	?????	2	ARSIDS
?	31-May-1979	26-Mar-1992	?????	?????	?????	1	OSA
M	19-Sep-1987	30-Mar-1992	108.0	19.00	?????	1	OSA
F	30-Apr-1986	30-Mar-1992	107.0	19.00	?????	1	NARCOLEPSY, FITS

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
?	09-Jun-1981	30-Mar-1992	?????	?????	?????	1	OSA
F	14-Feb-1992	31-Mar-1992	?????	3.360	?????	1	OSA, DESBUQUOIS
M	25-Jun-1980	31-Mar-1992	139.0	30.60	?????	1	CP, FITS, OSA
M	29-Mar-1985	01-Apr-1992	?????	?????	?????	3	OSA
M	25-Jun-1991	01-Apr-1992	72.00	9.200	?????	2	TRIGEMINAL
M	29-Oct-1981	02-Apr-1992	135.0	51.50	?????	3	PSEUDOHYPOPA, OSA, FITS
F	30-Aug-1986	02-Apr-1992	?????	?????	?????	1	OSA, ASTHMA, T&A
M	27-Aug-1991	07-Apr-1992	69.00	8.500	43.50	19	ARSIDS
F	06-Jan-1988	08-Apr-1992	97.50	15.00	51.00	1	OSA, NEUROFIBROMA
F	12-Feb-1985	08-Apr-1992	121.0	20.70	?????	1	ARSIDS
M	08-Feb-1977	08-Apr-1992	?????	?????	?????	1	?
M	16-May-1983	09-Apr-1992	126.0	23.20	?????	1	CLEFT, TRACHEOSTOMY
M	03-Dec-1991	09-Apr-1992	?????	2.270	35.00	2	CNLD
F	01-Oct-1987	13-Apr-1992	?????	20.00	51.00	1	ARSIDS, NIGHT WAKING
M	09-Oct-1984	13-Apr-1992	128.0	26.50	51.00	1	OSA, T&A
M	02-Aug-1983	14-Apr-1992	132.0	28.50	?????	1	NIGHT TERROR, FITS
F	27-Feb-1991	14-Apr-1992	75.00	11.40	?????	1	ARSIDS
F	07-Jan-1991	15-Apr-1992	?????	?????	?????	1	CNLD
F	12-Oct-1983	15-Apr-1992	134.0	30.00	?????	1	OSA, T&A, OBESE, EDS
M	10-Oct-1984	16-Apr-1992	126.0	27.70	?????	1	OSA, EDS
M	15-Dec-1988	16-Apr-1992	?????	11.00	?????	1	DEVEL DELAY, OSA, FITS
M	08-Jun-1989	21-Apr-1992	101.0	17.00	?????	1	OSA, T&A
M	27-Aug-1991	21-Apr-1992	?????	?????	?????	20	ARSIDS
M	21-Jan-1982	22-Apr-1992	140.0	47.50	54.00	1	OSA, POST T&A
F	16-Dec-1985	22-Apr-1992	115.0	23.50	54.00	2	OSA, APERTS
M	14-Jul-1984	23-Apr-1992	117.0	20.00	?????	1	OSA, T/B MALACIA, ASTHMA
F	03-Apr-1977	23-Apr-1992	?????	?????	?????	2	OSA
M	19-Jun-1984	23-Apr-1992	115.0	22.00	?????	1	PIERRE ROBIN, TRACHEOSTOMY
F	03-Apr-1977	24-Apr-1992	?????	?????	?????	3	OSA, CPAP
M	22-Jun-1985	27-Apr-1992	124.0	23.50	?????	2	FITS, CENTRAL APNEA
M	01-Jul-1989	27-Apr-1992	100.0	16.50	?????	1	DEVEL DELAY, OSA, T&A, FITS
F	17-Sep-1981	28-Apr-1992	149.0	47.70	?????	1	NARCOLEPSY, EDS
M	27-Aug-1991	28-Apr-1992	69.00	8.400	44.00	21	ARSIDS
F	17-Sep-1981	29-Apr-1992	?????	?????	?????	2	NARCOLEPSY, EDS
M	05-Jun-1989	29-Apr-1992	92.50	15.95	?????	1	OSA, ASTHMA
M	30-Aug-1985	29-Apr-1992	121.0	20.80	50.00	4	C HYPOVENT, VENTILATED
F	06-Aug-1990	30-Apr-1992	79.00	9.100	44.00	7	OSA, DOWNS, TB MALACIA
F	20-Aug-1981	04-May-1992	147.0	58.50	56.00	1	OSA
F	23-Apr-1977	04-May-1992	159.0	54.50	?????	1	CF, OSA
?	26-Jun-1976	04-May-1992	?????	?????	?????	1	OSA, AROUSALS
M	05-Apr-1989	05-May-1992	92.70	13.10	?????	2	OSA, T&A
M	05-Jun-1989	06-May-1992	92.50	14.70	?????	2	OSA, ASTHMA
F	20-Aug-1989	06-May-1992	83.00	10.95	48.00	1	SPINA BIFIDA, ARNOLD-CHIAR
M	29-Oct-1981	07-May-1992	136.5	48.50	55.00	4	PSEUDOHYPOPA, OSA, POST T&A
M	11-Oct-1989	07-May-1992	89.00	13.00	49.00	1	OSA, T&A
M	08-Feb-1990	11-May-1992	?????	?????	?????	1	ARSIDS
M	27-Dec-1988	12-May-1992	94.00	14.50	?????	1	OSA, T&A
M	08-Sep-1987	12-May-1992	103.0	18.00	?????	2	OSA, POST T&A
M	29-Mar-1985	13-May-1992	?????	?????	?????	4	OSA
M	27-Aug-1991	13-May-1992	70.50	9.280	?????	22	ARSIDS
M	16-Jun-1981	14-May-1992	146.0	33.50	?????	1	NIGHT TERROR, FITS

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
M	26-Mar-1991	14-May-1992	76.60	12.70	?????	1	OSA
M	21-Sep-1991	18-May-1992	95.00	13.70	?????	1	OSA, T&A
F	02-Aug-1990	18-May-1992	81.50	11.20	?????	1	CNLD
F	24-Jul-1986	19-May-1992	?????	?????	?????	2	C HYPOVENT, FITS, VENTILATED
F	17-Dec-1987	19-May-1992	106.0	15.20	48.00	1	CNLD
M	03-Mar-1991	20-May-1992	74.50	10.70	39.70	1	OSA, T&A
F	13-Oct-1991	20-May-1992	50.50	3.380	39.70	1	CNLD
M	21-Jan-1992	21-May-1992	64.00	5.340	41.00	2	ARSIDS
F	31-Mar-1992	21-May-1992	?????	4.000	38.00	1	CNLD
M	10-Aug-1979	25-May-1992	162.5	56.00	?????	5	OSA
M	05-Dec-1986	25-May-1992	?????	20.50	?????	1	OSA, CARDIAC
F	23-Apr-1977	25-May-1992	?????	?????	?????	2	CF, O2
F	07-Jan-1991	26-May-1992	58.00	4.930	?????	2	CNLD
F	11-Apr-1988	26-May-1992	106.0	19.20	?????	2	OSA
F	13-Oct-1991	26-May-1992	?????	?????	39.00	2	CNLD
F	23-Apr-1977	26-May-1992	?????	?????	?????	3	CF, CPAP
M	03-Jul-1978	26-May-1992	?????	?????	?????	2	MARFANS, OSA
M	14-Jun-1981	27-May-1992	151.5	74.10	?????	1	OSA, OBESE, T&A
M	19-Jul-1984	28-May-1992	132.0	35.40	?????	1	OSA, CLEFT, T&A
F	13-Oct-1991	28-May-1992	?????	?????	39.00	3	CNLD
F	26-Jul-1985	01-Jun-1992	108.0	19.00	42.00	1	OSA, CLEFT
M	12-Jun-1980	01-Jun-1992	?????	?????	57.00	1	OI
M	27-Aug-1991	02-Jun-1992	?????	?????	?????	23	ARSIDS
M	19-Mar-1988	02-Jun-1992	89.50	15.40	48.00	1	OSA, DOWNS
M	03-Jul-1978	02-Jun-1992	?????	?????	?????	3	MARFANS, OSA, CLOSING PRES
M	28-Feb-1983	03-Jun-1992	136.3	33.60	46.00	2	OSA, POST T&A
M	17-Jul-1989	03-Jun-1992	95.00	15.20	53.00	1	ARSIDS
F	30-Oct-1986	04-Jun-1992	104.0	16.50	49.00	1	OSA, T&A, FITS, CP
F	31-Mar-1992	04-Jun-1992	52.00	3.930	38.00	2	CNLD
F	29-Apr-1982	09-Jun-1992	141.2	42.40	?????	2	C HYPOVENT, EDS
F	26-May-1989	09-Jun-1992	92.00	12.50	?????	1	EDS
M	09-Jun-1988	10-Jun-1992	97.00	23.50	?????	3	OSA, ACHONDROPLAS, POST T&A
F	04-Feb-1985	10-Jun-1992	113.0	51.53	?????	1	OSA, TUBER SCLER, T&A
F	20-Sep-1990	11-Jun-1992	68.50	10.20	52.00	1	OSA, ACHONDROPLAS, T&A
F	02-Jun-1991	11-Jun-1992	66.50	9.600	46.00	1	SPINA BIFIDA, PRE-DECOMPRE
F	20-Nov-1980	15-Jun-1992	150.0	42.20	?????	1	EDS
M	12-Mar-1981	15-Jun-1992	140.0	45.80	?????	1	OSA, ASTHMA, T&A
F	16-Oct-1991	18-Jun-1992	58.00	5.030	40.00	1	CNLD
F	26-May-1989	18-Jun-1992	92.00	12.40	48.00	2	EDS
F	14-May-1984	22-Jun-1992	111.0	12.00	44.00	1	OSA, CP, POST T&A, FITS
M	27-Mar-1992	22-Jun-1992	61.00	6.600	42.00	1	RSV
M	27-Mar-1992	23-Jun-1992	61.00	6.600	42.00	2	RSV
F	29-May-1992	23-Jun-1992	?????	?????	37.00	1	ARSIDS
F	16-Dec-1976	24-Jun-1992	146.0	40.80	55.00	1	OSA, CF
F	24-Jul-1986	24-Jun-1992	125.0	31.00	?????	3	C HYPOVENT, FITS, VENTILATED
M	03-Jul-1991	25-Jun-1992	74.00	10.09	47.00	3	OSA, BREATHHOLD, POST T&A
M	09-Sep-1991	25-Jun-1992	71.00	7.000	45.00	1	OSA, BREATHHOLD, POST T&A
F	28-May-1992	29-Jun-1992	55.00	4.800	38.00	1	ARSIDS

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	17-Jan-1991	29-Jun-1992	79.50	11.90	47.50	1	OSA, ASTHMA, ARSIDS
M	21-Nov-1991	30-Jun-1992	62.00	6.000	39.00	1	OSA
M	16-May-1986	30-Jun-1992	124.3	24.30	?????	1	OSA, ASTHMA, T&A
F	17-Jan-1990	01-Jul-1992	?????	?????	?????	1	OSA, BECKWITH, T&A
F	29-May-1992	01-Jul-1992	89.00	14.10	?????	2	ARSIDS
M	04-Jan-1979	02-Jul-1992	179.0	59.00	56.50	1	ASTHMA, ACUTE OBSTRU
M	27-Aug-1991	02-Jul-1992	?????	?????	?????	24	ARSIDS
F	24-Feb-1984	06-Jul-1992	90.00	14.50	45.00	1	SPINA BIFIDA, BULBAR-PALSY, KYPHOSCOLIOS
M	09-Oct-1986	06-Jul-1992	112.0	22.50	56.00	1	OSA
F	31-Aug-1987	07-Jul-1992	107.5	18.50	51.00	1	KYPHOSCOLIOS, T&A
M	04-Mar-1992	07-Jul-1992	54.00	4.400	40.00	1	CNLD, PREM, ALTE
M	05-Apr-1992	08-Jul-1992	60.80	6.000	42.00	1	RSV, POST-INFECTI
M	04-Mar-1992	08-Jul-1992	54.00	4.400	40.00	2	CNLD, PREM, ALTE
M	05-Apr-1992	09-Jul-1992	60.80	6.000	42.00	2	RSV
F	29-May-1992	09-Jul-1992	55.50	3.910	37.50	3	ARSIDS
F	19-May-1985	13-Jul-1992	86.00	16.00	50.00	1	DESBUQUOIS, T&A
F	13-Oct-1989	13-Jul-1992	83.00	12.10	54.00	1	HYPOTONIA, CNLD, STEROIDS
M	30-Aug-1985	14-Jul-1992	123.0	21.50	49.50	5	C HYPOVENT, VENTILATED
M	12-Apr-1992	14-Jul-1992	61.50	6.100	42.00	1	OSA
F	06-Aug-1983	15-Jul-1992	130.0	28.00	51.00	1	OSA, POST T&A
F	17-Dec-1987	15-Jul-1992	108.0	16.10	49.00	2	CNLD, O2, T&A
F	03-May-1986	16-Jul-1992	117.5	26.90	?????	1	OSA, T&A
M	20-Apr-1982	16-Jul-1992	131.5	29.50	56.00	2	OSA, CROUZON
F	31-Mar-1992	20-Jul-1992	56.00	6.140	41.00	3	ARSIDS, OSA
F	14-Dec-1980	20-Jul-1992	149.0	53.70	58.00	1	OSA, EDS
M	27-Dec-1990	21-Jul-1992	85.50	13.00	48.50	2	OSA, ASTHMA, POST T&A
M	27-Mar-1992	21-Jul-1992	64.00	8.000	43.00	3	RSV, F/U
M	14-Jul-1984	22-Jul-1992	115.5	20.00	52.50	2	NOONAN, OSA
F	01-Oct-1989	22-Jul-1992	100.0	14.30	48.00	1	OSA, ALTE
F	25-May-1992	23-Jul-1992	59.00	5.390	39.00	1	ARSIDS
M	16-May-1989	23-Jul-1992	83.50	16.70	53.00	1	SPINA BIFIDA, BULBAR PALSY
F	29-May-1992	27-Jul-1992	56.00	4.380	41.00	4	ALTE, GOR
M	19-Dec-1982	27-Jul-1992	105.0	16.00	51.00	1	FITS
M	09-Sep-1976	27-Jul-1992	166.0	66.30	?????	1	OSA, CENTRAL APNEA
M	10-Oct-1991	28-Jul-1992	62.00	5.050	42.00	1	CNLD, PULM H/T
F	29-May-1992	28-Jul-1992	56.00	4.380	41.00	5	ALTE, GOR
M	24-Oct-1990	29-Jul-1992	86.60	10.00	50.00	1	OSA, T&A
M	10-Oct-1991	29-Jul-1992	62.00	5.050	42.00	2	CNLD, PULM H/T
F	26-Aug-1990	29-Jul-1992	83.00	9.600	46.00	1	OSA
F	20-Apr-1992	30-Jul-1992	62.00	6.075	39.00	1	ALTE, RSV
M	05-Apr-1992	30-Jul-1992	65.50	6.780	?????	3	RSV
M	06-Nov-1984	03-Aug-1992	125.0	17.50	53.00	4	VC PARESIS, OSA
M	09-Sep-1977	03-Aug-1992	149.5	30.50	53.00	1	CF, DEVEL DELAY
M	18-Oct-1991	04-Aug-1992	71.00	8.770	46.00	1	OSA, FHX
M	09-Sep-1977	04-Aug-1992	149.5	30.50	53.00	2	CF, DEVEL DELAY
F	23-Jan-1990	05-Aug-1992	88.50	12.90	47.50	1	DYSMORPHIC, ASTHMA, T&A, ASTHMA
M	21-Jan-1992	06-Aug-1992	67.00	6.300	?????	3	ARSIDS, F/U
M	11-Nov-1977	10-Aug-1992	133.0	41.50	53.00	1	OSA, DEVEL DELAY, FRAGILE X
F	26-May-1989	10-Aug-1992	90.00	12.20	49.00	3	EDS, NIGHT WAKING, DEVEL DELAY

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	25-May-1992	11-Aug-1992	62.00	5.640	40.00	2	ARSIDS, T&A
F	08-Jun-1987	11-Aug-1992	109.0	15.90	51.00	1	OSA
F	17-Feb-1991	12-Aug-1992	83.40	13.90	48.00	2	ARSIDS, APNEA
M	16-Oct-1985	12-Aug-1992	112.0	21.10	54.00	1	CF, APNEA
F	16-Oct-1991	13-Aug-1992	?????	5.920	40.50	2	CNLD, O2
M	30-Aug-1985	13-Aug-1992	121.0	22.00	50.00	6	C HYPOVENT, VENTILATED
F	24-Feb-1984	17-Aug-1992	80.00	15.00	48.00	2	SPINA BIFIDA, KYPHOSCOLIOS
F	15-Jun-1985	17-Aug-1992	136.2	46.70	58.00	1	OSA, OBESE, POST T&A
F	24-Feb-1984	18-Aug-1992	80.00	15.00	48.00	3	SPINA BIFIDA, KYPHOSCOLIOS
M	11-Feb-1992	18-Aug-1992	69.50	8.420	44.00	1	NIGHT WAKING, SNORE
F	25-May-1992	19-Aug-1992	61.00	5.590	40.00	3	ARSIDS, F/U
F	24-Jul-1986	19-Aug-1992	?????	?????	?????	4	C HYPOVENT, DEVEL DELAY, VENTILATED
F	25-May-1992	20-Aug-1992	61.00	5.590	40.00	4	ARSIDS, F/U
M	17-Oct-1990	20-Aug-1992	87.00	11.80	50.00	1	NIGHT WAKING
F	27-Oct-1990	24-Aug-1992	75.00	10.00	47.00	1	CNLD, O2
M	27-Aug-1991	24-Aug-1992	?????	?????	46.00	25	ARSIDS, F/U
F	27-Oct-1990	25-Aug-1992	75.00	10.00	47.00	2	CNLD, O2
M	21-Jul-1989	25-Aug-1992	98.00	15.90	50.00	1	ASTHMA, OSA, T&A
M	09-Sep-1976	25-Aug-1992	?????	?????	?????	2	OSA, CPAP
F	09-Apr-1991	26-Aug-1992	66.00	6.250	42.00	1	CNLD, O2, T&A
F	29-May-1992	26-Aug-1992	60.00	5.400	41.00	6	ARSIDS, F/U
M	01-Feb-1990	27-Aug-1992	?????	?????	48.00	1	ASTHMA, HEAD BANG
M	18-Jun-1983	31-Aug-1992	129.5	33.20	54.00	1	OSA
F	08-Oct-1987	31-Aug-1992	114.0	29.90	54.00	1	OSA, OBESE
F	13-Oct-1989	07-Sep-1992	82.80	12.70	54.50	2	CNLD, HYPOTONIA, STEROIDS
M	16-Feb-1979	07-Sep-1992	143.5	44.00	54.00	1	INSOMNIA
F	23-Aug-1988	08-Sep-1992	89.50	14.35	55.00	1	OSA, DYSMORPHIC
F	28-May-1992	08-Sep-1992	61.00	6.000	40.50	2	ARSIDS, CONTROL
F	17-Nov-1983	09-Sep-1992	125.0	24.20	52.00	1	ASTHMA, OSA, SCOLIOSIS
M	04-Jun-1989	09-Sep-1992	105.0	17.20	54.00	1	CP, HYDROCEPHALUS, MIXED APNEA
M	24-Dec-1986	10-Sep-1992	97.00	15.80	47.00	1	DOWNS, OSA
F	17-Jun-1985	10-Sep-1992	120.0	22.70	52.00	1	OSA
M	29-Dec-1985	14-Sep-1992	120.0	46.00	56.00	1	OBESE, OSA
M	20-Apr-1982	14-Sep-1992	131.9	?????	57.00	3	CROUZON, OSA
M	29-Dec-1985	15-Sep-1992	120.0	46.00	56.00	2	OBESE, OSA
F	06-Jun-1990	15-Sep-1992	83.50	11.30	48.00	1	FTT, OSA
F	25-Oct-1989	16-Sep-1992	89.00	12.00	50.00	1	APNEA, SHUDDERS
M	14-Jul-1990	16-Sep-1992	93.50	13.70	49.00	3	APNEA, T/B MALACIA
F	18-Jun-1981	17-Sep-1992	138.5	32.00	50.00	1	FITS, OSA
M	06-Sep-1992	17-Sep-1992	50.50	3.360	34.20	1	SPINA BIFIDA, PRE-SHUNT
M	03-Jul-1992	21-Sep-1992	57.00	5.600	41.00	1	GOR, APNEA, ARSIDS
M	28-Jul-1982	21-Sep-1992	140.0	31.85	55.00	1	OSA
F	25-May-1992	22-Sep-1992	63.00	6.470	41.00	5	ARSIDS
F	16-Oct-1991	23-Sep-1992	64.00	6.430	43.00	3	CNLD, PREM
M	30-Aug-1985	23-Sep-1992	124.5	22.45	54.00	7	C HYPOVENT, VENTILATED
M	09-Jul-1992	24-Sep-1992	59.00	7.290	43.50	1	TACHYPNOEA, T&A
F	31-Mar-1992	24-Sep-1992	64.00	7.750	43.50	4	PIERRE ROBIN, ARSIDS
M	02-Dec-1976	28-Sep-1992	172.0	43.58	51.50	1	CF
M	06-Sep-1992	28-Sep-1992	50.00	4.080	37.00	2	SPINA BIFIDA, INFANT
M	30-Dec-1983	29-Sep-1992	116.5	22.65	50.00	1	DOWNS, OSA, POST T&A

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	14-Aug-1992	29-Sep-1992	57.00	4.130	38.00	1	ALTE, ARSIDS
F	05-Jun-1990	30-Sep-1992	86.60	14.60	48.50	1	OSA, T&A, C HYPOVENT, BURNS
M	22-Dec-1988	30-Sep-1992	?????	?????	?????	1	ALTE, OSA
M	26-Jun-1983	01-Oct-1992	121.5	23.15	?????	3	C HYPOVENT, VENTILATED
F	03-Mar-1987	01-Oct-1992	82.60	13.90	52.00	4	ACHONDROPLAS, OSA
M	21-Jan-1992	06-Oct-1992	?????	?????	45.00	4	ARSIDS
M	15-Nov-1985	06-Oct-1992	122.5	?????	51.50	1	CLEFT, OSA, T&A
M	07-Jun-1989	07-Oct-1992	100.0	19.70	51.00	1	ALBRIGHTS, DEVEL DELAY, T&A
F	25-May-1992	07-Oct-1992	66.00	6.700	41.00	6	ARSIDS
M	13-Jan-1987	08-Oct-1992	115.5	22.60	51.00	1	OSA, T&A
F	09-Apr-1991	08-Oct-1992	66.00	7.390	43.00	2	CNLD, FTT
F	09-Apr-1991	12-Oct-1992	66.00	7.390	43.00	3	CNLD, O2
M	19-Aug-1991	12-Oct-1992	75.60	10.30	47.00	1	OSA, FALLOTS, T&A
F	24-Feb-1984	13-Oct-1992	?????	?????	?????	4	SPINA BIFIDA, KYPHOSCOLIOS
F	29-May-1992	13-Oct-1992	67.00	7.160	43.00	7	ALTE
F	29-May-1992	14-Oct-1992	67.00	7.160	43.00	8	ALTE
F	08-Dec-1990	14-Oct-1992	?????	?????	?????	1	ASD,VSD, PULM H/T, O2
M	10-Aug-1979	15-Oct-1992	167.9	64.30	55.00	6	OSA
F	14-Feb-1992	15-Oct-1992	58.00	5.620	?????	2	DESBUQUOIS, CLEFT
M	05-May-1986	19-Oct-1992	91.50	17.20	56.00	1	ACHONDROPLAS
F	20-Sep-1990	19-Oct-1992	72.50	11.40	33.00	2	ACHONDROPLAS, OSA, POST T&A
M	21-Jan-1992	20-Oct-1992	68.00	6.270	44.00	1	FTT, OSA
M	09-Sep-1991	20-Oct-1992	73.60	8.350	47.00	2	RHINORRHOEA, OSA, POST T&A
F	25-May-1992	21-Oct-1992	70.00	7.100	42.00	7	OSA, CPAP
F	06-May-1986	21-Oct-1992	112.0	22.10	55.00	2	DYSMORPHIC, OSA, FITS
F	25-May-1992	22-Oct-1992	70.00	7.100	42.00	8	ARSIDS
M	21-Jul-1989	22-Oct-1992	97.50	15.35	?????	2	ASTHMA, OSA
M	03-Sep-1989	26-Oct-1992	95.00	13.45	50.00	1	ASTHMA, OSA
M	29-Apr-1991	26-Oct-1992	80.00	12.20	51.00	2	CNLD, O2
M	29-Apr-1991	27-Oct-1992	80.00	12.20	51.00	4	CNLD
M	03-Dec-1991	27-Oct-1992	63.50	6.150	42.00	3	CNLD
M	05-Jan-1978	28-Oct-1992	?????	?????	60.00	1	OI, OBESE
M	03-Dec-1991	28-Oct-1992	63.50	6.150	?????	4	CNLD, O2
M	29-Apr-1991	29-Oct-1992	80.00	12.20	51.00	3	CNLD, O2, FTT
M	03-Dec-1991	29-Oct-1992	63.50	6.150	?????	5	CNLD, O2
F	21-Nov-1980	02-Nov-1992	160.0	51.95	57.00	2	OSA, FITS
F	04-Sep-1991	02-Nov-1992	77.00	10.40	47.00	1	GOR, APNEA
M	16-Sep-1987	03-Nov-1992	107.5	19.70	?????	2	OSA
M	16-Oct-1985	03-Nov-1992	112.0	21.15	53.00	2	CF
M	16-Oct-1985	04-Nov-1992	112.0	21.15	53.00	3	CF
F	02-Jan-1990	04-Nov-1992	94.50	14.50	50.00	1	DEVEL DELAY, ENCEPHALITIS
M	25-Sep-1988	05-Nov-1992	103.0	15.55	50.00	1	OSA
M	16-Oct-1985	05-Nov-1992	112.0	21.15	53.00	4	CF
M	21-May-1990	09-Nov-1992	79.00	10.65	50.00	1	SPINA BIFIDA, BULBAR PALSY
F	29-May-1992	09-Nov-1992	68.00	7.500	43.00	9	ALTE, GOR
F	07-Aug-1992	10-Nov-1992	54.00	4.400	39.00	1	PREM, APNEA
M	21-Dec-1986	10-Nov-1992	118.5	21.05	54.00	1	OSA

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	12-Jun-1979	10-Nov-1992	148.0	51.50	?????	6	NEUROMUSCULA, C HYPOVENT
F	07-Aug-1992	11-Nov-1992	54.00	4.400	39.00	2	PREM
M	14-Aug-1990	11-Nov-1992	86.00	14.00	50.00	2	PREM, CNLD, OSA
M	08-Feb-1977	11-Nov-1992	?????	?????	?????	2	HYPOVENTILAT, NEUROMUSCULA
F	21-Sep-1990	12-Nov-1992	79.50	10.80	48.00	1	GOLDENHAAR, OSA, POST T&A
F	04-Sep-1991	12-Nov-1992	77.00	10.40	47.00	2	APNEA
M	07-Sep-1992	16-Nov-1992	53.00	3.315	37.00	1	FTT, CNLD
F	17-Jun-1989	16-Nov-1992	91.00	14.05	37.00	1	SCHPRINTZEN, CLEFT, DYSMORPHIC
M	30-Dec-1989	17-Nov-1992	101.0	18.30	54.00	1	CNLD, O2
M	30-Dec-1989	18-Nov-1992	101.0	18.30	54.00	2	CNLD, O2
F	25-Jan-1989	18-Nov-1992	?????	25.00	50.00	1	EDS, OBESE, HYPOTHALAMIC
M	16-May-1983	19-Nov-1992	127.0	26.00	54.00	2	OSA, TRACHEOSTOMY
M	09-Sep-1977	19-Nov-1992	150.0	30.90	53.00	3	CF, C HYPOVENT
F	16-Oct-1991	23-Nov-1992	70.00	7.450	44.00	4	CNLD, O2
M	07-Apr-1990	23-Nov-1992	87.00	11.55	50.00	1	ASTHMA, OSA
M	16-Jul-1987	24-Nov-1992	112.5	27.30	54.00	10	DYSMORPHIC, FOETAL DILAN
F	25-Oct-1990	24-Nov-1992	86.00	16.50	54.00	3	DYSMORPHIC, POST T&A
F	16-Nov-1991	25-Nov-1992	60.00	6.480	46.30	1	ACHONDROPLAS, OSA
M	27-Mar-1981	25-Nov-1992	91.95	112.5	59.00	1	OSA, OBESE, RVH
F	17-Oct-1992	26-Nov-1992	?????	2.260	33.00	1	APNEA
M	27-Mar-1981	26-Nov-1992	159.0	91.95	59.00	2	OSA, OBESE, RVH
M	09-Sep-1977	30-Nov-1992	163.5	88.65	59.00	1	CP, OSA
M	10-Oct-1991	30-Nov-1992	75.00	6.310	44.00	3	CNLD
M	17-Jul-1990	01-Dec-1992	74.00	9.900	44.00	2	DOWNS, OSA
F	07-Aug-1992	01-Dec-1992	54.00	5.190	40.00	3	PREM, OSA
M	09-Sep-1977	01-Dec-1992	167.0	87.50	?????	2	OSA, DEVEL DELAY
F	14-Jul-1986	02-Dec-1992	129.0	32.30	53.00	1	C HYPOVENT, DEVEL DELAY, VENTILATED
F	12-Nov-1992	02-Dec-1992	53.00	4.200	38.00	1	OSA, PREM
M	19-Nov-1992	03-Dec-1992	52.00	3.336	35.00	1	APNEA, ACUTE OBSTRU
F	19-Sep-1992	03-Dec-1992	59.00	5.600	40.00	1	CONTROL
M	28-Dec-1988	07-Dec-1992	96.70	13.65	49.00	5	FALLOT, SCNLD, CPAP
F	19-Nov-1992	07-Dec-1992	57.00	4.080	37.00	1	SPINA BIFIDA, INFANT
M	28-Dec-1988	08-Dec-1992	96.70	13.65	49.00	6	FALLOT, SCNLD, CPAP
M	19-Nov-1992	08-Dec-1992	52.00	3.330	36.00	2	APNEA, ACUTE OBSTRU
M	06-Oct-1989	09-Dec-1992	92.50	14.40	50.00	1	NIGHT TERROR, STRIDOR
F	02-Jun-1991	09-Dec-1992	77.00	11.00	47.00	2	SPINA BIFIDA, POST DECOMPR
F	11-Dec-1991	10-Dec-1992	78.00	10.15	50.00	1	LARYNGOMALAC, NIGHT WAKING, OSA
M	13-Aug-1992	10-Dec-1992	69.00	6.940	42.00	1	ALTE, ARSIDS, COUSIN
M	04-May-1989	14-Dec-1992	94.50	14.65	52.00	1	OSA, EDS, T&A
F	05-Mar-1991	14-Dec-1992	86.60	8.500	49.00	1	OSA
F	28-May-1992	15-Dec-1992	?????	?????	?????	3	ARSIDS, SIBLING
F	17-Oct-1992	15-Dec-1992	?????	21.60	36.00	2	APNEA, ARSIDS, PREM
M	28-Sep-1990	16-Dec-1992	84.50	12.45	48.00	1	OSA, ASTHMA
M	23-Aug-1990	16-Dec-1992	92.60	16.65	52.00	1	OSA, POST T&A
M	01-Jan-1987	17-Dec-1992	104.0	14.40	50.00	1	OSA, T&A, EDS, PREM
M	15-Jan-1991	17-Dec-1992	85.40	11.60	49.00	1	NIGHT WAKING
M	27-Sep-1988	21-Dec-1992	108.0	?????	48.00	1	NIGHT WAKING, INSOMNIA
F	29-May-1992	21-Dec-1992	?????	8.200	43.00	10	ARSIDS, GOR

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
M	15-Mar-1989	22-Dec-1992	101.5	?????	51.00	1	NIGHT WAKING
M	24-Mar-1992	22-Dec-1992	?????	?????	44.00	1	ALTE, APNEA, FITS
M	28-Sep-1988	23-Dec-1992	112.5	?????	54.00	1	OSA, POST T&A
M	21-Aug-1989	23-Dec-1992	98.00	?????	53.00	1	OSA
F	04-Jun-1990	01-Jan-1993	86.50	12.00	50.00	1	OSA, AWAKE OBSTR
F	07-Jan-1988	07-Jan-1993	?????	?????	?????	1	OSA, ENEURESIS
M	09-Feb-1990	11-Jan-1993	147.0	34.00	51.00	1	OSA, POST T&A, T&A
F	06-May-1989	11-Jan-1993	98.50	15.45	52.00	2	APNEA, ARSIDS, ALTE
M	20-Jul-1990	12-Jan-1993	77.00	10.80	47.00	1	RUB-TAYBI, ASTHMA/GOR, T&A, OSA
F	21-Jul-1989	12-Jan-1993	92.00	13.85	51.00	1	OSA, ASTHMA, T&A
F	16-May-1989	13-Jan-1993	94.50	45.50	50.00	1	OSA, SNORING, T&A
M	13-Nov-1992	13-Jan-1993	62.00	5.700	41.00	3	ALTE
M	30-Aug-1982	14-Jan-1993	133.0	33.90	53.00	1	CLEFT, OSA, SCHPRINTZEN, CPAP
M	14-Apr-1986	18-Jan-1993	124.5	24.80	52.00	1	NIGHT TERROR
F	02-Jul-1989	18-Jan-1993	101.0	16.85	51.00	1	OSA, POST T&A, PALATE
M	27-Aug-1992	19-Jan-1993	63.00	7.230	42.00	1	ALTE
F	07-Jul-1987	19-Jan-1993	112.5	21.15	50.00	1	FITS, EDS
M	13-Feb-1987	20-Jan-1993	108.5	22.80	50.00	1	DOWNS, OSA, POST T&A
M	21-Jan-1992	20-Jan-1993	79.00	9.500	47.00	5	ARSIDS
M	29-Mar-1985	21-Jan-1993	127.0	36.35	53.00	5	OSA, CPAP
M	05-Jul-1988	21-Jan-1993	108.0	19.95	54.00	1	OSA, POST T&A
M	05-Oct-1989	25-Jan-1993	91.50	15.25	53.00	1	OSA, ASTHMA
M	15-Nov-1985	25-Jan-1993	126.0	23.90	53.00	2	POST T&A, CLEFT
M	06-Jan-1978	27-Jan-1993	148.0	74.50	65.50	1	OI, ASTHMA, OSA
M	15-Jul-1989	27-Jan-1993	?????	?????	?????	1	PREM, APNEA
F	21-Nov-1992	28-Jan-1993	57.00	5.230	38.00	1	ARSIDS
M	04-Sep-1989	28-Jan-1993	104.0	17.30	50.00	1	OSA, WHEEZE
M	15-Jun-1991	01-Feb-1993	?????	7.800	47.00	1	CP, OSA, CNLD, CHROMOSONAL
M	16-Jul-1992	01-Feb-1993	68.00	7.300	46.00	1	ALTE, CNLD, RESP FAILURE
F	30-Oct-1986	02-Feb-1993	108.0	16.00	48.00	2	CP, OSA, POST T&A
M	02-Feb-1993	02-Feb-1993	105.0	24.25	52.00	1	POST T&A, FITS
M	10-Mar-1990	03-Feb-1993	57.60	13.25	50.00	2	CNLD, O2
M	28-Nov-1992	03-Feb-1993	59.00	5.500	39.00	1	ALTE, GOR
M	28-Feb-1983	04-Feb-1993	139.5	37.00	56.00	3	ALTE, C HYPOVENT
M	30-Aug-1982	04-Feb-1993	135.0	35.00	55.00	2	SCHPRINTZEN, CPAP, OSA
F	14-Feb-1992	08-Feb-1993	61.00	6.240	43.00	3	OSA, DEBUQUOIS, KYPHOSIS
F	26-Aug-1989	08-Feb-1993	89.00	14.60	53.00	1	OSA, DYSMORPHIC, DEVEL DELAY
M	19-Jun-1981	09-Feb-1993	153.5	65.40	57.00	1	OSA, ASTHMA, OBESE
M	24-Mar-1992	09-Feb-1993	?????	?????	43.00	2	ALTE, FITS
F	17-Oct-1992	10-Feb-1993	52.00	4.640	38.00	3	APNEA
M	27-Aug-1991	10-Feb-1993	?????	?????	47.00	26	ARSIDS, ALTE
F	19-Sep-1992	11-Feb-1993	66.00	6.700	43.00	2	CONTROL, NORMAL
F	04-Jul-1988	11-Feb-1993	113.0	47.45	56.00	1	OBESE, OSA
M	17-Oct-1983	15-Feb-1993	127.0	29.25	54.00	2	EDS
M	13-Oct-1992	15-Feb-1993	65.00	7.350	44.00	1	ALTE, OSA
M	13-Oct-1992	16-Feb-1993	65.00	7.350	44.00	2	ALTE
F	21-Nov-1992	16-Feb-1993	?????	5.900	40.00	2	ARSIDS
M	14-Mar-1991	17-Feb-1993	76.00	8.680	45.00	1	CP, KYPHOSIS, OSA, PALLIATIVE
M	11-Apr-1990	17-Feb-1993	?????	?????	?????	1	QUADRIPLEGIA, C HYPOVENT
M	19-Jul-1991	18-Feb-1993	81.50	12.70	48.00	3	ARSIDS, OSA

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	02-Sep-1981	18-Feb-1993	140.0	27.45	?????	1	FITS, OSA, APNEA, FITS
F	08-Nov-1987	22-Feb-1993	110.0	20.75	54.00	2	POST T&A, DOWNS
F	08-Dec-1986	22-Feb-1993	122.0	23.00	52.00	1	OSA
F	16-Nov-1991	23-Feb-1993	62.00	6.900	48.00	2	POST T&A, ACHONDROPLAS, CPAP
F	14-Sep-1988	23-Feb-1993	105.0	5.950	52.00	2	POST T&A
F	09-Dec-1986	24-Feb-1993	149.2	29.60	?????	1	OSA, POST T&A, T&A
M	15-Sep-1990	24-Feb-1993	93.00	15.20	51.00	1	OSA, NIGHT WAKING, NIGHT TERROR
M	26-Mar-1990	25-Feb-1993	99.50	12.50	51.00	1	NIGHT WAKING, ASTHMA, OSA, FHX SIDS
F	23-Sep-1992	25-Feb-1993	?????	2.950	37.00	1	CNLD, HYDROCEPHALU
M	02-Oct-1990	01-Mar-1993	94.00	17.05	54.00	1	OSA, NIGHT WAKING
F	11-Apr-1988	01-Mar-1993	111.0	21.25	50.00	3	POST T&A, OSA
M	21-Aug-1983	02-Mar-1993	120.0	23.95	49.00	1	OSA, DOWNS, CLEFT
F	09-Jan-1987	02-Mar-1993	114.0	20.10	52.00	2	POST T&A, OSA
M	27-Aug-1992	03-Mar-1993	68.00	7.700	43.00	2	ALTE, TRACHEOSTOMY
M	07-Dec-1992	03-Mar-1993	64.00	6.080	41.00	1	ALTE
M	27-Mar-1981	04-Mar-1993	134.0	23.00	51.00	1	TRACHEOSTOMY, OSA, DEVEL DELAY, LARYN WEB
M	29-Jan-1993	04-Mar-1993	55.00	4.095	47.00	2	APNEA, CYANOSIS
F	05-May-1984	08-Mar-1993	138.7	29.10	50.00	1	OSA, FHX
F	05-Jul-1983	08-Mar-1993	134.0	45.90	55.00	1	OSA, OBESE, ATOPY
M	07-Apr-1990	09-Mar-1993	88.00	12.75	51.00	2	POST T&A, OSA
F	31-Mar-1992	09-Mar-1993	77.50	10.50	46.50	5	ARSIDS
M	03-Jul-1991	10-Mar-1993	75.00	10.50	47.50	1	PREM, OSA, TB MALACIA, POST T&A
F	12-Jul-1988	10-Mar-1993	96.50	14.60	54.00	1	OSA, ASTHMA, POST T&A
F	11-Dec-1992	11-Mar-1993	60.50	5.200	41.00	1	ALTE, GOR
M	26-May-1990	11-Mar-1993	95.50	14.50	47.00	1	POST T&A, OSA, SNORE
F	25-May-1992	15-Mar-1993	75.00	9.400	46.00	9	ARSIDS, CPAP
M	16-Jun-1981	15-Mar-1993	148.2	35.25	52.50	2	NIGHT TERROR, RIVOTRIL
F	27-Nov-1991	16-Mar-1993	77.00	8.360	47.00	1	C HYPOVENT
M	27-Jul-1992	16-Mar-1993	?????	4.950	42.00	1	PREM, CNLD
M	07-Feb-1992	17-Mar-1993	77.00	10.00	46.00	1	OSA, NIGHT TERROR
F	14-Sep-1988	17-Mar-1993	105.0	15.95	52.00	3	OSA, POST T&A
F	17-Oct-1992	18-Mar-1993	60.00	5.840	41.00	4	APNEA
M	14-Apr-1989	18-Mar-1993	103.9	16.00	49.00	1	OSA, EDS
F	21-Nov-1992	22-Mar-1993	62.00	6.600	40.00	3	ARSIDS, SIBLING, FHX
F	23-Jan-1990	22-Mar-1993	95.50	16.05	48.00	2	ASTHMA, DEVEL DELAY, POST T&A
M	13-Nov-1992	23-Mar-1993	70.00	8.100	43.00	4	ALTE
M	29-Jan-1993	23-Mar-1993	58.50	4.770	37.00	3	ALTE, TB MALACIA
M	29-Jan-1993	24-Mar-1993	58.50	4.770	37.00	4	ALTE, CPAP
M	07-May-1992	24-Mar-1993	71.50	8.650	48.00	1	CHOANAL, STEN OSA, TRACHEOSTOMY, ALTE
F	19-Sep-1992	25-Mar-1993	68.00	7.230	43.00	3	CONTROL, NORMAL
F	02-Jul-1990	25-Mar-1993	84.20	14.90	48.50	3	DOWNS, OSA, POST T&A, ENT
M	27-Jul-1992	29-Mar-1993	61.00	4.950	42.00	2	ALTE, O2
M	20-Mar-1993	29-Mar-1993	47.70	3.125	34.00	1	SPINA BIFIDA, APNEA, ARNOLD-CHIAR
F	25-Feb-1993	30-Mar-1993	51.00	3.610	35.50	1	ALTE, GOR
M	27-Jul-1992	30-Mar-1993	61.00	4.950	42.00	3	ALTE, O2
F	30-Nov-1992	31-Mar-1993	?????	?????	?????	1	ARSIDS, FHX, SIBLING, PREM

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
F	15-Aug-1981	31-Mar-1993	149.0	60.79	54.00	1	DIDMOA, OBESE, DIABETES, C HYPOVENT
M	20-Mar-1993	01-Apr-1993	?????	3.300	35.00	2	SPINA BIFIDA, APNEA
M	18-Aug-1989	01-Apr-1993	93.50	15.50	52.00	1	OSA
M	23-Jan-1991	05-Apr-1993	90.00	14.50	48.00	1	POST T&A, OSA
M	07-May-1992	05-Apr-1993	71.50	8.800	49.00	2	CHONAL, ATRES OSA, ALTE
F	18-Nov-1990	06-Apr-1993	86.50	12.20	48.00	1	OSA, RHINITIS, ATOPY
M	04-Apr-1991	06-Apr-1993	91.20	17.25	51.00	1	HYDROCEPHALUS, OSA, EDS
M	09-Dec-1990	07-Apr-1993	91.00	15.85	49.00	1	OSA, T&A
M	02-Oct-1988	07-Apr-1993	109.3	19.25	51.00	1	OSA, T&ASEX DOB
M	18-Apr-1991	08-Apr-1993	91.00	16.00	51.00	1	OSA, BEHAVIOUR, NIGHT WAKING
F	17-Jan-1990	08-Apr-1993	95.50	16.00	53.00	2	OSA, BECKWITH, POST T&A
F	03-Mar-1987	13-Apr-1993	86.50	14.00	53.00	5	ACHONDROPLAS, OSA, CPAP
M	17-Dec-1989	13-Apr-1993	96.00	15.50	52.00	2	POST T&A, OSA
M	29-Feb-1988	14-Apr-1993	117.0	22.00	53.00	1	PARASOMNIA, HEAD BANG
M	29-Jan-1988	14-Apr-1993	60.00	5.300	89.00	1	OFF CPAP, ARSIDS
F	19-Apr-1990	15-Apr-1993	152.0	37.00	54.00	1	QUADRIPLEGIA, TRAUMATIC, C HYPOVENT
F	23-Jan-1987	15-Apr-1993	103.0	14.60	48.50	1	SPINA BIFIDA, ARNOLD-CHIAR, OSA, CLD
F	13-Oct-1989	19-Apr-1993	89.00	13.45	56.00	3	CNLD, O2
M	26-Dec-1988	19-Apr-1993	104.0	14.00	?????	2	POST T&A, OSA
F	13-Oct-1989	20-Apr-1993	89.00	13.45	56.00	4	CLD, O2
F	10-Oct-1985	20-Apr-1993	126.0	32.60	53.00	1	OSA, EDS
F	23-Sep-1992	21-Apr-1993	53.00	3.710	38.50	2	EX-PREM, CNLD, HYDROCEPHALUS, O2
F	27-Nov-1991	21-Apr-1993	?????	9.550	46.00	2	C HYPOVENT, VENTILATED
F	23-Sep-1992	22-Apr-1993	53.00	3.710	38.50	3	CNLD, O2, HYDROCEPHALUS
M	22-Feb-1990	22-Apr-1993	95.00	14.10	49.00	1	CNLD, INTERSTITIAL, O2, OSA
F	03-Aug-1975	27-Apr-1993	159.0	40.10	58.00	2	CF, CPAP, O2
M	20-Feb-1992	27-Apr-1993	74.00	9.000	49.00	1	CP, COR, OSA
F	17-Oct-1992	28-Apr-1993	63.00	7.350	43.00	5	APNEA, ARSIDS
F	21-Aug-1984	28-Apr-1993	105.0	16.50	55.00	1	CROUZONS, OSA, UPPP, POST T&A
F	28-Mar-1993	29-Apr-1993	49.00	3.270	34.80	1	SPINA BIFIDA, ARNOLD-CHIAR, APNEA
M	04-Mar-1993	29-Apr-1993	?????	5.600	44.00	1	ALTE, UTI
F	14-Feb-1992	03-May-1993	63.00	7.040	44.00	4	DESBUQUOIS, CLEFT, OSA, CPAP
M	05-Feb-1991	03-May-1993	80.00	11.20	46.00	1	DOWNS, OSA, ASTHMA
F	31-Oct-1991	04-May-1993	81.00	11.20	46.00	1	ARSIDS, APNEA
F	28-Mar-1993	04-May-1993	19.00	3.300	35.00	2	SPINA BIFIDA, ARNOLD-CHIAR, CPAP
M	26-Jul-1989	05-May-1993	99.00	16.75	?????	1	ASTHMA
F	05-Feb-1993	05-May-1993	?????	?????	?????	1	EX-PREM, APNEA
M	19-Dec-1990	06-May-1993	89.00	14.60	?????	1	OSA, EX-PREM, TWIN
M	11-Sep-1980	06-May-1993	170.0	94.00	59.00	1	OSA, OBESE, NORMAL
F	16-Feb-1990	06-May-1993	?????	?????	?????	1	APNEA, ARSIDS
M	03-May-1985	10-May-1993	123.2	47.85	54.50	1	OSA, PARASOMNIA, VON WILLEBRA
F	04-Aug-1988	10-May-1993	90.00	12.15	46.00	1	NIGHT WAKING, DEVEL DELAY, FITS
M	11-Jun-1992	11-May-1993	69.50	8.020	?????	1	APNEA, GOR, EX-PREM

Sex	DOB	Study	HT	WT	HC	Stud	Diagnoses
M	29-Jan-1993	11-May-1993	63.00	12.00	41.00	5	ALTE, APNEA
M	05-Apr-1990	12-May-1993	72.10	7.200	44.00	1	OSA, TOF, ASTHMA, GOLDENHAAR
M	20-Mar-1993	12-May-1993	55.00	4.570	38.00	3	APNEA, OSA, SPINA BIFIDA, CPAP
M	18-Jul-1992	13-May-1993	79.00	10.40	47.00	1	ARSIDS, ALTE
M	14-Mar-1993	13-May-1993	56.00	5.390	40.00	1	ARSIDS, CONTROL, SIBLING
F	21-Nov-1992	17-May-1993	67.00	7.300	42.00	4	ARSIDS, SIBLING
M	24-Dec-1981	17-May-1993	139.3	54.05	52.50	1	OBESE, OSA, NOCTURIA, NOCTURIA, ACANTHOSIS N
M	14-Mar-1991	18-May-1993	76.00	8.850	47.00	2	CP, KYPHOSCOLIOS, GER, OSA
M	24-Dec-1981	18-May-1993	139.3	54.05	52.50	2	OBESE, OSA, CPAP
F	19-Mar-1993	19-May-1993	54.50	4.330	39.30	1	NORMAL, CONTROL
M	11-Feb-1992	19-May-1993	58.00	4.760	42.00	1	OSA, NIGHT WAKING
M	23-Jan-1987	20-May-1993	129.5	41.40	55.00	1	OSA, OBESE, ASTHMA, POST T&A
M	21-Aug-1989	20-May-1993	102.5	19.50	?????	2	OSA, POST T&A
M	27-Feb-1988	24-May-1993	111.0	18.00	51.00	1	OSA, T&A
F	25-Jun-1992	24-May-1993	72.00	9.350	?????	1	APNEA, CYANOSIS, BRADYCARDIA
M	13-Nov-1992	25-May-1993	76.00	9.030	47.00	5	ALTE, APNEA
F	11-Mar-1987	25-May-1993	116.0	20.20	48.00	1	OSA, DEVEL DELAY
M	27-Jul-1992	26-May-1993	70.00	7.000	44.00	1	EX-PREM, BRONCHIOLITI, TRIPLET
M	27-Jul-1992	26-May-1993	59.00	5.590	42.00	4	EX-PREM, CNLD, TRIPLET
F	25-May-1992	27-May-1993	74.00	18.90	46.00	10	ARSIDS, SIBLING, EX-CPAP
M	10-Apr-1993	27-May-1993	61.00	6.200	44.00	1	ARSIDS, COUSIN
M	12-Feb-1993	31-May-1993	40.50	1.595	32.80	1	EX-PREM, CNLD
M	17-Sep-1991	31-May-1993	86.00	12.15	51.50	1	OSA
M	12-Feb-1993	01-Jun-1993	40.50	1.595	32.80	2	EX-PREM, CNLD
M	30-Aug-1985	01-Jun-1993	125.0	23.45	51.50	8	C HYPOVENT
F	28-May-1992	02-Jun-1993	69.90	8.540	46.20	4	ARSIDS, APNEA, NIGHT TERROR
M	08-Dec-1992	02-Jun-1993	70.00	8.100	46.00	1	BRADYCARDIA, URTI, APNEA
F	29-May-1992	03-Jun-1993	?????	?????	46.00	11	ARSIDS, APNEA, EX-CPAP, GER
M	07-Oct-1992	03-Jun-1993	?????	7.100	45.00	1	APNEA, CYANOSIS
F	05-Feb-1993	07-Jun-1993	62.00	6.320	40.50	2	ALTE, OSA
F	14-Dec-1992	07-Jun-1993	49.50	3.220	39.50	1	CNLD, EX-PREM, O2
F	18-Feb-1993	08-Jun-1993	45.00	3.100	36.00	1	CNLD, EX-PREM, O2
F	14-Dec-1992	08-Jun-1993	49.50	3.220	39.50	2	CNLD, EX-PREM, O2
M	07-Oct-1992	09-Jun-1993	65.00	7.380	45.00	2	CNLD, ARSIDS, C HYPOVENT
F	25-Jun-1992	10-Jun-1993	71.00	8.500	?????	2	APNEA, CYANOSIS, BRADYCARDIA
M	07-Oct-1992	10-Jun-1993	65.00	7.380	45.00	3	CNLD, ARSIDS, C HYPOVENT

b. RESPONSE OF OSA TO ADENOTONSILLECTOMY

Subj	Study	Date	Totca	Totca	Totoa	Totoa
CA	1	05-May-92	31.00	231.0	57.00	593.0
	2	30-Jun-93	9.000	85.00	.0000	.0000
TDC	1	04-Jun-92	9.000	70.00	28.00	219.0
	2	02-Feb-93	5.000	42.00	1.000	10.00
JD	1	08-Oct-90	16.00	110.0	148.0	1324.
	2	19-Apr-93	17.00	122.0	28.00	282.0
MF	1	13-May-91	14.00	219.0	91.00	1747.
	2	01-Apr-92	6.000	50.00	17.00	190.0
WG	1	01-Jul-92	16.00	106.0	32.00	207.0
	2	08-Apr-93	14.00	103.0	16.00	101.0
MJ	1	16-May-91	19.00	157.0	51.00	679.0
	2	22-Feb-93	13.00	90.00	8.000	47.00
ML	1	12-Jun-91	22.00	128.0	71.00	335.0
	2	25-Mar-93	52.00	400.0	20.00	136.0
NM	1	13-Aug-90	38.00	286.0	63.00	515.0
	2	22-Jun-93	41.00	303.0	15.00	116.0
DN	1	09-Jan-91	13.00	86.00	53.00	432.0
	2	17-Mar-93	5.000	32.00	28.00	248.0
MOD	1	19-Nov-90	20.00	117.0	158.0	1267.
	2	13-Apr-93	30.00	171.0	3.000	21.00
AR	1	07-May-92	24.00	262.0	28.00	255.0
	2	29-Jun-93	34.00	331.0	3.000	23.00
JS	1	09-Mar-92	16.00	171.0	24.00	189.0
	2	11-Mar-93	31.00	310.0	7.000	51.00
RW	1	12-Dec-91	12.00	124.0	86.00	1124.
	2	01-Mar-93	13.00	109.0	18.00	127.0

Subj	Study	Totma	Totma	Totch	Totch	Totoh	Totoh	Totmh	Totmh	Remca	Remca	Remoa	Remoa	Remma
CA	1	4.000	32.00	2.000	23.00	75.00	992.0	1.000	12.00	28.00	141.0	11.00	96.00	.0000
	2	2.000	20.00	1.000	5.000	30.00	313.0	3.000	19.00	6.000	48.00	.0000	.0000	.0000
TDC	1	2.000	15.00	2.000	18.00	126.0	1682.	5.000	81.00	5.000	31.00	3.000	24.00	.0000
	2	.0000	.0000	39.00	466.0	15.00	189.0	13.00	179.0	8.000	47.00	.0000	.0000	.0000
JD	1	3.000	30.00	29.00	201.0	135.0	1095.	38.00	240.0	42.00	297.0	114.0	847.0	12.00
	2	2.000	19.00	.0000	.0000	6.000	70.00	2.000	15.00	23.00	157.0	13.00	140.0	5.000
MF	1	1.000	12.00	1.000	15.00	100.0	1428.	18.00	263.0	.0000	.0000	105.0	2824.	4.000
	2	8.000	109.0	.0000	.0000	65.00	813.0	16.00	193.0	16.00	152.0	13.00	198.0	4.000
WG	1	3.000	28.00	7.000	45.00	261.0	1882.	45.00	356.0	13.00	65.00	42.00	305.0	2.000
	2	9.000	79.00	1.000	6.000	16.00	125.0	83.00	1053.	4.000	25.00	11.00	82.00	2.000
MJ	1	4.000	44.00	6.000	59.00	54.00	514.0	33.00	262.0	12.00	80.00	.0000	.0000	.0000
	2	.0000	.0000	14.00	103.0	4.000	19.00	6.000	38.00	9.000	61.00	7.000	40.00	.0000
ML	1	2.000	14.00	2.000	9.000	173.0	974.0	4.000	23.00	17.00	88.00	2.000	13.00	.0000
	2	21.00	235.0	34.00	350.0	50.00	307.0	16.00	160.0	39.00	241.0	5.000	31.00	16.00
NM	1	1.000	8.000	13.00	102.0	74.00	544.0	20.00	153.0	3.100	185.0	30.00	214.0	8.000
	2	1.000	8.000	6.000	37.00	.0000	.0000	2.000	17.00	39.00	212.0	6.000	44.00	.0000
DN	1	7.000	69.00	1.000	5.000	36.00	348.0	2.000	19.00	27.00	152.0	47.00	467.0	1.000
	2	2.000	27.00	1.000	8.000	132.0	1429.	4.000	38.00	8.000	43.00	21.00	178.0	3.000
MOD	1	9.000	75.00	4.000	25.00	59.00	548.0	6.000	43.00	22.00	118.0	201.0	2365.	16.00
	2	2.000	15.00	4.000	22.00	.0000	.0000	.0000	61.00	382.0	1.000	7.000	1.000	
AR	1	9.000	115.0	.0000	.0000	41.00	417.0	7.000	68.00	41.00	335.0	9.000	95.00	9.000
	2	.0000	.0000	5.000	39.00	45.00	401.0	5.000	60.00	23.00	183.0	6.000	62.00	1.000
JS	1	3.000	25.00	3.000	36.00	25.00	264.0	6.000	65.00	24.00	154.0	18.00	146.0	9.000
	2	2.000	26.00	9.000	81.00	22.00	183.0	6.000	56.00	8.000	55.00	2.000	10.00	1.000
RW	1	11.00	135.0	.0000	.0000	23.00	399.0	1.000	10.00	24.00	227.0	189.0	2152.	23.00
	2	4.000	29.00	7.000	62.00	6.000	45.00	2.000	22.00	41.00	245.0	8.000	58.00	.0000

Subj	Study	Remma	Remch	Remch	Remoh	Remoh	Remmh	Remmh	Twt	Ts1	Ts2	Tsws	Tnrem	TRem
CA	1	.0000	.0000	.0000	22.00	199.0	2.000	24.00	51.90	41.60	304.8	121.8	468.2	86.00
	2	.0000	.0000	.0000	13.00	149.0	2.000	21.00	83.60	45.50	241.2	88.80	375.6	45.90
TDC	1	.0000	.0000	.0000	1.000	8.000	1.000	6.000	170.1	17.30	148.7	162.3	328.3	43.70
	2	.0000	1.000	16.00	4.000	55.00	.0000	.0000	79.40	12.90	159.8	220.3	393.0	47.60
JD	1	148.0	14.00	105.0	13.00	143.0	6.000	76.00	22.80	101.2	112.6	129.0	342.8	123.4
	2	61.00	1.000	12.00	21.00	222.0	3.000	36.00	10.90	40.40	161.7	186.7	388.8	101.3
MF	1	100.0	.0000	.0000	15.00	392.0	4.000	75.00	114.6	63.50	155.6	117.3	336.4	95.00
	2	34.00	1.000	10.00	110.0	1886.	8.000	100.0	27.30	13.70	151.3	179.2	344.2	118.5
WG	1	15.00	1.000	20.00	189.0	1556.	22.00	210.0	100.2	32.50	220.8	108.3	361.5	145.2
	2	20.00	.0000	.0000	16.00	152.0	8.000	60.00	90.90	105.3	170.2	124.1	399.6	70.50
MJ	1	.0000	5.000	48.00	3.000	34.00	1.000	15.00	126.0	19.00	3.700	268.3	456.2	53.80
	2	.0000	15.00	104.0	2.000	20.00	1.000	10.00	57.90	36.90	229.9	140.3	407.1	72.00
ML	1	.0000	5.000	19.00	9.000	49.00	7.000	42.00	134.3	1.900	173.5	170.7	346.0	40.70
	2	180.0	15.00	118.0	11.00	85.00	12.00	149.0	21.60	61.00	173.6	133.2	367.8	117.6
NM	1	60.00	1.000	11.00	22.00	184.0	15.00	153.0	13.00	77.90	266.5	83.90	428.3	98.80
	2	.0000	.0000	.0000	.0000	.0000	.0000	.0000	24.00	32.90	242.9	154.6	430.4	56.60
DN	1	14.00	2.000	20.00	26.00	262.0	4.000	32.00	34.50	42.60	90.70	218.6	351.9	122.6
	2	52.00	1.000	6.000	71.00	705.0	11.00	127.0	10.00	103.7	234.4	102.0	440.2	93.80
MOD	1	167.0	.0000	.0000	32.00	573.0	2.000	15.00	39.70	36.60	163.4	93.00	293.0	187.3
	2	5.000	13.00	105.0	.0000	.0000	.0000	.0000	45.90	15.00	282.1	179.4	476.5	109.7
AR	1	114.0	.0000	.0000	33.00	554.0	10.00	111.0	103.4	13.60	214.8	144.8	373.2	112.3
	2	15.00	8.000	49.00	60.00	575.0	22.00	215.0	.0000	2.000	300.6	142.1	444.7	135.3
JS	1	103.0	8.000	58.00	7.000	69.00	10.00	92.00	27.00	17.90	207.5	119.2	344.6	88.40
	2	6.000	6.000	48.00	2.000	15.00	.0000	.0000	84.10	102.2	264.0	151.2	517.3	47.60
RW	1	215.0	.0000	.0000	63.00	928.0	4.000	61.00	8.000	25.00	102.0	165.0	292.0	141.0
	2	.0000	2.000	15.00	.0000	.0000	.0000	.0000	84.20	79.30	176.7	139.8	395.8	125.1

Subj	Study	S1%	S2%	SWS%	Nrem%	Rem%	Tst	Tstdy	Effic	Sighs	Siind	Arous	Arind	Moves
CA	1	7.500	55.00	22.00	84.50	15.50	91.40	606.1	91.40	35.00	3.800	88.00	9.500	38.00
	2	10.80	57.20	21.10	89.10	10.90	421.4	505.0	83.40	10.00	1.400	20.00	2.800	9.000
TDC	1	4.700	40.00	43.60	88.30	11.70	371.9	542.0	68.60	15.00	2.400	17.00	2.700	32.00
	2	2.900	36.30	50.00	89.20	10.80	440.6	520.0	84.70	15.00	2.000	19.00	2.600	51.00
JD	1	21.70	24.10	27.70	73.50	26.50	466.2	489.0	95.30	43.00	5.500	28.00	3.600	39.00
	2	8.200	33.00	38.10	79.30	20.70	490.1	501.0	97.80	15.00	1.800	23.00	2.800	20.00
MF	1	14.70	36.10	27.20	78.00	22.00	431.4	546.0	79.00	14.00	1.900	35.00	4.900	13.00
	2	3.000	32.70	38.70	74.40	25.60	462.7	490.0	94.40	7.000	.9000	64.00	8.300	10.00
WG	1	6.400	43.60	21.40	71.30	28.70	506.8	607.0	83.50	53.00	6.300	24.00	2.800	47.00
	2	22.40	36.20	26.40	85.00	15.00	470.0	560.9	83.80	28.00	3.600	71.00	9.100	46.00
MJ	1	3.700	52.60	33.10	89.40	10.60	510.0	636.0	80.20	6.000	.7000	34.00	4.000	57.00
	2	7.700	48.00	29.30	85.00	15.00	479.1	537.0	89.20	1.000	.1000	20.00	2.500	20.00
ML	1	.5000	44.90	44.10	89.50	10.50	386.7	521.0	74.20	65.00	10.10	13.00	2.000	11.00
	2	12.60	35.80	27.40	75.80	24.20	485.5	507.1	95.70	21.00	2.600	13.00	1.600	126.0
NM	1	14.80	50.60	15.90	81.30	18.70	527.0	540.0	97.60	24.00	2.700	28.00	3.200	80.00
	2	6.800	50.00	31.70	88.40	11.60	487.0	511.0	95.30	5.000	.6000	48.00	5.900	20.00
DN	1	9.000	19.10	46.10	74.20	25.80	474.5	509.0	93.20	47.00	5.900	30.00	3.800	10.00
	2	19.40	43.90	19.10	82.40	17.60	534.0	544.0	98.20	9.000	1.000	36.00	4.000	19.00
MOD	1	7.600	34.00	19.40	61.00	39.00	480.3	520.0	92.40	41.00	5.100	17.00	2.100	22.00
	2	2.600	48.10	30.60	81.30	18.70	586.2	632.0	92.70	5.000	.5000	46.00	4.700	26.00
AR	1	2.800	44.20	29.80	76.90	23.10	485.6	589.3	82.40	35.00	4.300	37.00	4.600	64.00
	2	1.300	54.80	24.50	76.70	23.30	580.0	580.0	100.0	6.000	.6000	20.00	2.100	62.00
JS	1	4.100	47.90	27.50	79.60	20.40	433.0	460.0	94.10	4.000	.6000	57.00	7.900	32.00
	2	18.10	46.70	26.80	91.60	8.400	564.9	649.3	87.00	30.00	3.200	91.00	9.700	65.00
RW	1	5.800	23.60	38.10	67.40	32.60	433.0	441.0	98.20	8.000	1.100	15.00	2.100	.0000
	2	15.20	33.90	26.80	76.00	24.00	520.8	605.0	86.10	27.00	3.100	33.00	3.800	3.000

Subj	Study	Mvind	NO	Group	Sex	Date2	Dlay	Dlay2	NremA	Remad	ADI	NREMH
CA	1	4.100	1.000	3.000	M	30-Jun-93	25-Feb-02	.0164	11.79	27.21	99.39	9.996
	2	1.300	1.000	3.000		?	?	?????	1.757	7.843	7.566	5.431
TDC	1	5.200	2.000	3.000	F	02-Feb-93	31-Aug-01	.3260	7.128	10.98	14.29	24.31
	2	7.000	2.000	3.000		?	?	?????	.9160	10.08	8.817	10.23
JD	1	5.000	3.000	3.000	M	19-Apr-93	13-Jul-03	.0055	29.23	81.69	189.5	35.36
	2	2.400	3.000	3.000		?	?	?????	7.253	24.28	46.75	1.235
MF	1	1.800	4.000	3.000	M	01-Apr-92	20-Nov-01	.0027	18.91	68.84	123.7	21.22
	2	1.300	4.000	3.000		?	?	?????	5.404	16.71	37.02	14.12
WG	1	5.600	5.000	3.000	F	08-Apr-93	08-Oct-01	.0849	8.465	23.55	63.04	51.95
	2	5.900	5.000	3.000		?	?	?????	5.856	14.47	21.98	15.02
MJ	1	6.700	6.000	3.000	F	22-Feb-93	10-Oct-02	.1260	9.733	13.38	20.71	12.23
	2	2.500	6.000	3.000		?	?	?????	3.095	13.33	18.63	3.537
ML	1	1.700	7.000	3.000	F	25-Mar-93	14-Oct-02	.0521	16.47	28.01	33.74	31.04
	2	15.60	7.000	3.000		?	?	?????	15.17	30.61	71.49	16.31
NM	1	9.100	8.000	3.000	M	22-Jun-93	10-Nov-03	.0055	14.29	24.96	52.71	14.99
	2	2.500	8.000	3.000		?	?	?????	7.946	47.70	52.02	1.115
DN	1	1.300	9.000	3.000	F	17-Mar-93	09-Mar-03	.0027	12.45	36.70	84.23	6.650
	2	2.100	9.000	3.000		?	?	?????	4.771	20.47	35.93	18.67
MOD	1	2.700	10.00	3.000	M	13-Apr-93	26-May-03	.0329	38.29	76.56	262.4	14.13
	2	2.700	10.00	3.000		?	?	?????	4.407	34.46	66.58	.5037
AR	1	7.900	11.00	3.000	M	29-Jun-93	22-Feb-02	.2356	9.807	31.52	66.54	7.717
	2	6.400	11.00	3.000		?	?	?????	4.992	13.30	33.83	7.421
JS	1	4.400	12.00	3.000	M	11-Mar-93	02-Jan-02	.2712	7.487	34.62	56.96	5.920
	2	6.900	12.00	3.000		?	?	?????	4.639	13.87	15.25	4.292
RW	1	.0000	13.00	3.000	F	01-Mar-93	21-Mar-02	.1918	22.40	100.4	251.1	4.932
	2	.3000	13.00	3.000		?	?	?????	5.306	23.50	53.03	2.274

Subj	Study	RemHd	HDI	TRDI	TADT	THDT	TRDT	Y	rrREM	rrSWS	Sat-H	Sat-L	Sat-B	Sat-R
CA	1	16.74	75.20	153.0	18.22	20.83	39.05	1.882	20.00	19.00	97.00	88.00	94.00	9.000
	2	19.61	19.84	9.397	2.550	8.450	11.00	1.319	17.00	18.00	99.00	92.00	96.00	7.000
TDC	1	2.746	23.46	29.36	5.983	29.92	35.90	1.388	20.00	18.00	100.0	90.00	98.00	10.00
	2	6.303	14.12	11.71	1.650	15.08	16.73	1.180	18.00	18.00	100.0	91.00	98.00	9.000
JD	1	16.05	59.00	73.36	45.93	31.00	76.93	1.778	15.00	13.00	100.0	84.00	97.00	16.00
	2	14.80	25.98	14.81	13.02	5.917	18.93	1.431	17.00	15.00	99.00	93.00	98.00	6.000
MF	1	12.00	35.55	49.10	81.70	36.22	117.9	1.563	18.00	16.00	98.00	39.00	94.00	59.00
	2	60.25	129.5	34.23	12.22	50.03	62.25	2.116	20.00	14.00	99.00	76.00	95.00	23.00
WG	1	87.60	249.1	74.94	12.10	67.82	79.92	2.398	27.00	28.00	100.0	85.00	97.00	15.00
	2	20.43	36.77	22.98	6.833	23.27	30.10	1.577	24.00	28.00	100.0	90.00	98.00	10.00
MJ	1	10.04	19.94	22.12	16.00	15.53	31.53	1.321	17.00	20.00	99.00	90.00	97.00	9.000
	2	15.00	21.01	9.894	3.967	4.900	8.867	1.343	20.00	21.00	100.0	88.00	98.00	12.00
ML	1	30.96	48.77	48.72	9.633	18.60	28.23	1.697	30.00	32.00	96.00	83.00	93.00	13.00
	2	19.39	50.36	35.96	20.38	19.48	39.87	1.711	23.00	27.00	100.0	89.00	96.00	11.00
NM	1	23.08	50.18	32.80	21.13	19.12	40.25	1.709	22.00	22.00	98.00	86.00	96.00	12.00
	2	.0000	.9856	13.55	11.38	.9000	12.28	.2979	17.00	20.00	100.0	90.00	98.00	10.00
DN	1	15.66	36.93	27.69	20.33	11.43	31.77	1.579	24.00	22.00	99.00	86.00	95.00	13.00
	2	53.09	98.39	32.25	9.667	38.55	48.22	1.997	20.00	23.00	99.00	82.00	97.00	17.00
MOD	1	10.89	42.62	66.08	68.48	20.07	88.55	1.640	26.00	29.00	100.0	50.00	93.00	50.00
	2	7.110	13.41	11.77	10.02	2.117	12.13	1.159	25.00	18.00	100.0	88.00	98.00	12.00
AR	1	22.97	48.93	26.07	19.60	19.17	38.77	1.698	16.00	17.00	99.00	80.00	95.00	19.00
	2	39.91	95.69	21.93	10.23	22.32	32.55	1.985	19.00	20.00	98.00	90.00	96.00	8.000
JS	1	16.97	29.71	21.20	13.13	9.733	22.87	1.487	24.00	23.00	99.00	90.00	95.00	9.000
	2	10.08	11.93	10.20	7.633	6.383	14.02	1.112	24.00	20.00	100.0	88.00	98.00	12.00
RW	1	28.51	70.33	60.42	66.28	23.30	89.58	1.853	21.00	17.00	99.00	92.00	98.00	7.000
	2	.9592	3.728	11.64	9.467	2.400	11.87	.6747	16.00	18.00	100.0	90.00	99.00	10.00

Subj	Study	CO2-H	CO2-L	CO2-B	CO2-R	TREMa	Tnrem	Tremh	Tnrem	DOB	Age	S1-2%
CA	1	51.00	44.00	47.00	7.000	39.00	92.00	24.00	78.00	05-Apr-89	3.085	62.50
	2	55.00	40.00	49.00	15.00	6.000	11.00	15.00	34.00	05-Apr-89	4.238	68.00
TDC	1	42.00	25.00	38.00	17.00	8.000	39.00	2.000	133.0	30-Oct-86	5.600	44.70
	2	66.00	42.00	58.00	24.00	8.000	6.000	5.000	67.00	30-Oct-86	6.266	39.20
JD	1	52.00	43.00	48.00	9.000	168.0	167.0	33.00	202.0	26-Dec-88	1.784	45.80
	2	50.00	44.00	45.00	6.000	41.00	47.00	25.00	8.000	26-Dec-88	4.315	41.20
MF	1	72.00	45.00	57.00	27.00	109.0	106.0	19.00	119.0	29-Mar-85	6.126	50.80
	2	73.00	45.00	55.00	28.00	33.00	31.00	119.0	81.00	29-Mar-85	7.014	35.70
WG	1	53.00	38.00	43.00	15.00	57.00	51.00	212.0	313.0	17-Jul-90	1.959	50.00
	2	48.00	42.00	35.00	6.000	17.00	39.00	24.00	100.0	17-Jul-90	2.729	58.60
MJ	1	42.00	32.00	37.00	10.00	12.00	74.00	9.000	93.00	08-Nov-87	3.521	56.30
	2	50.00	33.00	43.00	17.00	16.00	21.00	18.00	24.00	08-Nov-87	5.296	55.70
ML	1	56.00	36.00	47.00	20.00	19.00	95.00	21.00	179.0	02-Jul-90	.9452	45.40
	2	51.00	38.00	48.00	13.00	60.00	93.00	38.00	100.0	02-Jul-90	2.732	48.40
NM	1	?????	?????	?????	?????	41.10	102.0	38.00	107.0	30-Jul-89	1.038	65.40
	2	47.00	35.00	43.00	12.00	45.00	57.00	.0000	8.000	30-Jul-89	3.899	56.80
DN	1	73.00	38.00	44.00	35.00	75.00	73.00	32.00	39.00	14-Sep-88	2.321	28.10
	2	48.00	37.00	44.00	11.00	32.00	35.00	83.00	137.0	14-Sep-88	4.507	63.30
MOD	1	63.00	45.00	50.00	18.00	239.0	187.0	34.00	69.00	17-Dec-89	.9233	41.60
	2	47.00	32.00	43.00	15.00	63.00	35.00	13.00	4.000	17-Dec-89	3.323	50.70
AR	1	45.00	35.00	36.00	10.00	59.00	61.00	43.00	48.00	11-Oct-89	2.573	47.00
	2	48.00	41.00	43.00	7.000	30.00	37.00	90.00	55.00	11-Oct-89	3.718	56.10
JS	1	46.00	38.00	41.00	8.000	51.00	43.00	25.00	34.00	26-May-90	1.789	52.00
	2	45.00	34.00	43.00	11.00	11.00	40.00	8.000	37.00	26-May-90	2.795	64.80
RW	1	53.00	42.00	48.00	11.00	236.0	109.0	67.00	24.00	11-Apr-88	3.671	29.40
	2	52.00	35.00	44.00	17.00	49.00	35.00	2.000	15.00	11-Apr-88	4.890	49.10

Subj	Study	OAI	OHI	T&A's	Dlay1	TADlay	Dlay3	Dlay4	Dlay5	Ordi	Crdi	Totc	Toto
CA	1	64.22	89.44	11-May-92	1.153	19-Feb-02	1.137	.1973	13.64	112.9	40.04	61.00	172.0
	2	.0000	31.85	?	?????	?	?????	?????	?????	7.119	2.278	16.00	50.00
TDC	1	28.48	126.2	01-Oct-92	.6658	04-May-01	.3397	3.912	4.077	26.78	2.581	16.00	166.0
	2	1.000	15.54	?	?????	?	?????	?????	?????	4.494	7.217	53.00	33.00
JD	1	162.7	136.7	10-Oct-90	2.532	25-Oct-03	2.526	.0658	30.31	60.36	13.00	101.0	469.0
	2	29.59	8.571	?	?????	?	?????	?????	?????	9.794	5.019	41.00	80.00
MF	1	105.6	102.1	14-May-91	.8877	29-Nov-01	.8849	.0329	10.62	47.01	2.086	15.00	338.0
	2	18.69	79.26	?	?????	?	?????	?????	?????	31.25	2.982	23.00	241.0
WG	1	36.97	283.4	01-Aug-92	.7699	07-Sep-01	.6849	1.019	8.219	70.56	4.380	37.00	596.0
	2	17.40	18.04	?	?????	?	?????	?????	?????	20.55	2.426	19.00	161.0
MJ	1	51.00	54.35	01-Jul-91	1.775	25-Aug-02	1.649	1.512	19.79	17.18	4.941	42.00	146.0
	2	8.877	4.250	?	?????	?	?????	?????	?????	3.507	6.387	51.00	28.00
ML	1	71.31	174.4	01-Jul-91	1.786	25-Sep-02	1.734	.6247	20.81	41.58	7.137	46.00	268.0
	2	20.62	51.36	?	?????	?	?????	?????	?????	18.66	17.30	140.0	151.0
NM	1	66.42	76.50	15-Aug-90	2.860	22-Nov-03	2.855	.0658	34.26	26.53	6.273	55.10	233.0
	2	15.74	.0000	?	?????	?	?????	?????	?????	2.957	10.60	86.00	24.00
DN	1	58.94	39.29	10-Jan-91	2.186	08-Mar-03	2.184	.0329	26.20	22.26	5.437	43.00	176.0
	2	30.36	140.0	?	?????	?	?????	?????	?????	30.56	1.685	15.00	272.0
MOD	1	183.1	63.00	01-Dec-90	2.400	14-May-03	2.367	.3945	28.41	60.34	5.746	46.00	483.0
	2	3.102	.0000	?	?????	?	?????	?????	?????	.7165	11.05	108.0	7.000
AR	1	29.11	45.08	01-Aug-92	1.145	28-Nov-01	.9096	2.827	10.92	18.04	8.031	65.00	146.0
	2	3.621	51.21	?	?????	?	?????	?????	?????	14.69	7.241	70.00	142.0
JS	1	26.49	25.97	16-Jun-92	1.005	25-Sep-01	.7342	3.255	8.811	14.13	7.067	51.00	102.0
	2	7.212	22.21	?	?????	?	?????	?????	?????	4.461	5.736	54.00	42.00
RW	1	112.2	31.73	20-Feb-92	1.219	10-Jan-02	1.027	2.301	12.33	55.43	4.988	36.00	400.0
	2	18.92	6.000	?	?????	?	?????	?????	?????	4.378	7.258	63.00	38.00

Subj	Sex	Age1	DOB	Diagnosis	Study
AA	m	1.644	12-Jun-91	CP	01-Feb-93
VA	f	15.04	25-Jan-73	OSA, Sotos syndrome	04-Feb-88
DA	m	8.756	30-Dec-83	Downs	29-Sep-92
ZA	m	1.655	17-Jul-90	Downs	12-Mar-92
AA	f	.2959	06-Aug-90	Downs/tracheobroncho	22-Nov-90
NB	m	8.907	16-May-83	Cleft palate/pharyng	09-Apr-92
JB	m	6.718	29-Dec-85	Obesity	15-Sep-92
AB	m	12.21	10-Aug-79	Obesity	21-Oct-91
LB	m	.4137	13-Jul-91	Breatholding attacks	11-Dec-91
DB	m	3.849	29-Oct-81	Pseudohypoparathyroi	08-Nov-90
SB	m	10.38	30-Aug-82	Schprintzen	14-Jan-93
NB	m	7.781	14-Jul-84	Noonan's/Rvocalcordp	23-Apr-92
FC	m	1.770	03-Jun-91	Ex-premature	10-Mar-93
AC	m	3.337	07-Jun-89	Albrights osteodystr	07-Oct-92
CC	m	1.981	25-Nov-89	Laryngomalacia	18-Nov-91
SC	f	4.274	26-Nov-87	CP	04-Mar-92
CC	f	2.145	21-Sep-90	Goldenhaar	12-Nov-92
SD	m	12.92	03-Jul-78	Marfans	02-Jun-91
RE	f	1.384	07-Jan-91	CNLD/Respiratory fai	26-May-92
ME	f	6.115	03-Mar-87	Achondroplasia	12-Apr-93
NF	m	.1945	30-Sep-91	C hypoventilation	10-Dec-91
CF	f	8.367	24-Feb-84	Spina bifida/scolios	05-Jul-92
MF	m	6.132	29-Mar-85	T&A hypertrophy	13-May-91
RG	m	.9808	27-Dec-90	T&A hypertrophy	20-Dec-91
SG	m	1.923	28-Dec-88	Tetralogy/BPD	30-Nov-90
AH	m	11.95	27-Mar-81	Devel delay	04-Mar-93
AH	m	3.189	16-May-89	Spina bifida	23-Jul-92
RH	m	13.60	30-Jan-72	Laryngeal nerve pals	03-Sep-85
MH	m	5.921	21-Dec-86	T&A hypertrophy	20-Nov-92
SH	m	2.323	04-Jul-88	Achondroplasia	30-Oct-90
KH	f	8.690	21-Aug-84	Crouzon's	28-Apr-93
TH	m	1.112	23-Oct-90	T&A hypertrophy/asth	03-Dec-91
BJ	m	9.707	09-Sep-77	Developmental delay	23-May-87
CJ	f	.5562	26-Apr-91	Trisomy 18	15-Nov-91
JK	m	3.238	09-Jun-88	Achondroplasia	04-Sep-91
NK	m	1.427	08-Sep-87	Achondroplasia	10-Feb-89
RK	f	1.027	16-Nov-91	Achondroplasia	25-Nov-92
SK	f	.1260	14-Feb-92	Desbuquois syndrome	15-Oct-92
BK	m	4.090	08-Sep-87	T&A hypertrophy	09-Oct-91
HL	f	6.123	16-Dec-85	Aperts	29-Jan-92

Subj	Sex	Age1	DOB	Diagnosis	Study
TL	m	15.27	03-Sep-74	Pseudohypoparathyoi	07-Dec-89
JL	m	14.53	15-Oct-76	CF, behaviour prob.	24-Apr-91
AL	f	12.26	15-Nov-77	Rhinotricophalangeal	14-Feb-90
ENM	f	4.258	06-Jan-88	Neurofibroma	08-Apr-92
MM	f	.0877	28-Mar-93	Spina bifida	29-Apr-93
PM	m	2.600	16-Jul-87	Foetal dilantin synd	10-Mar-88
DM	m	3.164	22-Feb-90	CNLD / interstitial	22-Apr-93
LM	m	11.67	27-Mar-81	Obesity	25-Nov-92
KN	f	11.63	15-Aug-81	DIDMODE	31-Mar-93
GN	m	11.98	12-Jun-80	Osteogenesis Imperfe	01-Jun-92
MOD	m	.9233	17-Dec-89	T&A hypertrophy	19-Nov-90
AO	m	2.556	21-May-90	Spina bifida	09-Dec-92
AO	m	3.189	02-Sep-89	T&A hypertrophy (acu	12-Aug-92
CO	m	6.129	16-May-86	T&A hypertrophy	30-Jun-92
FP	f	1.726	20-Sep-90	Achondroplasia	11-Jun-92
PP	f	.4849	18-Nov-91	CNLD	13-May-92
TP	f	2.712	20-Aug-89	Spina bifida	06-May-92
LR	m	.7945	09-Sep-91	T&A hypertrophy	25-Jun-92
WR	m	12.12	27-Oct-67	Fragile X	05-Dec-79
AR	m	1.838	26-Jan-90	T&A hypertrophy	25-Nov-91
NR	m	.9699	14-Jul-90	Tracheomalacia (seve	03-Jul-91
SR	f	3.033	18-Feb-86	Achondroplasia	01-Mar-89
DS	m	12.22	30-Aug-74	Morquio's	14-Nov-86
NS	f	11.61	14-Dec-80	T&A hypertrophy	20-Jul-92
PS	m	7.378	07-Nov-85	Obese	23-Mar-93
HS	m	.9315	14-Mar-92	CP	17-Feb-93
SS	m	7.063	15-Sep-85	Cleft lip/palate (bi	06-Oct-92
DS	m	5.474	05-Dec-86	T&A hypertrophy/MVal	25-May-92
MT	m	4.351	16-Sep-87	T&A hypertrophy	21-Jan-92
BT	m	.0329	20-Mar-93	Spina bifida	29-Mar-93
PT	m	11.40	24-Dec-81	Obese	17-May-93
KT	f	.8411	29-Sep-91	CP	01-Aug-92
AU	m	6.540	20-Apr-82	Crouzons	01-Sep-88
DW	m	14.91	09-Sep-77	CF	02-Aug-92
JW	f	8.718	26-Mar-82	Hurlers	11-May-90
EW	m	13.67	05-Aug-79	Obese	01-Apr-93
TW	m	.8795	07-May-92	Choanal stenosis	24-Mar-93
MW	m	5.512	06-Nov-84	Vocal cord paresis	11-May-90
DW	m	15.32	23-Aug-73	Aperts	14-Dec-88
JY	m	1.405	20-Jun-89	T&A hypertrophy	15-Nov-90

	Explntn	Masktype	Notes	Current	Synd	Cause
AA	O2 only	Paed C	Trial in Hunter Baillie ward while in-patient; for training	f	N	B
VA	still	A	Good response to CPAP remains on treatment 7 years	y	S	T
DA	O2 only	B	Behavioural - would not tolerate masks, Rx not initiated, home on O2	f	S	B
ZA	O2 only	Paed C	Behavioural - unsuccessful pre-op T&A's.	f	S	B
AA	age	Prongs	Off CPAP 4-dec-92:Normal sleep study 30-4-92, CO2 45-51 - Wait & see	n	S	G
NB	still	?	CPAP commenced Melbourne, Tracheal fistula	y	M	T
JB	still	B	Post T&A's. Variable compliance, 48 kg, needs follow up	y	O	T
AB	wt loss	?	Stopped CPAP Sept 1992.	n	O	R
LB	T&A	Paed C	Adenoidectomy16-12-91:6.5 cm post-op Home1-92 w/o CPAP(mother):study 25-6-92	n	TA	R
DB	better study	B	Adenoids 10/90,T&A's oct'86,cease CPAP10/92,seizures during study	n	S	G
SB	still	A	Stabilised on CPAP, mother -> new chin strap.	y	S	T
NB	still	Paed C	Tolerating CPAP well	y	S	T
FC	T&A	Paed C	Adenoidectomy 21-jul-92, T&A's 10-Apr-93	n	R	R
AC	still	Paed C	Slow to tolerate CPAP, T&A's Nov 92, 31.12.92 training well 4 hrs per night	y	S	T
CC	failed	Paed C	Not attempted by parents ? why	f	R	B
SC	died	Paed bubble	Died after using CPAP palliative care,easier nursing, approx date death Sep	d	N	T
CC	still	Paed C	Residual symptoms post T&A's but some significant improvement. Trial CPAP	y	S	T
SD	still (offtestos	A	Apnoea worse with Testosterone therapy. Stopped treatment and apnoea.	y	S	T
RE	parents stopped	Paed bubble	Unsuccessful in long term/unable to wear mask over nasal prong/parents choice	n	R	Q
ME	training	Paed C	Multiple studies. T&A's before CPAP, submucous cleft palate/achondroplasia	t	S	ND
NF	died	Paed	Home on CPAP, refused second study, died Mar 92	d	R	T
CF	still	?	Home on CPAP tolerated well	y	M	T
MF	still	B	Mesam diagnosis 10-5-91 RPAH,rpt study 13-10-92 5cm	y	TA	T
RG	T&A	Paed C	Adenoidectomy Dec91,started CPAP in HB,difficult at home,7/92 off CPAP after	n	TA	R
SG	still	Prongs, now Paed C	10/2/91 11cm 0.5L,off O2 July 92, 6.5cm Dec 92	y	M	T
AH	fail/behaviour	B	Short limbed dwarf, laryngeal web, post tracheostomy. In patient to start.	n	N	B
AH	in training	Paed C	Diagnosis 23-jul-92, in training	t	M	ND
RH	graft Dec 89	A	Tolerated CPAP well for ~4 years (started at 12) Off CPAP Nov91 Post-op	n	R	R
MH	T&A	B	Bad apnoea with CO2 retention, pectus and nocturnal enuresis, Pre-op CPAP	n	TA	R
SH	ICP	Paed C	T's dec 90, no change, CPAP stopped Oct92 raised ICP	n	S	R
KH	mask training	B bubble	Past adenotonsillectomy and UPPP	t	S	ND
TH	T&A	Paed C	T&A's HB 12/91, CPAP Pre-peri and post-op until discharge	n	TA	R
BJ	restrt 1-12-92	A	CPAP re-do 1-sep-92, secondary hypoventilation initially	y	N	T

	Explntn	Masktype	Notes	Current	Syndr	Cause
CJ	died	Paed bubble	Died 7-jul-92, CPAP well tolerated (palliative)	d	S	T
JK	still	Paed C	Post T&A 17-dec-92 persistent partial obs. 6/92 apnoea, machine 28-jul-92	y	S	T
NK	still	Paed C	T&A's 25.1.89, Repeat study 3-12-90, REM co2 up to 56, awake gas 40 mmHG.	y	S	T
RK	still	Paed C	Dx study,presented with burns&respiratory failure 6/12 later.CPAP as inpatient	y	S	T
SK	improved	Paed C	Skeletal dyspl. & severe cervical spine deformity, cleft, progressive OSA	n	S	G
BK	T&A	Paed C	Tolerated poorly pre T&A,not on CPAP post-op, mild to mod OSA persists	n	TA	R
HL	restart	Paed C	CPAP education and trial successful. Retry because of inadvertent high pressure	n	S	C
TL	still	A	Tolerates CPAP well	y	S	T
JL	died	A	Required oxygen as well as CPAP - stable on CPAP at present.	d	N	T
AL	still	Respironics Paed	CPAP 9cm mar 92	y	S	T
ENM	still	B	Home on CPAP - parents say tolerating well. CPAP PD unsuccessful study.	y	S	T
MM	still	Infant	Disorganised breathing and bulbar symptoms	y	M	T
PM	still	Paed C	Last study 24-nov-92, 11 cm no O2, am ABG CO2 49	y	S	T
DM	still	Paed C	OSA, interstitial lung disease. Lung biopsy, ? transplant. Trial CPAP.	y	R	T
LM	still	A	Hypertensive, far West/ Nyngan	Y	O	T
KN	still	A	Diabetes inspidus, diabetes mellitus, obese, hypothalamic. Bro. ventilated	y	S	T
GN	died	A bubble	Died first week sept 92	d	S	T
MOD	T&A	Paed C	CPAP pre-adenotonsillectomy	n	TA	R
AO	mask 14-12-92	Paed C	In training 9-Dec-92	t	M	ND
AO	failed 12-8-92	Paed C	Unsuccessful in ward (Clubbe)	f	TA	Q
CO	T&A	A	T&A 10-9-92 Repeat study NAD	n	TA	R
FP	training mask	Paed C	20-11-92 not doing well, still encouraging to wear mask. Mod persis OSA	t	S	ND
PP	died	C bubble	Died in HB 28-7-92.	d	R	T
TP	failed	Paed C	Training aborted 20-11-92 Parents request	f	M	Q
LR	nose treated	Paed C	Off CPAP 30-11-92, profuse nasal discharge	n	TA	R
WR	still	A	24-Aug-91 10 cm repeat study. Fits, ongoing CPAP therapy.	y	S	T
AR	T&A	Paed C	CPAP post T&A then discharged without CPAP	n	TA	R
NR	age	Prongs + Paed	Compliance variable, CPAP stopped March 92 Dr.Rossier,Inpatient trial B 12/	n	R	G
SR	failed	Nazih	Trial CPAP in LTICU unsuccessful	f	S	B
DS	died	A	Morquio's, kyphosis, IPPV trial initially because of respiratory failure	d	S	T
NS	T&A	A	Cured by T's and A's, obesity also a factor	n	TA	R
PS	mask training	B	Small mid-face, obese, T&A's at 3 yrs, A's at 5 years.	t	O	ND
HS	mother no	Paed C	Cerebral palsy with fits,obstruction,arousals. Started in hospital.	n	N	Q
SS	T&A	B	Pre-operative CPAP, F/U post T's & A's no longer needs CPAP	n	M	R

	Explntn	Masktype	Notes	Current	Syndr	Cause
DS	doctor	B	On Warfarin, Prof. Beveridge ceased CPAP	n	TA	C
MT	still	Paed C	4-Nov-92 remains on 8cm	y	TA	T
BT	still	infant	Started in Grace. Disorganised breathing.	y	M	T
PT	T&A	B bubble	Obese, one of twins. Pre-operative CPAP.	n	O	R
KT	trial went off	C bubble	Unable to tolerate CPAP because of desaturation and destabilisation of resp.	f	N	C
AU	still	A	Mid face advancement Nov91, off CPAP 3-jun-92 until 14/9/92 at our request-	y	S	T
DW	died	B	Died in Hall ward 8-dec-92. Repeat PD 19-nov-92, 10cm. 4 litres O2	d	R	T
JW	failed	Training only frame	Tolerated mask, but unable to tolerate CPAP. discontinued	f	S	B
EW	mask training	B	Obese, post-adenotonsillectomy.	t	O	ND
TW	still	C bubble	ALTE's during wake-sleep transition. Post tracheostomy. Choanal stenosis.	y	M	T
MW	still	B bubble	8cm 26-4-91:14.5cm 3-aug-92	y	R	T
DW	failed	old adult	Unable to tolerate CPAP	f	S	Q
JY	T&A	Paed C	Asthma and upper airway obstruction. Rx one week pre-op in hospital. NO RV	n	TA	R

d. CHANGES IN SLEEP AND BREATHING ON NASAL CPAP

Subj	Study	Date	Totca	Totca	Totoa	Totoa	Mvind	NO	GROUP	NREMA	REMAD	ADI	NREMH
JB	1	14-Sep-92	16.00	110.0	26.00	170.0	.6000	1.000	1.000	5.731	14.89	15.25	20.60
	2	15-Sep-92	4.000	25.00	4.000	40.00	.5000	1.000	1.000	1.364	7.792	13.11	1.212
AB	1	31-Oct-91	.0000	.0000	225.0	3201.	8.900	1.000	2.000	38.38	219.7	88.90	11.60
	2	09-Mar-92	9.000	78.00	.0000	.0000	2.100	1.000	2.000	2.349	3.448	6.704	3.132
SB	1	14-Jan-93	86.00	1041.	1.000	4.000	19.60	2.000	2.000	17.64	15.59	42.31	15.89
	2	04-Feb-93	149.0	1447.	.0000	.0000	3.600	2.000	2.000	20.10	20.50	49.52	1.889
NB	1	23-Apr-92	13.00	131.0	26.00	345.0	.4000	3.000	2.000	6.152	14.60	16.55	15.16
	2	22-Jul-92	27.00	265.0	.0000	.0000	.4000	3.000	2.000	4.074	10.95	23.19	2.716
SC	1	04-Mar-92	5.000	38.00	37.00	281.0	.9000	4.000	2.000	7.079	25.96	66.17	6.607
	2	11-Mar-92	14.00	125.0	5.000	30.00	.2000	4.000	2.000	3.736	17.65	21.14	.1868
SD	1	13-Aug-91	12.00	108.0	45.00	530.0	.7000	2.000	1.000	9.293	12.82	19.15	44.84
	2	03-Sep-91	9.000	85.00	3.000	22.00	2.000	2.000	1.000	2.637	7.287	11.14	.3766
MF	1	13-May-91	14.00	219.0	91.00	1747.	1.800	5.000	2.000	18.91	68.84	123.7	21.22
	2	13-May-92	7.000	78.00	.0000	.0000	.7000	5.000	2.000	1.612	15.86	24.28	4.299
CG	1	23-Apr-92	.0000	.0000	12.00	136.0	2.700	3.000	1.000	2.045	6.366	9.684	3.238
	2	24-Apr-92	4.000	30.00	1.000	7.000	1.500	3.000	1.000	1.063	3.704	3.907	1.489
HL	1	29-Jan-92	13.00	104.0	18.00	219.0	1.000	6.000	2.000	4.044	14.06	18.55	17.22
	2	22-Apr-92	24.00	213.0	2.000	15.00	3.400	6.000	2.000	3.633	9.123	19.88	3.354
AL	1	14-Feb-90	50.00	390.0	5.000	32.00	2.400	7.000	2.000	8.472	9.462	28.27	10.74
	2	24-Mar-92	3.000	22.00	21.00	134.0	.9000	7.000	2.000	3.833	1.835	4.526	.3194
ENM	1	08-Apr-92	12.00	63.00	5.000	38.00	6.100	8.000	2.000	2.464	35.40	43.16	8.007
	2	15-Jul-92	28.00	162.0	.0000	.0000	4.900	8.000	2.000	5.184	9.335	15.26	2.036
LM	1	25-Nov-92	1.000	12.00	28.00	211.0	.6000	4.000	1.000	5.166	10.45	11.61	11.94
	2	26-Nov-92	6.000	61.00	.0000	.0000	.0000	4.000	1.000	.9724	11.19	5.907	.0000
DS	1	25-May-92	23.00	153.0	26.00	185.0	2.100	9.000	2.000	6.161	9.669	23.94	8.298
	2	15-Jul-92	21.00	231.0	2.000	13.00	1.200	9.000	2.000	3.128	2.556	6.598	1.043
PT	1	17-May-93	2.000	15.00	112.0	1124.	20.70	5.000	1.000	32.24	26.00	54.07	57.95
	2	18-May-93	17.00	120.0	.0000	.0000	2.400	5.000	1.000	2.437	20.67	32.02	8.170
AU	1	04-Mar-92	1.000	17.00	8.000	52.00	1.000	10.00	2.000	1.870	10.12	17.44	3.926
	2	14-Sep-92	6.000	65.00	4.000	33.00	3.700	10.00	2.000	1.852	8.920	16.49	.7124
DW	1	03-Aug-92	6.000	43.00	1.000	5.000	2.500	6.000	1.000	1.565	.0000	1.254	5.671
	2	04-Aug-92	3.000	26.00	1.000	5.000	3.100	6.000	1.000	.6940	3.081	4.567	2.256
TW	1	24-Mar-93	59.00	400.0	17.00	75.00	16.30	11.00	2.000	10.92	18.25	58.98	3.551
	2	05-Apr-93	46.00	286.0	3.000	20.00	10.60	11.00	2.000	8.894	32.48	108.7	5.514
MW	1	11-May-90	22.00	1.000	8.000	.0000	9.400	12.00	2.000	4.060	.6390	4.350	17.05
	2	03-Aug-92	37.00	325.0	.0000	.0000	3.500	12.00	2.000	5.652	11.30	17.81	.4582

Subj	Study	Totma	Totma	Totch	Totch	Totoh	Totoh	Totmh	Totmh	Remca	Remca	Remoa	Remoa	Remma
JB	1	.0000	.0000	8.000	60.00	135.0	1140.	8.000	63.00	3.000	15.00	7.000	43.00	.0000
	2	1.000	10.00	.0000	.0000	7.000	45.00	1.000	10.00	9.000	48.00	2.000	16.00	1.000
AB	1	.0000	.0000	.0000	.0000	67.00	992.0	1.000	27.00	.0000	.0000	52.00	689.0	.0000
	2	.0000	.0000	10.00	125.0	.0000	.0000	2.000	5.000	5.000	41.00	.0000	.0000	.0000
SB	1	14.00	173.0	14.00	183.0	8.000	82.00	69.00	1039.	20.00	166.0	7.000	60.00	2.000
	2	.0000	.0000	14.00	136.0	.0000	.0000	.0000	.0000	33.00	298.0	.0000	.0000	.0000
NB	1	4.000	64.00	.0000	.0000	102.0	1565.	4.000	72.00	7.000	49.00	4.000	60.00	.0000
	2	.0000	.0000	15.00	161.0	.0000	.0000	3.000	29.00	20.00	189.0	.0000	.0000	.0000
SC	1	3.000	30.00	.0000	.0000	39.00	303.0	3.000	41.00	8.000	41.00	51.00	262.0	2.000
	2	1.000	7.000	1.000	12.00	.0000	.0000	.0000	.0000	18.00	99.00	.0000	.0000	.0000
SD	1	.0000	.0000	.0000	.0000	272.0	4426.	3.000	32.00	3.000	28.00	7.000	85.00	1.000
	2	2.000	20.00	1.000	8.000	1.000	12.00	.0000	.0000	8.000	81.00	1.000	15.00	.0000
MF	1	1.000	12.00	1.000	15.00	100.0	1428.	18.00	263.0	.0000	.0000	105.0	2824.	4.000
	2	2.000	23.00	.0000	.0000	3.000	35.00	21.00	274.0	20.00	156.0	2.000	21.00	1.000
CG	1	.0000	.0000	.0000	.0000	16.00	224.0	3.000	26.00	4.000	33.00	4.000	52.00	.0000
	2	.0000	.0000	.0000	.0000	3.000	31.00	4.000	43.00	2.000	19.00	1.000	7.000	.0000
HL	1	.0000	.0000	3.000	33.00	122.0	1392.	7.000	77.00	7.000	51.00	6.000	87.00	2.000
	2	.0000	.0000	4.000	36.00	18.00	218.0	2.000	18.00	17.00	143.0	.0000	.0000	.0000
AL	1	1.000	12.00	2.000	22.00	61.00	667.0	8.000	79.00	20.00	141.0	2.000	31.00	.0000
	2	.0000	.0000	.0000	.0000	2.000	17.00	.0000	.0000	1.000	6.000	.0000	.0000	.0000
ENM	1	3.000	23.00	.0000	.0000	57.00	524.0	8.000	68.00	38.00	191.0	3.000	33.00	.0000
	2	.0000	.0000	4.000	27.00	6.000	47.00	1.000	8.000	11.00	58.00	.0000	.0000	.0000
LM	1	.0000	.0000	.0000	.0000	64.00	959.0	3.000	32.00	.0000	.0000	7.000	79.00	.0000
	2	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	1.000	5.000	.0000	.0000
DS	1	.0000	.0000	2.000	16.00	60.00	614.0	4.000	38.00	5.000	32.00	13.00	111.0	1.000
	2	1.000	15.00	6.000	52.00	.0000	.0000	2.000	18.00	3.000	22.00	1.000	9.000	.0000
PT	1	103.0	1157.	.0000	.0000	297.0	3091.	93.00	1068.	1.000	8.000	24.00	283.0	1.000
	2	.0000	.0000	11.00	114.0	.0000	.0000	46.00	476.0	30.00	175.0	.0000	.0000	.0000
AU	1	1.000	15.00	2.000	19.00	18.00	189.0	1.000	6.000	5.000	45.00	10.00	60.00	1.000
	2	3.000	30.00	2.000	33.00	2.000	27.00	1.000	13.00	7.000	42.00	6.000	42.00	2.000
DW	1	1.000	6.000	11.00	90.00	5.000	36.00	13.00	113.0	.0000	.0000	.0000	.0000	.0000
	2	.0000	.0000	9.000	96.00	4.000	25.00	.0000	.0000	4.000	21.00	.0000	.0000	.0000
TW	1	7.000	47.00	13.00	78.00	7.000	59.00	7.000	50.00	38.00	197.0	12.00	169.0	1.000
	2	1.000	5.000	10.00	85.00	.0000	.0000	21.00	199.0	94.00	567.0	5.000	32.00	4.000
MW	1	.0000	.0000	.0000	.0000	124.0	1855.	2.000	22.00	1.000	8.000	.0000	.0000	.0000
	2	.0000	.0000	.0000	.0000	3.000	26.00	.0000	.0000	12.00	112.0	1.000	12.00	.0000

Subj	Study	Remma	Remch	Remch	Remoh	Remoh	Remmh	Remmh	Twt	Ts1	Ts2	Tsws	Tnrem	TRem
JB	1	.0000	.0000	.0000	19.00	174.0	5.000	47.00	5.000	97.30	218.7	123.7	439.7	40.30
	2	8.000	1.000	6.000	4.000	33.00	1.000	10.00	48.60	44.70	141.1	210.2	396.0	92.40
AB	1	.0000	.0000	.0000	27.00	418.0	.0000	.0000	1.100	6.700	307.7	37.30	351.7	14.20
	2	.0000	1.000	5.000	9.000	73.00	3.000	33.00	188.1	3.000	97.60	129.3	229.9	87.00
SB	1	33.00	3.000	24.00	3.000	55.00	2.000	42.00	76.90	65.60	151.5	126.5	343.6	111.6
	2	.0000	1.000	11.00	1.000	15.00	1.000	10.00	39.80	26.90	265.7	152.1	444.7	96.60
NB	1	.0000	.0000	.0000	26.00	464.0	1.000	9.000	62.40	25.60	318.8	75.00	419.4	45.20
	2	.0000	3.000	27.00	.0000	.0000	1.000	10.00	58.80	24.90	221.2	151.4	397.6	109.6
SC	1	19.00	.0000	.0000	33.00	221.0	.0000	.0000	3.700	62.60	265.5	53.30	381.4	141.0
	2	.0000	2.000	16.00	.0000	.0000	.0000	.0000	92.50	61.90	188.4	71.00	321.2	61.20
SD	1	12.00	.0000	.0000	20.00	301.0	.0000	.0000	41.50	43.50	209.8	117.7	368.0	51.50
	2	.0000	4.000	39.00	.0000	.0000	2.000	27.00	24.30	2.900	Q130.6	185.1	318.6	74.10
MF	1	100.0	.0000	.0000	15.00	392.0	4.000	75.00	114.6	63.50	14.70	117.3	336.4	95.00
	2	14.00	2.000	19.00	4.000	50.00	.0000	.0000	126.0	18.00	143.0	174.0	335.0	87.00
CG	1	.0000	2.000	14.00	6.000	110.0	6.000	71.00	104.5	19.00	180.2	152.9	352.1	75.40
	2	.0000	2.000	18.00	.0000	.0000	3.000	29.00	71.40	39.70	133.8	108.6	282.1	48.60
HL	1	22.00	.0000	.0000	16.00	209.0	12.00	134.0	60.10	99.10	142.1	218.7	459.9	64.00
	2	.0000	3.000	42.00	.0000	.0000	.0000	.0000	12.90	58.40	157.3	213.7	429.4	111.8
AL	1	.0000	1.000	12.00	91.00	830.0	12.00	150.0	13.00	5.000	162.4	229.2	396.6	139.5
	2	.0000	.0000	.0000	1.000	9.000	.0000	.0000	69.60	43.80	62.10	269.9	375.7	32.70
ENM	1	.0000	2.000	15.00	74.00	1030.	3.000	131.0	32.50	13.00	267.6	206.4	487.1	69.50
	2	.0000	12.00	83.00	.0000	.0000	1.000	7.000	122.2	21.90	167.1	135.2	324.1	70.70
LM	1	.0000	.0000	.0000	47.00	855.0	1.000	13.00	20.90	91.90	175.3	69.60	336.8	40.20
	2	.0000	.0000	.0000	.0000	.0000	.0000	.0000	42.90	42.80	203.0	124.4	370.2	26.80
DS	1	12.00	2.000	13.00	94.00	926.0	5.000	58.00	32.90	61.90	227.2	188.1	477.2	117.9
	2	.0000	3.000	32.00	.0000	.0000	.0000	.0000	4.800	44.70	253.1	162.5	460.3	93.90
PT	1	5.000	.0000	.0000	12.00	145.0	9.000	103.0	93.20	93.10	1519.	151.3	403.8	60.00
	2	.0000	14.00	126.0	.0000	.0000	5.000	56.00	31.30	29.60	224.4	164.6	418.6	87.10
AU	1	11.00	1.000	12.00	25.00	329.0	2.000	35.00	59.20	52.10	134.7	134.0	320.9	94.90
	2	17.00	1.000	8.000	.0000	.0000	1.000	16.00	15.00	56.00	208.9	156.2	421.1	100.9
DW	1	.0000	3.000	30.00	7.000	65.00	9.000	68.00	41.20	22.70	146.6	137.5	306.8	76.00
	2	.0000	4.000	32.00	8.000	54.00	.0000	.0000	92.40	16.30	122.3	207.1	345.8	77.90
TW	1	8.000	4.000	22.00	5.000	29.00	23.00	141.0	19.10	106.5	203.9	145.7	456.2	167.7
	2	34.00	8.000	56.00	7.000	64.00	4.000	42.00	111.5	75.50	137.5	124.3	337.3	190.3
MW	1	.0000	.0000	.0000	20.00	376.0	39.00	506.0	61.70	38.90	274.2	130.4	443.4	93.90
	2	.0000	.0000	.0000	.0000	.0000	.0000	.0000	61.20	78.70	237.3	76.80	392.8	69.00

Subj	Study	S1%	S2%	SWS%	Nrem%	Rem%	Tst	Tstdy	Effic	Sighs	Siind	Arous	Arind	Moves
JB	1	20.30	45.60	25.80	91.60	8.400	480.0	485.0	99.00	9.000	1.100	42.00	5.300	5.000
	2	9.100	28.90	43.00	81.10	18.90	488.4	537.0	91.00	6.000	.7000	20.00	2.500	4.000
AB	1	1.800	84.10	10.30	96.10	4.000	365.9	367.0	99.70	.0000	.0000	67.00	11.00	54.00
	2	1.000	30.80	40.80	72.50	27.50	316.9	505.0	62.80	10.00	1.900	46.00	8.700	11.00
SB	1	14.40	33.30	27.80	75.50	24.50	455.2	532.0	85.60	24.00	3.200	76.00	10.00	149.0
	2	5.000	49.10	28.10	82.20	17.80	541.2	581.0	93.20	5.000	.6000	55.00	6.100	32.00
NB	1	5.500	68.60	16.10	90.30	9.700	464.6	527.0	88.20	9.000	1.200	43.00	5.600	3.000
	2	4.900	43.60	29.90	78.40	21.60	507.2	566.0	89.60	21.00	2.500	85.00	10.10	3.000
SC	1	12.00	50.80	10.20	73.00	27.00	522.3	526.0	99.30	6.000	.7000	12.00	1.400	8.000
	2	16.20	49.20	18.60	84.00	16.00	382.5	475.0	80.50	11.00	1.700	25.00	3.900	1.000
SD	1	10.40	50.00	27.30	87.70	12.30	419.5	461.0	91.00	.0000	.0000	91.00	13.00	5.000
	2	.7000	33.20	47.10	81.10	18.97	392.7	417.0	94.20	2.000	.3000	19.00	2.900	13.00
MF	1	14.70	36.10	27.20	78.00	22.00	431.4	546.0	79.00	14.00	1.900	35.00	4.900	13.00
	2	4.300	33.90	41.20	79.40	20.60	422.0	548.0	77.00	3.000	.4000	24.00	3.400	5.000
CG	1	4.400	42.20	35.80	82.40	17.60	427.5	532.0	80.40	1.000	.1000	41.00	5.800	19.00
	2	12.00	40.50	32.80	85.30	14.70	330.6	402.0	82.30	3.000	.5000	50.00	9.100	8.000
HL	1	18.90	27.01	41.70	87.80	12.20	523.9	584.0	89.77	71.00	8.100	49.00	5.600	9.000
	2	10.80	29.10	39.50	79.30	20.70	541.1	554.0	97.70	16.00	1.800	35.00	3.900	31.00
AL	1	.9000	30.30	42.80	74.00	26.07	536.0	549.0	97.60	37.00	4.100	29.00	3.200	21.00
	2	10.70	15.20	66.10	92.00	8.000	408.4	477.0	85.60	5.000	.7000	57.00	8.400	6.000
ENM	1	2.400	48.10	37.10	87.50	12.50	556.5	589.0	94.50	22.00	2.400	62.00	6.700	57.00
	2	5.500	42.30	34.20	82.10	17.90	394.8	517.0	76.40	9.000	1.400	43.00	6.500	32.00
LM	1	24.40	46.50	18.50	89.30	10.70	377.1	398.0	94.70	12.00	1.900	69.00	11.00	4.000
	2	10.80	55.10	31.30	93.20	6.800	397.1	440.0	90.20	6.000	.9000	38.00	5.700	.0000
DS	1	10.40	38.20	31.60	80.20	19.80	595.1	628.0	94.80	11.00	1.100	97.00	9.800	21.00
	2	8.100	45.70	29.30	83.10	16.90	554.2	559.0	99.10	16.00	1.700	61.00	6.600	11.00
PT	1	20.10	34.40	32.60	87.10	12.97	463.8	557.0	83.30	37.00	4.800	120.0	15.50	160.0
	2	5.800	44.40	32.50	82.80	17.20	505.7	537.0	94.20	25.00	3.000	27.00	3.200	20.00
AU	1	12.50	32.40	32.20	77.30	22.80	415.8	475.0	87.50	17.00	2.500	51.00	7.400	7.000
	2	10.70	40.00	29.90	80.70	19.30	522.0	537.0	97.20	16.00	1.800	44.00	5.000	32.00
DW	1	5.900	38.30	35.90	80.10	19.90	382.9	424.1	90.30	27.00	4.200	21.00	3.300	16.00
	2	3.900	28.90	48.90	81.60	18.40	423.6	516.0	82.10	49.00	6.900	27.00	3.800	22.00
TW	1	17.10	32.70	23.40	73.10	26.90	623.8	643.0	97.00	365.0	35.10	38.00	3.700	169.0
	2	14.30	26.10	23.60	63.90	36.70	527.6	639.0	82.60	311.0	35.40	.0000	.0000	93.00
MW	1	7.200	51.00	24.30	82.50	17.50	537.3	599.0	89.70	34.00	3.800	23.00	2.600	84.00
	2	17.00	51.40	16.60	85.10	14.90	461.8	523.0	88.30	13.00	1.700	1.400	13.50	27.00

Subj	Study	REMHD	HDI	TRDI	TADT	THDT	TRDT	Y	RRREM	RRSWS	SAT-H	SAT-L	SAT-B	SAT-R
JB	1	35.73	42.88	28.38	5.633	24.73	30.37	13.00	32.00	23.00	99.00	86.00	97.00	13.00
	2	3.896	6.983	4.300	2.450	1.733	4.183	9.000	25.00	21.00	99.00	90.00	98.00	9.000
AB	1	114.1	38.15	61.00	64.83	23.95	88.78	13.00	14.00	17.00	97.00	84.00	94.00	13.00
	2	8.966	15.27	7.384	1.983	4.017	6.000	4.000	15.00	14.00	100.0	96.00	98.00	4.000
SB	1	4.301	19.99	30.18	24.62	23.75	48.37	4.000	14.00	16.00	100.0	96.00	98.00	4.000
	2	1.863	4.552	22.06	29.08	2.867	31.95	8.000	17.00	12.00	100.0	92.00	98.00	8.000
NB	1	35.84	40.69	24.15	10.82	35.17	45.98	26.00	12.00	15.00	100.0	74.00	99.00	26.00
	2	2.190	6.129	8.162	7.567	3.783	11.35	2.000	12.00	17.00	100.0	98.00	98.00	2.000
SC	1	14.04	37.82	20.79	11.18	9.417	20.60	4.000	19.00	19.00	100.0	96.00	98.00	4.000
	2	1.961	2.157	6.431	4.350	.4667	4.817	9.000	13.00	18.00	99.00	90.00	99.00	9.000
SD	1	23.30	59.33	51.92	12.72	79.32	92.03	9.000	15.00	16.00	99.00	90.00	95.00	9.000
	2	4.858	6.306	4.736	3.717	1.433	5.150	6.000	15.00	15.00	98.00	92.00	94.00	6.000
MF	1	12.00	35.55	49.10	81.70	36.22	117.9	59.00	18.00	15.00	98.00	39.00	94.00	59.00
	2	4.138	9.412	8.815	4.867	6.300	11.17	8.000	18.00	15.00	100.0	92.00	98.00	8.000
CG	1	11.14	16.67	7.439	3.683	7.417	11.10	12.00	25.00	18.00	99.00	87.00	97.00	12.00
	2	6.173	6.270	3.630	1.050	2.017	3.067	8.000	17.00	14.00	100.0	92.00	96.00	8.000
HL	1	26.25	43.12	23.59	8.050	30.75	38.80	8.000	14.00	14.00	98.00	90.00	95.00	8.000
	2	1.610	5.661	7.762	6.183	5.233	11.42	14.00	14.00	11.00	99.00	85.00	99.00	14.00
AL	1	44.73	111.9	28.32	10.10	29.33	39.43	21.00	20.00	20.00	97.00	76.00	94.00	21.00
	2	1.835	1.294	4.114	2.700	.4333	3.133	12.00	17.00	17.00	100.0	88.00	99.00	12.00
ENM	1	68.20	86.01	22.10	5.800	29.47	35.27	3.000	23.00	19.00	99.00	96.00	98.00	3.000
	2	11.03	14.67	9.574	3.667	2.867	6.533	11.00	21.00	23.00	97.00	86.00	93.00	11.00
LM	1	71.64	58.66	24.03	5.033	30.98	36.02	11.00	18.00	20.00	99.00	88.00	97.00	11.00
	2	.0000	.0000	1.662	1.033	.0000	1.033	9.000	15.00	16.00	99.00	90.00	96.00	9.000
DS	1	51.40	107.7	23.69	8.217	27.75	35.97	8.000	26.00	20.00	99.00	91.00	98.00	8.000
	2	1.917	3.866	4.222	4.833	1.700	6.533	4.000	24.00	22.00	100.0	96.00	99.00	4.000
PT	1	21.00	71.45	84.61	43.20	73.45	116.7	24.00	20.00	35.00	100.0	76.00	98.00	24.00
	2	13.09	25.76	14.59	4.917	12.87	17.78	14.00	17.00	25.00	99.00	85.00	98.00	14.00
AU	1	17.70	31.03	10.82	3.333	9.833	13.17	611.0	16.00	18.00	700.0	89.00	98.00	611.0
	2	1.189	2.575	4.023	3.817	1.617	5.433	2.000	24.00	18.00	98.00	96.00	98.00	2.000
DW	1	15.00	23.54	8.775	.9000	6.700	7.600	15.00	21.00	23.00	95.00	80.00	93.00	15.00
	2	9.243	13.84	4.674	.8667	3.450	4.317	3.000	20.00	20.00	97.00	94.00	95.00	3.000
TW	1	11.45	34.60	18.56	14.93	6.317	21.25	11.00	36.00	29.00	99.00	88.00	96.00	11.00
	2	5.991	22.53	23.09	15.73	7.433	23.17	7.000	22.00	23.00	100.0	93.00	98.00	7.000
MW	1	37.70	73.07	24.12	.1500	45.98	46.13	9.000	18.00	16.00	98.00	89.00	95.00	9.000
	2	.0000	.3898	6.886	7.483	.4333	7.917	13.00	15.00	9.000	98.00	85.00	96.00	13.00

Subj	Study	CO2-H	CO2-L	CO2-B	CO2-R	TREMa	TNREM	Tremh	Tnrem	DOB	Age	S1-2%
JB	1	60.00	33.00	45.00	27.00	10.00	42.00	24.00	151.0	29-Dec-85	6.715	65.90
	2	46.00	35.00	38.00	11.00	12.00	9.000	6.000	8.000	29-Dec-85	6.718	38.00
AB	1	50.00	39.00	40.00	11.00	52.00	225.0	27.00	68.00	10-Aug-79	12.23	85.90
	2	46.00	42.00	45.00	4.000	5.000	9.000	13.00	12.00	10-Aug-79	12.59	31.80
SB	1	77.00	42.00	65.00	35.00	29.00	101.0	8.000	91.00	30-Aug-82	10.38	47.70
	2	51.00	40.00	46.00	11.00	33.00	149.0	3.000	14.00	30-Aug-82	10.44	54.10
NB	1	50.00	33.00	47.00	17.00	11.00	43.00	27.00	106.0	14-Jul-84	7.781	74.10
	2	48.00	28.00	46.00	20.00	20.00	27.00	4.000	18.00	14-Jul-84	8.027	48.50
SC	1	48.00	38.00	43.00	10.00	61.00	45.00	33.00	42.00	26-Nov-87	4.274	62.80
	2	44.00	35.00	38.00	9.000	18.00	20.00	2.000	1.000	26-Nov-87	4.293	65.40
SD	1	46.00	38.00	40.00	8.000	11.00	57.00	20.00	275.0	30-Jul-78	13.05	60.40
	2	?????	?????	?????	?????	9.000	14.00	6.000	2.000	30-Jul-78	13.10	33.90
MF	1	72.00	45.00	57.00	27.00	109.0	106.0	19.00	119.0	29-Mar-85	6.126	50.80
	2	46.00	37.00	38.00	9.000	23.00	9.000	6.000	24.00	29-Mar-85	7.129	38.20
CG	1	57.00	40.00	50.00	17.00	8.000	12.00	14.00	19.00	03-Apr-77	15.07	46.60
	2	46.00	38.00	43.00	8.000	3.000	5.000	5.000	7.000	03-Apr-77	15.07	52.50
HL	1	52.00	40.00	44.00	12.00	15.00	31.00	28.00	132.0	16-Dec-85	6.123	45.91
	2	52.00	35.00	50.00	17.00	17.00	26.00	3.000	24.00	16-Dec-85	6.353	39.90
AL	1	62.00	50.00	56.00	12.00	22.00	56.00	104.0	71.00	15-Nov-77	12.26	31.20
	2	50.00	40.00	46.00	10.00	1.000	24.00	1.000	2.000	15-Nov-77	14.36	25.90
ENM	1	60.00	35.00	38.00	25.00	41.00	20.00	79.00	65.00	06-Jan-88	4.258	50.50
	2	50.00	40.00	41.00	10.00	11.00	28.00	13.00	11.00	06-Jan-88	4.526	47.80
LM	1	48.00	38.00	45.00	10.00	7.000	29.00	48.00	67.00	27-Mar-81	11.67	70.90
	2	45.00	38.00	43.00	7.000	5.000	6.000	.0000	.0000	27-Mar-81	11.68	65.90
DS	1	45.00	35.00	40.00	10.00	19.00	49.00	101.0	66.00	15-Dec-86	5.447	48.60
	2	70.00	44.00	47.00	26.00	4.000	24.00	3.000	8.000	15-Dec-86	5.586	53.80
PT	1	72.00	38.00	60.00	34.00	26.00	217.0	21.00	390.0	24-Dec-81	11.40	54.50
	2	56.00	41.00	53.00	15.00	30.00	17.00	19.00	57.00	24-Dec-81	11.41	50.20
AU	1	60.00	43.00	48.00	17.00	16.00	10.00	28.00	21.00	20-Mar-82	9.964	44.90
	2	52.00	47.00	50.00	5.000	15.00	13.00	2.000	5.000	20-Mar-82	10.50	50.70
DW	1	53.00	40.00	50.00	13.00	.0000	8.000	19.00	29.00	09-Sep-77	14.91	44.20
	2	58.00	43.00	52.00	15.00	4.000	4.000	12.00	13.00	09-Sep-77	14.91	32.80
TW	1	58.00	41.00	45.00	17.00	51.00	83.00	32.00	27.00	07-May-92	.8795	49.80
	2	50.00	37.00	45.00	13.00	103.0	50.00	19.00	31.00	07-May-92	.9123	40.40
MW	1	50.00	46.00	47.00	4.000	1.000	30.00	59.00	126.0	06-Nov-84	5.512	58.20
	2	50.00	38.00	45.00	12.00	13.00	37.00	.0000	3.000	06-Nov-84	7.745	68.40

Subj	Study	OAI	OHI	Ordi	Crdi	Totc	Toto
JB	1	26.88	137.4	25.00	3.375	27.00	200.0
	2	4.246	7.491	2.580	1.720	14.00	21.00
AB	1	233.5	71.43	61.00	.0000	.0000	372.0
	2	.0000	1.704	2.651	4.733	25.00	14.00
SB	1	1.923	8.395	13.97	16.21	123.0	106.0
	2	.0000	.1109	.2217	21.84	197.0	2.000
NB	1	26.52	105.4	21.57	2.583	20.00	167.0
	2	.0000	.0000	.4732	7.689	65.00	4.000
SC	1	42.86	42.79	19.30	1.493	13.00	168.0
	2	5.000	.0000	.9412	5.490	35.00	6.000
SD	1	46.00	274.9	49.77	2.145	15.00	348.0
	2	3.153	1.000	1.375	3.361	22.00	9.000
MF	1	105.6	102.1	47.01	2.086	15.00	338.0
	2	.2844	3.569	4.692	4.123	29.00	33.00
CG	1	12.56	16.84	6.596	.8421	6.000	47.00
	2	1.181	3.000	2.178	1.452	8.000	12.00
HL	1	18.69	123.8	20.96	2.634	23.00	183.0
	2	2.000	18.00	2.439	5.322	48.00	22.00
AL	1	5.224	71.19	20.15	8.172	73.00	180.0
	2	21.00	2.147	3.526	.5877	4.000	24.00
ENM	1	5.323	64.98	16.50	5.606	52.00	153.0
	2	.0000	6.000	1.216	8.359	55.00	8.000
LM	1	29.11	71.48	23.87	.1591	1.000	150.0
	2	.7555	.0000	.7555	.9066	6.000	5.000
DS	1	27.31	69.48	20.47	3.226	32.00	203.0
	2	2.108	.0000	.6496	3.573	33.00	6.000
PT	1	115.1	298.6	84.22	.3881	3.000	651.0
	2	.0000	.0000	6.051	8.543	72.00	51.00
AU	1	9.443	21.61	9.524	1.299	9.000	66.00
	2	4.690	2.000	2.184	1.839	16.00	19.00
DW	1	1.000	6.097	5.641	3.134	20.00	36.00
	2	1.000	5.133	1.841	2.833	20.00	13.00
TW	1	18.15	7.481	7.599	10.97	114.0	79.00
	2	3.569	.7961	5.118	17.97	158.0	45.00
MW	1	8.000	126.2	21.55	2.568	23.00	193.0
	2	.1299	3.000	.5197	6.366	49.00	4.000

d. SPINA BIFIDA

Subj	Notes	Date	Totca	Totca	Totoa	Totoa	Mvind	NO	Group	Sex	NREMA	REMAD	ADI	NREMH
CF1		06-Jul-92	3.000	20.00	.0000	.0000	2.600	1.000	4.000	F	.5660	1.791	.7790	9.057
CF2		17-Aug-92	3.000	21.00	3.000	17.00	.1000	1.000	7.000		1.028	6.590	12.78	3.768
CF3	on CPAP	13-Oct-92	11.00	60.00	3.000	18.00	.0000	2.000	8.000		2.190	12.89	16.85	1.251
CF4	on CPAP	18-Aug-92	.0000	.0000	.0000	.0000	.0000	2.000	7.000		.0000	.0000	.0000	1.395
CF5	off CPAP	18-Aug-92	15.00	90.00	5.000	37.00	.0000	3.000	7.000		5.143	5.517	11.80	20.57
AHC		23-Jul-92	159.0	1681.	27.00	298.0	3.200	2.000	4.000	M	24.51	44.46	28.79	21.32
MM1		29-Apr-93	4.000	25.00	135.0	1089.	18.90	3.000	6.000	F	37.82	40.37	34.71	31.55
MM2		04-May-93	122.0	525.0	33.00	173.0	16.90	4.000	8.000		24.81	46.03	108.1	6.202
MM3	w/o NG	24-Jun-93	13.00	69.00	13.00	75.00	5.700	4.000	7.000		22.73	74.29	43.70	7.307
MM4	with NG	24-Jun-93	25.00	112.0	10.00	33.00	8.200	5.000	7.000		16.02	45.07	89.16	7.590
MM5	on CPAP	24-Jun-93	34.00	170.0	.0000	.0000	14.90	5.000	7.000		18.04	46.64	36.43	2.653
AO		09-Nov-92	24.00	147.0	13.00	85.00	2.200	4.000	4.000	M	6.292	17.34	7.808	15.96
JP1	pre-shunt	17-Sep-92	5.000	16.00	7.000	29.00	8.300	1.000	6.000		35.26	25.16	30.37	17.94
JP2	post-shunt	28-Sep-93	27.00	143.0	3.000	16.00	3.500	1.000	5.000	M	7.681	16.94	49.90	9.815
TP		06-May-92	46.00	374.0	23.00	234.0	.7000	5.000	4.000	F	13.43	41.34	21.82	7.836
BR		07-Dec-92	15.00	60.00	4.000	15.00	23.10	6.000	6.000	F	5.530	28.56	14.36	34.36
NT1		11-Jun-92	19.00	121.0	1.000	15.00	2.000	2.000	4.000		4.312	13.94	6.998	.6468
NT2		09-Dec-92	50.00	344.0	6.000	32.00	3.400	2.000	5.000	F	8.766	28.88	60.78	3.600
BT1		29-Mar-93	87.00	650.0	30.00	186.0	8.100	7.000	6.000	M	30.48	36.48	33.76	48.48
BT2	on CPAP	01-Apr-93	68.00	371.0	3.000	21.00	8.100	7.000	8.000		22.29	41.21	147.7	22.57
BT3		12-May-93	41.00	219.0	19.00	96.00	9.300	7.000	7.000		12.05	16.24	62.36	18.83
BT4		23-Jun-93	142.0	696.0	6.000	36.00	9.400	8.000	7.000		21.38	67.49	144.8	4.044
JW		15-Apr-93	39.00	246.0	3.000	16.00	1.900	8.000	4.000	F	6.006	2.135	5.371	14.66

Subj	Totma	Totma	Totch	Totch	Totoh	Totoh	Totmh	Totmh	Remca	Remca	Remoa	Remoa	Remma
CF1	.0000	.0000	3.000	33.00	6.000	56.00	39.00	403.0	1.000	5.000	1.000	5.000	.0000
CF2	2.0000	.0000	19.00	168.0	3.000	23.00	.0000	.0000	12.00	63.00	.0000	.0000	.0000
CF3	.0000	.0000	7.000	56.00	.0000	.0000	1.000	6.000	14.00	77.00	1.000	6.000	.0000
CF4	.0000	.0000	4.000	47.00	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
CF5	1.000	8.000	83.00	905.0	1.000	8.000	.0000	.0000	7.000	30.00	.0000	.0000	1.000
AHC	14.00	158.0	.0000	.0000	20.00	233.0	154.0	1712.	89.00	804.0	6.000	59.00	4.000
MM1	48.00	452.0	4.000	25.00	139.0	1141.	13.00	112.0	1.000	5.000	113.0	928.0	24.00
MM2	5.000	33.00	28.00	173.0	10.00	61.00	2.000	13.00	80.00	349.0	5.000	22.00	4.000
MM3	2.000	9.000	6.000	26.00	1.000	5.000	2.000	8.000	24.00	113.0	2.000	9.000	.0000
MM4	3.000	14.00	8.000	36.00	2.000	11.00	8.000	54.00	67.00	269.0	8.000	42.00	5.000
MM5	.0000	.0000	5.000	30.00	.0000	.0000	.0000	.0000	22.00	97.00	.0000	.0000	.0000
AO	4.000	27.00	18.00	118.0	62.00	461.0	24.00	171.0	13.00	82.00	.0000	.0000	5.000
JP1	2.000	5.000	8.000	52.00	6.000	61.00	.0000	.0000	62.00	166.0	36.00	143.0	3.000
JP2	6.000	30.00	15.00	113.0	4.000	17.00	27.00	137.0	20.00	86.00	18.00	87.00	7.000
TP	15.00	219.0	32.00	297.0	10.00	109.0	7.000	73.00	69.00	447.0	19.00	240.0	23.00
BR	9.000	68.00	132.0	845.0	21.00	113.0	21.00	139.0	67.00	298.0	13.00	155.0	10.00
NT1	.0000	.0000	1.000	9.000	2.000	14.00	.0000	.0000	20.00	119.0	5.000	34.00	.0000
NT2	.0000	.0000	11.00	64.00	7.000	55.00	5.000	39.00	51.00	238.0	3.000	16.00	.0000
BT1	10.00	88.00	176.0	1499.	1.000	4.000	25.00	200.0	99.00	499.0	46.00	305.0	38.00
BT2	10.00	83.00	74.00	474.0	.0000	.0000	8.000	84.00	88.00	435.0	8.000	50.00	40.00
BT3	4.000	28.00	47.00	326.0	13.00	94.00	40.00	258.0	48.00	218.0	3.000	13.00	4.000
BT4	.0000	.0000	27.00	161.0	.0000	.0000	1.000	3.000	127.0	577.0	1.000	5.000	.0000
JW	1.000	8.000	38.00	278.0	11.00	74.00	56.00	475.0	3.000	20.00	.0000	.0000	.0000

Subj	Remma	Remch	Remch	Remoh	Remoh	Remmh	Remmh	Twt	Ts1	Ts2	Tsws	Tnrem	TRem
CF1	.0000	.0000	.0000	.0000	.0000	37.00	434.0	194.9	8.600	181.5	128.0	318.0	67.00
CF2	.0000	34.00	386.0	.0000	.0000	.0000	.0000	135.5	19.70	143.2	187.4	350.3	109.2
CF3	.0000	26.00	284.0	.0000	.0000	1.000	10.00	135.6	4.300	96.40	282.9	383.6	69.80
CF4	.0000	.0000	.0000	.0000	.0000	.0000	.0000	49.00	?????	99.00	73.00	172.0	16.00
CF5	5.000	47.00	176.0	.0000	.0000	.0000	.0000	8.000	?????	154.0	91.00	245.0	87.00
AHC	50.00	1.000	10.00	7.000	82.00	67.00	857.0	54.80	6.000	263.2	220.3	489.6	133.6
MM1	231.0	5.000	31.00	51.00	389.0	9.000	65.00	36.40	3.600	200.9	92.20	296.7	205.1
MM2	28.00	31.00	178.0	3.000	13.00	2.000	12.00	162.0	14.00	180.0	193.0	387.0	116.0
MM3	.0000	8.000	39.00	.0000	.0000	.0000	.0000	8.000	.0000	6.500	67.40	73.90	21.00
MM4	27.00	10.00	55.00	2.000	6.000	8.000	53.00	15.30	1.100	29.70	111.5	142.3	106.5
MM5	.0000	3.000	27.00	.0000	.0000	2.000	16.00	53.60	16.60	30.20	66.30	113.1	28.30
AO	57.00	14.00	91.00	7.000	73.00	22.00	175.0	148.6	22.00	174.0	195.0	391.0	62.30
JP1	22.00	14.00	66.00	27.00	250.0	3.000	20.00	120.5	?????	5.600	181.5	187.2	202.3
JP2	49.00	13.00	57.00	19.00	86.00	33.00	133.0	159.5	?????	75.90	205.2	281.2	159.4
TP	391.0	45.00	514.0	4.000	44.00	5.000	81.00	107.7	21.90	248.7	104.6	375.2	161.1
BR	63.00	188.0	1134.	5.000	27.00	28.00	210.0	134.3	?????	86.10	217.7	303.8	189.1
NT1	.0000	10.00	68.00	1.000	9.000	.0000	.0000	5.200	5.800	214.8	57.60	278.3	107.6
NT2	.0000	8.000	42.00	3.000	14.00	3.000	28.00	40.50	59.50	185.6	138.3	383.3	112.2
BT1	298.0	400.0	3145.	4.000	27.00	42.00	336.0	81.00	?????	?????	?????	250.0	301.0
BT2	226.0	163.0	1144.	.0000	.0000	18.00	141.0	119.0	?????	?????	?????	218.0	198.0
BT3	29.00	89.00	588.0	5.000	29.00	39.00	249.0	94.40	1.000	109.7	207.9	318.6	203.2
BT4	.0000	16.00	81.00	.0000	.0000	.0000	.0000	121.9	65.40	156.7	193.3	415.4	113.8
JW	.0000	6.000	35.00	2.000	18.00	28.00	328.0	52.10	50.10	262.9	116.6	429.6	84.30

Subj	S1%	S2%	SWS%	Nrem%	Rem%	Tst	Tstdy	Effic	Sighs	Siind	Arous	Arind	Moves
CF1	2.200	47.10	33.00	82.60	17.40	385.1	580.0	66.40	32.00	5.000	53.00	8.300	17.00
CF2	4.300	31.20	40.80	76.20	23.80	459.5	5958.	77.20	108.0	14.10	52.00	6.800	1.000
CF3	.9000	21.30	62.40	84.60	15.40	453.4	589.0	77.00	54.00	7.100	27.00	3.600	.0000
CF4	?????	57.60	42.40	91.50	8.500	188.0	237.0	79.30	21.00	6.700	20.00	6.400	.0000
CF5	?????	46.40	27.40	73.80	26.20	332.0	340.0	97.70	32.00	10.20	37.00	11.80	.0000
AHC	1.000	42.20	35.40	78.60	21.40	623.2	678.0	91.90	63.00	6.100	7.000	.7000	33.00
MM1	.7000	40.00	18.40	59.10	40.90	561.8	538.2	93.20	37.00	4.200	39.00	4.200	177.0
MM2	2.800	35.80	38.40	76.90	23.10	503.0	665.0	75.60	45.00	5.400	76.00	9.100	142.0
MM3	.0000	6.800	71.00	77.90	22.17	94.90	102.9	92.20	11.00	7.000	9.000	5.700	9.000
MM4	.4000	11.90	44.80	57.20	42.80	248.8	264.1	94.20	15.00	3.600	20.00	4.800	34.00
MM5	11.70	21.40	46.90	80.00	20.00	141.4	195.0	72.50	9.000	3.800	10.00	4.200	35.00
AO	4.900	38.40	43.00	86.20	13.80	453.4	602.0	75.30	25.00	3.300	4.000	.5000	17.00
JP1	?????	1.400	46.60	48.10	51.90	389.5	510.0	76.40	47.00	7.200	19.00	2.900	54.00
JP2	?????	17.20	46.60	63.80	36.20	440.5	600.0	73.40	28.00	3.800	149.0	20.30	26.00
TP	4.100	46.40	19.50	70.00	30.00	536.3	644.0	83.30	23.00	2.600	21.00	2.300	6.000
BR	?????	17.50	44.20	61.60	38.40	492.9	627.2	78.60	198.0	24.10	22.00	2.700	192.0
NT1	1.500	55.70	14.90	72.10	27.90	385.8	391.0	98.70	5.000	.8000	13.00	2.000	13.00
NT2	12.00	37.50	27.90	77.40	22.60	495.5	536.0	92.40	27.00	3.300	41.00	5.000	28.00
BT1	?????	?????	?????	45.40	54.60	551.0	632.0	87.20	118.0	12.90	31.00	3.400	74.00
BT2	?????	?????	?????	52.30	47.60	416.0	535.0	77.80	39.00	5.600	25.00	3.600	56.00
BT3	.2000	21.00	39.80	61.10	38.90	521.8	616.2	84.70	47.00	5.400	77.00	8.900	81.00
BT4	12.40	29.60	36.50	78.50	21.50	529.2	651.0	81.30	62.00	7.000	44.00	5.000	83.00
JW	9.800	51.20	22.70	83.60	16.40	513.9	566.0	90.80	91.00	10.60	17.00	2.000	16.00

Subj	REMhd	HDI	TRDI	TADT	THDT	TRDT	Y	rrREM	rrSWS	Sat-H	Sat-L	Sat-B	Sat-R
CF1	33.13	13.24	14.02	.5000	15.43	15.93	1.702	40.00	25.00	97.00	85.00	92.00	12.00
CF2	18.67	36.87	9.663	1.683	9.617	11.30	1.562	21.00	25.00	95.00	90.00	93.00	5.000
CF3	23.21	28.06	8.469	2.683	5.933	8.617	1.365	25.00	19.00	99.00	85.00	97.00	14.00
CF4	.0000	1.277	1.277	.0000	.7833	.7833	?????	21.00	23.00	98.00	90.00	95.00	8.000
CF5	32.41	62.18	28.92	2.833	18.15	20.98	?????	17.00	21.00	98.00	80.00	95.00	18.00
AHC	33.68	23.97	52.76	50.83	48.23	99.07	?????	14.00	14.00	99.00	85.00	97.00	14.00
MM1	19.02	23.60	58.31	45.50	29.38	74.88	1.620	55.00	52.00	100.0	78.00	97.00	22.00
MM2	18.62	40.77	38.77	18.83	7.500	26.33	1.598	35.00	33.00	100.0	87.00	98.00	13.00
MM3	22.86	13.69	44.89	4.583	1.300	5.883	.8921	38.00	39.00	100.0	92.00	99.00	8.000
MM4	11.27	24.34	37.62	8.283	3.583	11.87	1.124	45.00	36.00	100.0	85.00	99.00	15.00
MM5	10.60	7.122	28.01	4.450	1.217	5.667	1.533	23.00	20.00	100.0	85.00	100.0	15.00
AO	41.41	19.45	27.26	6.633	18.15	24.78	?????	21.00	19.00	99.00	90.00	96.00	9.000
JP1	11.89	14.96	26.65	?????	?????	?????	?????	62.00	53.00	98.00	88.00	97.00	10.00
JP2	24.47	71.27	26.15	6.850	9.050	15.90	?????	44.00	48.00	99.00	90.00	97.00	9.000
TP	20.11	11.52	33.34	15.23	12.08	27.32	?????	24.00	21.00	99.00	57.00	97.00	42.00
BR	70.12	48.08	62.45	8.480	37.98	46.47	?????	52.00	54.00	99.00	81.00	96.00	18.00
NT1	6.134	2.177	9.176	4.817	1.667	6.483	1.765	26.00	21.00	98.00	90.00	96.00	8.000
NT2	7.487	16.79	17.80	10.50	4.033	14.53	1.703	17.00	21.00	100.0	89.00	98.00	11.00
BT1	88.90	70.56	104.3	33.77	86.85	120.6	?????	38.00	59.00	100.0	80.00	98.00	20.00
BT2	54.85	192.8	69.23	19.77	30.72	50.48	?????	39.00	44.00	100.0	87.00	98.00	13.00
BT3	39.27	144.5	40.48	10.05	25.73	35.78	1.346	43.00	42.00	99.00	82.00	96.00	17.00
BT4	8.436	19.17	36.28	21.90	4.083	25.98	1.633	34.00	33.00	100.0	84.00	99.00	16.00
JW	25.62	16.46	21.83	4.833	20.13	24.97	?????	19.00	25.00	99.00	88.00	97.00	11.00

Subj	CO2-H	CO2-L	CO2-B	CO2-R	Trema	Tnrem	Tremh	Tnrem	DOB	Age	S1-2%
CF1	43.00	33.00	42.00	10.00	2.000	3.000	37.00	48.00	24-Feb-84	8.370	49.30
CF2	64.00	40.00	45.00	24.00	12.00	6.000	34.00	22.00	24-Feb-84	8.485	35.50
CF3	61.00	40.00	47.00	21.00	15.00	14.00	27.00	8.000	24-Feb-84	8.641	22.20
CF4	45.00	40.00	43.00	5.000	.0000	.0000	.0000	4.000	24-Feb-84	8.488	?????
CF5	51.00	33.00	45.00	18.00	8.000	21.00	47.00	84.00	24-Feb-84	8.488	?????
AHC	34.00	23.00	25.00	11.00	99.00	200.0	75.00	174.0	16-May-89	3.189	43.27
MM1	65.00	45.00	50.00	20.00	138.0	187.0	65.00	156.0	28-Mar-93	.0877	40.70
MM2	48.00	40.00	43.00	8.000	89.00	160.0	36.00	40.00	28-Mar-93	.1014	38.60
MM3	50.00	36.00	37.00	14.00	26.00	28.00	8.000	9.000	28-Mar-93	.2411	6.800
MM4	70.00	48.00	50.00	22.00	80.00	38.00	20.00	18.00	28-Mar-93	.2411	12.30
MM5	43.00	33.00	38.00	10.00	22.00	34.00	5.000	5.000	28-Mar-93	.2411	33.10
AO	42.00	33.00	40.00	9.000	18.00	41.00	43.00	104.0	21-May-90	2.474	43.30
JP1	50.00	33.00	46.00	17.00	91.00	114.0	43.00	58.00	06-Sep-92	.0301	?????
JP2	50.00	36.00	44.00	14.00	45.00	36.00	65.00	46.00	06-Sep-92	1.060	?????
TP	46.00	32.00	41.00	14.00	111.0	84.00	54.00	49.00	20-Aug-89	2.712	50.50
BR	55.00	35.00	49.00	20.00	90.00	28.00	221.0	174.0	19-Nov-92	.0493	?????
NT1	45.00	40.00	41.00	5.000	25.00	20.00	11.00	3.000	02-Jun-91	1.027	57.20
NT2	55.00	35.00	49.00	20.00	54.00	56.00	14.00	23.00	02-Jun-91	1.523	49.50
BT1	60.00	35.00	53.00	25.00	183.0	127.0	446.0	202.0	20-Mar-93	.0247	?????
BT2	53.00	46.00	50.00	7.000	136.0	81.00	181.0	82.00	20-Mar-93	.0329	?????
BT3	52.00	35.00	45.00	17.00	55.00	64.00	133.0	100.0	20-Mar-93	.1452	21.20
BT4	60.00	28.00	33.00	32.00	128.0	148.0	16.00	28.00	20-Mar-93	.2603	42.00
JW	50.00	35.00	47.00	15.00	3.000	43.00	36.00	105.0	23-Jan-87	6.230	61.00

Subj	OAI	OHI	Ordi	Crdi	Totc	Toto
CF1	.1558	12.78	12.93	1.091	7.000	83.00
CF2	3.000	3.000	.7835	8.879	68.00	6.000
CF3	3.132	.0000	.7940	7.675	58.00	6.000
CF4	.0000	.0000	.0000	1.277	4.000	.0000
CF5	5.000	1.000	1.446	27.47	152.0	8.000
AHC	4.910	23.88	28.79	23.97	249.0	299.0
MM1	34.18	22.64	56.82	1.495	14.00	532.0
MM2	33.60	10.36	7.634	31.13	261.0	64.00
MM3	14.26	1.000	12.64	32.24	51.00	20.00
MM4	11.93	2.482	11.09	26.53	110.0	46.00
MM5	.0000	.0000	.8487	27.16	64.00	2.000
AO	2.911	15.22	18.13	9.131	69.00	137.0
JP1	12.74	9.630	12.94	13.71	89.00	84.00
JP2	5.452	6.588	15.94	10.22	75.00	117.0
TP	8.950	2.909	11.86	21.48	192.0	106.0
BR	4.382	9.130	13.51	48.93	402.0	111.0
NT1	.9331	.4666	1.400	7.776	50.00	9.000
NT2	6.363	7.363	3.269	14.53	120.0	27.00
BT1	13.50	7.840	21.34	82.98	762.0	196.0
BT2	4.154	.0000	12.55	56.68	393.0	87.00
BT3	19.34	13.57	14.60	25.87	225.0	127.0
BT4	6.113	.0000	.9070	35.37	312.0	8.000
JW	.4670	11.33	11.79	10.04	86.00	101.0