Obstructive sleep apnoea syndrome in infants and children: established facts and unsettled issues

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The obstructive sleep apnoea (OSA) syndrome was first identified in infants and children by Guilleminault *et al* in 1976.¹ Since then, a great deal has been learned about infancy and childhood obstructive apnoea, although several areas remain largely unexplored. Since the first description of the OSA syndrome during infancy and childhood, we have learnt that the clinical symptoms of an increased upper airway resistive load during sleep are not always associated with complete airways obstruction during sleep.² Episodes of partial airways obstruction without obstructive apnoea are frequently observed in infants and children,³ so adult diagnostic criteria for the OSA syndrome may not identify infants and children with sleep-related increases in upper airway resistive loads.^{3,4} As recommended by Carroll and Loughlin,⁴ we should consider that infancy and childhood OSA syndrome is not a form of adult OSA but a separate syndrome with specific symptoms, diagnostic criteria, and therapeutic requirements.

Prevalence

We still know little about the prevalence of increased respiratory resistive loads during sleep in infants and children. Reliable data on the incidence of the OSA syndrome during infancy and childhood are not available. Series of patients with OSA published in the paediatric medical literature suggest that the peak incidence is in the 2-5 year age group. This age group may be particularly susceptible to OSA because of the prominence of pharyngeal lymphoid tissue during these years.⁵ In children, in contrast to adults, there is no clear male predominance of OSA.⁴

The prevalence of snoring in two large populations of children has been evaluated by questionnaire.^{6,7} Between four and six years of age the reported prevalence of snoring was 7-10%.^{6,7} In one of these studies children aged 4-5 years were studied at home by overnight video recording and oximetry.⁷ The prevalence of sleep and breathing disorders in this age group was estimated at 0.7%. Another questionnaire based study in a wider age range (six

months to six years) estimated the prevalence of OSA at 1.6-3.4%.⁸ Large scale, well designed studies assessing the prevalence of an increased upper airway resistive load during sleep in infants and children are needed. A reasonable priority would be to develop and validate a questionnaire, use it in the general population to detect high risk individuals, and subject these to polysomnographic recordings.

Clinical symptoms

A careful history of sleep-associated symptoms is the first step in detecting a sleep-related increase in upper airway resistive loads in an infant or child. However, more than a year often elapses between the onset of symptoms and diagnosis. This explains why severe complications such as cardiorespiratory failure are sometimes the presenting complaint.⁹

Clinical symptoms in children differ in several ways from those in adults. Excessive daytime sleepiness, the typical presenting complaint in adults, is not frequent in children.⁴ The two major symptoms are sleep-related breathing difficulties and snoring.^{3,9,10} Parents sometimes report that during sleep their child stops breathing, sweats profusely, is restless, and assumes unusual positions in an attempt to relieve upper airways obstruction. Enuresis has been reported in children with the OSA syndrome.¹¹ Mouth breathing during wakefulness is common when nasal obstruction is severe. Upper respiratory tract infections are frequently reported in young children.^{9,10} The severity of the symptoms usually increases during these infections and decreases after recovery. Behavioural disorders, including hyperactivity, aggressiveness, and rebellious behaviour, have been reported.^{9,10,12} In school age children learning problems may occur.¹³ However, it should not be concluded that a sleep-related increase in upper airway resistive loads invariably causes behavioural abnormalities. Psychological testing before and after treatment can be useful for determining the contribution of upper airway problems to behavioural abnormalities.

Obesity has been reported in a large pro-

portion of adults with OSA but has been found in only a few of the patients in paediatric series.⁴ The risk of occurrence of a sleep-related increase in upper airway resistive loads is not clearly established in obese children. However an abnormally high prevalence of OSA without clinical symptoms has been found in overweight infants.¹⁴ In obese children both low and high percentages of sleep-disordered breathing have been reported.^{15,16} Silvestri *et al*¹⁶ recommended that obese children with a history of sleep-related breathing difficulties should be referred for polysomnographic evaluation.

Failure to thrive is a not unusual characteristic of infants with OSA.^{4,9} Investigations to look for a sleep-related increase in upper airway resistive loads should be routinely performed as part of the evaluation of growth retarded infants and children and adequate treatment of the upper airways obstruction results in rapid catch-up growth.⁹ The mechanisms of growth retardation are not well understood but may include an increase in the metabolic rate during sleep. In a recent preliminary study oxygen consumption during sleep decreased after treatment in children with OSA.¹⁷ These data suggest that children gain weight after treatment because of a decrease in energy expenditure and that before treatment the increase in the work of breathing during sleep is responsible for an increase in the consumption of oxygen by respiratory muscles, leaving less oxygen available for growth. Alternatively and/or simultaneously, repeated interruption of sleep may interfere with the release of growth hormone. One study showed normalisation of growth hormone release after treatment of upper airways obstruction.¹⁸

Cardiovascular complications

The syndrome combining hypoventilation, pulmonary hypertension, cor pulmonale, and pulmonary oedema was described in the middle of the 1960s in infants and children with chronic upper airways obstruction.¹⁹ Sofer *et al*²⁰ described the haemodynamics of this syndrome in a 22 month old child and suggested that the pulmonary oedema was secondary to both right and left heart failure. In their patient pulmonary arterial pressures returned to normal within 48 hours of surgery. Acute cardiorespiratory failure seems to occur mainly in patients with long-standing neglected clinical symptoms. Upper respiratory tract infection is usually the triggering event. Patients with an unrecognised sleep-related increase in upper airway resistive loads are still at risk of acute cardiorespiratory failure. Paediatricians should be aware of this potential complication because it can result in sudden death.^{21,22}

Cardiovascular symptoms are common in adults with the OSA syndrome. It is therefore of interest to review their frequency in infants and children without cardiac failure. However, data on this issue are scant. Radiological and/or electrocardiographic evidence of right ventricular hypertrophy was reported in 55% of a group of infants and children with OSA.^{19,23} In contrast, in a series of 92 children referred for

adenoidectomy and tonsillectomy Wilkinson *et al* found electrocardiographic evidence of right ventricular hypertrophy in only 3.3% of cases.²² Thus, available data do not provide an adequate basis for estimating the prevalence of right ventricular dysfunction in infants and children with complete and/or partial upper airways obstruction during sleep. Interestingly, low pre-treatment right ventricular ejection fraction values have been shown to increase significantly after tonsillectomy.²⁴ Recently developed echocardiography techniques allow examination of interventricular septum behaviour during sleep-related upper airways obstruction. In one 11 year old child Guillemainault *et al* reported a leftward shift of the septum, even during heavy snoring.²⁵ In a preliminary study the severity of clinical symptoms and/or polysomnographic abnormalities was not related to the presence of echocardiographic abnormalities.²⁶

Systemic hypertension is found in a large percentage of adult patients with the OSA syndrome.⁴ In a series of 50 cases diurnal systemic hypertension was found in 10% of patients, all of whom were older than 10 years.¹³ More recently, no abnormalities in systolic or diastolic arterial pressures were observed in 22 children aged 6 (0.4) years.²⁷ Non-invasive continuous blood pressure measurements were performed in two children whose fingers were big enough to allow use of a cuff designed for adults and pulsus paradoxus was found in one.²⁵

There are conflicting data with regard to ECG abnormalities in children with the OSA syndrome. A study carried out in the early 1980s in a group of 50 children with OSA found sinus arrests lasting from 2.5 to 9 seconds in 52% of cases, second degree atrioventricular block in 28%, and paradoxical tachycardia in 16%.¹³ However, a more recent study in 12 subjects aged eight months to 14 years with complete and/or partial airways obstruction during sleep failed to find significant changes in heart rate during numerous episodes of severe hypoxaemia.²⁸ No episodes of severe bradycardia or cardiac arrhythmia were detected. These findings are of clinical relevance since ambulatory ECG monitoring has been used in adults to screen for sinus brady-tachy-arrhythmia as a marker for OSA.²⁹ The data suggest that this method would not detect all children with increased upper airway resistive loads during sleep.

Finally, a recent study of heart rate variability evaluated by power spectral analysis demonstrated a predominance of sympathetic activity throughout the night with surges during periods with apnoeas.³⁰ This might indicate an increased risk of systemic hypertension at an older age in the event of persistent sleep-related breathing disorders.

Methods of diagnosis

A standardised questionnaire developed by Brouillette *et al*³¹ has proved useful for suspected OSA in children aged one to 10 years. However, more recently Carroll *et al* reported that primary snoring cannot be differentiated

from OSA by clinical history alone in children.³² In a population of infants with an abnormal obstructive apnoea index Kahn *et al* found that a history of profuse sweating and noisy breathing during sleep in the absence of upper respiratory infection was useful as an aid to the diagnosis of sleep-related obstructed breathing episodes in infants.³³ Thus, there is no consensus on whether or not an age-specific questionnaire is an adequate tool for identifying infants and children with increased upper airway resistive loads during sleep.

Polysomnographic examination remains the gold standard diagnostic investigation. However, a full overnight polysomnographic study is technically difficult and can be performed only by trained personnel. Some laboratories study a daytime nap. One study compared nap and overnight polysomnography recordings in 40 children aged one month to 16.3 years, two thirds of whom received chloral hydrate sedation for the nap polysomnography.³⁴ The results showed that nap studies had a sensitivity of 74%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 17% for the diagnosis of sleep-disordered breathing. Thus, a negative nap study does not rule out the diagnosis and must be completed by an overnight sleep study. Natural sleep for a daytime polysomnographic study is sometimes difficult to obtain. Sleep deprivation or sedation has been used to induce daytime sleep. However, sleep deprivation has been shown to increase significantly the number of obstructive respiratory events in healthy infants,³⁵ and sedation by chloral hydrate is sometimes associated with a dramatic worsening of upper airways obstruction.^{36,37}

Use of home monitoring using either a microphone³⁸ or video recording and oximetry^{39,40} has been suggested. However, none of these techniques has been validated against overnight polysomnography in a large number of subjects with different levels of severity of OSA. More work is needed to verify the reliability of ambulatory methods of diagnosis of sleep-related resistive load increases in infants and children.

Polysomnographic findings

There are few data on the occurrence of obstructive apnoea during overnight sleep in normal infants and children. In infants older than six weeks the index of obstructive apnoea episodes lasting more than three seconds was found to be less than 1.^{41,42} No episodes of obstructive apnoea were detected in children⁴³ or in a small group of adolescents.⁴⁴ However, in a more recent study of 50 children aged 1–18 years there were 0.1 (0.5) (range 0–3.1) obstructive apnoeas lasting less than 10 seconds per hour of total sleep time.⁴⁵ We clearly need more normative data to improve our ability to interpret polysomnographic data in paediatric patients.

Polysomnographic recordings can be divided into two categories – those with and those without obstructive apnoeas. When obstructive apnoeas are found, their duration and rate of occurrence are usually greatest during REM

sleep. Associated with obstructive apnoeas, polygraphic recording shows laboured breathing during the ventilatory periods. Wide swings in oesophageal pressure have been found during ventilatory periods.^{46,47} Paradoxical inward rib cage motion during inspiration has been reported throughout REM sleep periods in children and during non-REM sleep.⁴⁸ Accessory respiratory muscles, including abdominal muscles, are recruited during non-REM sleep with snoring.⁴⁹ Compared with non-REM sleep, REM sleep is associated with inhibition of accessory respiratory muscle activity which results in an increase in the diaphragmatic work of breathing.

Guilleminault *et al* were the first to point out in 1982 that some children with clinical symptoms do not have obstructive apnoeas during sleep.² However, these children have significantly increased respiratory resistive loads during sleep and wide swings in oesophageal pressure. Their breathing is most laboured during REM sleep. Recently, Rosen *et al*³ documented partial airways obstruction during sleep in a group of 20 patients aged eight months to 16 years; 80% of their patients had sustained partial airways obstruction characterised by cyclic decreases in Sao_2 , hypercarbia, laboured paradoxical respiratory efforts, and snoring. Such episodes of partial airways obstruction are described as obstructive hypopnoeas in adult patients.⁵⁰ However, there is no consensus among laboratories on the definition of obstructive hypopnoea. Studies are needed to determine the clinical usefulness of oesophageal pressure measurements during sleep in symptomatic infants or children with no obstructive apnoeas on polysomnographic recordings. However, data on the normal range of oesophageal pressure swings during sleep in children are scant. The lowest negative oesophageal pressures have been reported to range from –8 to –20 cm H_2O in two groups of healthy children aged 2–14 years.^{2,47}

Early studies in children with the OSA syndrome found abnormalities in the sleep pattern with a decrease in the duration of slow wave sleep.¹³ These findings were not borne out by recent investigations in which the sleep pattern was normal.⁵¹ Differences in the severity and duration of the disease may at least partially explain these discrepancies.

Different categories of arousal have been characterised, such as behavioural arousal, EEG arousal, and movement arousal.⁵² However, several laboratories are still working on the development of standardised criteria for arousal detection in infants and children. Few reports have documented the occurrence of arousal at the end of sleep-related obstructive events in infants or children. In a study of preterm infants with apnoeas, behavioural arousal occurred more frequently after obstructive apnoeas than after central apnoeas,⁵³ but no attempt was made to characterise EEG arousal. An important study in infants with increased upper airway resistive load during sleep found an abnormal number of EEG arousals compared with age matched control infants.⁵⁴ Interestingly, EEG arousals occurred

at the nadirs of the oesophageal pressure recording. In a group of prepubertal children with OSA the end of non-REM sleep apnoea was marked by EEG arousal in 12% of events and by movement arousal in the remaining events.⁴⁹ During REM sleep only movement arousals occurred.⁴⁹ Another study reported a similar low rate of occurrence of EEG arousal in children and adults.⁵⁵ The fact that EEG and behavioural arousals are uncommon in children may be related to the less frequent occurrence of excessive daytime sleepiness in children than in adults.⁴ However, more extensive multicentre studies using standardised criteria for arousal detection and assessment of daytime behavioural disturbances are needed in different age groups of infants and children with increased upper airway resistive loads.

Pathophysiology

The pathophysiology of increased upper airway resistive load in infants and children is not fully understood. Several factors may place infants and children at risk for developing the OSA syndrome. The leading cause of sleep-related increases in upper airway resistive load in the paediatric population is the prominence of lymphoid tissues.^{9,10} However, the severity of OSA is not always proportional to the size of the tonsils and adenoids.^{56,57} This suggests involvement of other risk factors such as abnormal ventilatory drive and/or mechanical and anatomical abnormalities of the upper airways.

Few studies have evaluated ventilatory drive in children with OSA. One early study found that some children had low hypercapnic ventilatory responses when awake several years after adenotonsillectomy.⁵⁸ However, Marcus *et al* recently reported normal hypercapnic ventilatory responses when awake in children with tonsilloadenoidal hypertrophy.⁵⁹ The ventilatory response to chemical stimuli during sleep has not been studied. It can be speculated that the sleep-related decrease in ventilatory responses to chemical stimuli may differ between healthy children and children with chronic upper airways obstruction. On the other hand, children with OSA appear to have normal central control of the upper airway muscles during sleep. Continuous upper airway muscle activity was found during airway obstruction, and this muscle activity increased with the degree of hypercapnia and hypoxaemia.⁶⁰ Furthermore, a decrease in genioglossus muscle activity at the onset of obstructive apnoeas has been found in adults⁶¹ but not in children.⁶² In children, obstructive apnoeas may, rather, be the result of a sudden increase in upper airways resistance. Fibroscopic⁶³ and fluoroscopic⁶⁴ studies in children with enlarged tonsils have shown that inspiratory movements of the tonsils and pharyngeal walls tend to narrow the upper airways and occasionally lead to occlusion. A narrow airway is an additional risk factor. A relationship has been reported between the size of the posterior airway and the severity of the OSA syndrome.^{57,65} A recent study evaluated the mechanical properties of the pharynx in chil-

dren with OSA.⁶⁶ Closing pressure is increased in children with OSA compared with age matched subjects with primary snoring; similar findings have been reported in adults.⁶⁷ Interestingly, closing pressure was lower in children than in adults with snoring, suggesting differences in upper airways collapsibility between children and adults. Further investigations are needed to document changes in the mechanical properties of the upper airways in healthy children. Currently, data are available only in healthy infants.⁶⁸ Little attention has been paid to the functional and anatomical consequences of chronic obstruction on the growth of the upper airways. Experiments in rhesus monkeys have demonstrated interactions between abnormal nasal breathing and abnormal growth of the mandible starting at birth.⁶⁹ These environmental factors may explain why residual symptoms are sometimes seen after tonsillectomy⁷⁰ and why symptoms can recur after puberty.⁷¹ Finally, a racial predisposition for OSA due to hypertrophy of the lymphoid tissues has been suggested, since young black subjects have more lymphoid tissue than young white subjects.⁷²

Of the craniofacial abnormalities that have been found to be responsible for sleep-related upper airways obstruction, the Pierre Robin syndrome has been extensively studied.⁷³ Using flexible fiberoptic endoscopy Sher *et al* showed that obstruction of the airways is due not only to glossoptosis but also to many other abnormalities.⁷⁴ In infants with micrognathia the pharyngeal airway closing pressure during nasal occlusion trials was correlated with genioglossus muscle activity, suggesting that this muscle contributes to pharyngeal airway patency in micrognathic infants.⁷⁵

Endoscopic observations in children with the OSA syndrome due to other craniofacial anomalies such as Crouzon syndrome, Treacher-Collins syndrome, and other disorders have shown that the mechanism of airway collapse is variable.⁷⁶ The midfacial and mandibular hypoplasia and glossoptosis seen in Down's syndrome increase the risk of OSA. Undiagnosed OSA may contribute to the unexplained pulmonary hypertension seen in some of these children.⁷⁷

Other disorders associated with an increased risk of OSA in children include sickle cell anaemia,⁷⁸ brainstem disorders such as Arnold-Chiari malformation⁷⁹ and myelomeningocele,^{79,80} achondroplasia,⁸¹ neuromuscular disorders,⁸² and Prader Willi syndrome.⁸³ In infants laryngomalacia can be responsible for severe OSA.⁸⁴

Familial factors

A familial basis for the OSA syndrome is suggested by reports of families with several affected members.^{84,85} One recent pilot study showed an increased frequency of sleep-disordered breathing in relatives of non-obese adult patients with sleep apnoea/hypnoea syndrome.⁸⁶ Preliminary data on the prevalence of snoring in the parents of children who snore

have been reported.⁸⁷ Ventilatory control dysfunction and craniofacial morphology abnormalities have a familial basis⁸⁵ and may be risk factors for OSA in adults. Guilleminault *et al* reported five families in which several members, covering three generations, had OSA associated with a small upper airway.⁸⁸ Thus, there is evidence that familial factors influence the risk of developing an increase in upper airway resistive loads. Adult physicians and paediatricians should look for symptoms of sleep-disordered breathing in the relatives of their patients.

OSA and sudden infant death syndrome (SIDS)

It is unclear whether the risk factors for SIDS and OSA operate similarly, but there is some evidence that SIDS and OSA aggregate within the same families. Guilleminault *et al*⁸⁸ observed clinical symptoms of OSA and abnormal numbers of obstructive apnoeas among the parents or grandparents of SIDS or near-miss SIDS cases in five families. The risk was apparently related to the presence of a small posterior airway, which was found in several family members including children. Infants with near-miss SIDS were followed up and found to develop OSA during childhood.^{89,90} These are the first patients who have been studied during the development of OSA. More recently the same group found sleep-related increases in upper airways resistance in infants with a family history of SIDS, apparent life-threatening events, and parental sleep-related breathing disorders.⁵⁴ These infants may be at the highest end of the spectrum of at risk infants. However, these findings are in agreement with those of a Belgian case control study that found a significant increase in the rate of occurrence of obstructive events in infants who later died of SIDS compared with control infants.⁹¹ In two ongoing studies of the familial aggregation of OSA, families with both OSA in adults and SIDS or near-miss SIDS have been identified.^{85,92} All these data suggest that there is a subset of families at risk for both disorders. From a clinical point of view, paediatricians and adult physicians should look for familial histories of both disorders and should recommend a careful investigation in at risk infants.

Treatment

The optimal treatment strategies for paediatric OSA are still the focus of intensive research, taking into account not only obstructive apnoeas but also sleep-related increases in upper airways resistive load. Treatment should be considered only after objective testing to determine the severity of the syndrome and after otorhinolaryngological and maxillofacial studies. The pretreatment examination should include radiological evaluation,^{93,94} cephalometric measurements,⁹⁵ fluoroscopic and fibroscopic studies,^{63,64,96} computed tomographic scanning and magnetic resonance imaging.⁷⁰ The respective indications of these procedures are not yet standardised in infants

and children. Further investigations and multicentre studies are needed to clarify their clinical usefulness for elucidating the pathophysiology of OSA and for determining the best treatment strategy.

Tonsillectomy and adenoidectomy have been the most commonly recommended treatments. However, associated problems such as an abnormally long soft palate, retroposition of the mandible, or soft tissue infiltration behind the base of the tongue must receive attention. Such problems may lead to residual symptoms after tonsillectomy. Long term monitoring is required in infants and children treated for sleep-related upper airway symptoms. Follow up evaluations should include a physical examination, detailed questionnaires, and polysomnographic recordings if necessary. Symptoms sometimes recur after puberty, especially in boys.⁷¹ The usefulness of orthodontic treatment in children with mandibular abnormalities after tonsillectomy is still under investigation.

In 1986 Guilleminault suggested that nasal continuous positive airway pressure (CPAP) could be used as an alternative to tracheostomy in young patients with OSA due to craniofacial abnormalities.⁹⁷ The preliminary findings of a multicentre study conducted in North America and France have recently been reported.^{98,99} The patients were obese or had craniofacial abnormalities or residual problems after tonsillectomy.¹⁰⁰ The mean level of positive pressure used was lower than in adults with OSA. However, pressure requirements changed with growth, suggesting that CPAP requirements should be routinely re-evaluated at regular intervals. In general, the level of pressure was set to maintain the SaO_2 above 95%. However, further investigations are needed to establish the best criteria for selecting the optimal pressure. In infants with sleep-related increases in upper airway resistance Guilleminault recommended that the level of nasal pressure should be selected to maintain the oesophageal pressure no lower than $-8 \text{ cm H}_2\text{O}$ during sleep.⁵⁴ Commercial masks for infants are available, but in patients with craniofacial abnormalities custom-made masks may be necessary. Finally, the BiPAP system may be useful in some cases. Further studies are needed to determine the specific indications of both CPAP and the BiPAP system.

In patients with craniofacial abnormalities treatment with CPAP enables the patient to wait until optimal surgery can be performed and avoids the use of a tracheostomy in young patients. Close follow up is mandatory. In patients with the Pierre Robin syndrome some studies have found that clinical and polysomnographic abnormalities persisted during childhood and adolescence.^{96,101} Finally, laryngomalacia can be treated successfully by epiglottoplasty.⁸⁴

Summary

The presence of increased upper airway resistive loads during sleep can now be diagnosed by paediatricians. However, diagnostic criteria

need to be further clarified to allow accurate identification of episodes of partial airway obstruction. New technological advances can be expected to help to determine the clinical usefulness of ambulatory testing during sleep and thus to establish the indications for polysomnographic investigations in the laboratory. A thorough investigation of the anatomical abnormalities that contribute to airways obstruction is essential for selecting the most appropriate therapy. However, the order in which these investigations should be performed remains unclear. The diagnostic tools, including questionnaires and sleep testing, and methods aimed at investigating pathophysiological mechanisms should be standardised for multicentre studies. Familial factors should be taken into account. The best strategy for preventing the complications of the OSA syndrome is to identify the disorder as early as possible. This requires close cooperation between adult physicians and paediatricians called upon to evaluate sleep-related disorders.

- 1 Guilleminault C, Eldridge F, Simmons F, Dement WC. Sleep apnea in eight children. *Pediatrics* 1976;58:23-31.
- 2 Guilleminault C, Winkle R, Korobkin R, Simmons B. Children and nocturnal snoring: evaluation of the effects of sleep related respiratory resistive load and day time functioning. *Eur J Pediatr* 1982;139:165-71.
- 3 Rosen CL, D'Andrea L, Haddad GG. Adult criteria for obstructive sleep apnea do not identify children with serious obstruction. *Am Rev Respir Dis* 1992;146:1231-4.
- 4 Carroll JL, Loughlin GM. Diagnosis criteria for obstructive sleep apnea syndrome in children. *Pediatr Pulmonol* 1992;14:71-4.
- 5 Jeans WD, Fernando DC, Maw AR, Leighton BC. A longitudinal study of the growth of the nasopharynx and its contents in normal children. *Br J Radiol* 1981;54:117-21.
- 6 Teculescu DB, Caillier I, Perrin P, Rebstock E, Rauch A. Snoring in French preschool children. *Pediatr Pulmonol* 1992;13:239-44.
- 7 Ali NJ, Pitson DJ, Stradling JR. Snoring, sleep disturbance, and behaviour in 4-5 year olds. *Arch Dis Child* 1993;68:360-6.
- 8 Benediktssdottir B, Gislason T. Sleep related breathing disturbances among children 6 months to 6 years old (abstract). *European Sleep Research Society, Strasbourg* 20-25 May 1990.
- 9 Brouillette R, Fernbach SK, Hunt CE. Obstructive sleep apnea in infants and children. *J Pediatr* 1982;100:31-40.
- 10 Frank Y, Kravath RE, Pollak CP, Weitzman ED. Obstructive sleep apnea and its therapy: clinical and polysomnographic manifestations. *Pediatrics* 1983;71:737-42.
- 11 Weider DJ, Hauri PJ. Nocturnal enuresis in children with upper airway obstruction. *Int J Pediatr Otorhinolaryngol* 1985;9:173-82.
- 12 Potts WP, Pasquariello PS, Corsobaranak C, Marsh RR, Miller LM. Relief of upper airway obstruction by adenotonsillectomy. *Otolaryngol Head Neck Surg* 1986;94:476-80.
- 13 Guilleminault C, Korobkin R, Winkle R. A review of 50 children with obstructive sleep apnea syndrome. *Lung* 1981;159:275-87.
- 14 Kahn A, Mozin MJ, Rebuffat E, Sottiaux M, Burniat W, Shepherd S, Muller MF. Sleep pattern alterations and brief airway obstructions in overweight infants. *Sleep* 1989;12:430-8.
- 15 Mallory GB, Fiser DH, Jackson R. Sleep-associated breathing disorders in morbidly obese children and adolescents. *J Pediatr* 1989;115:892-7.
- 16 Silvestri JM, Weese-Mayer DE, Bass MT, Kenny AS, Hauptman SA, Pearsall SM. Polysomnography in obese children with a history of sleep-associated breathing disorders. *Pediatr Pulmonol* 1993;16:124-9.
- 17 Marcus CL, Koerner CB, Pysik Ph, Loughlin GM. Determinants of growth failure in children with the obstructive sleep apnea syndrome. *J Pediatr* 1994;125:556-62.
- 18 Goldstein SJ, Wu RHK, Thorpy MJ, Shprintzen J, Marion RE, Saenger P. Reversibility of deficient sleep entrained growth hormone secretion in a boy with achondroplasia and obstructive sleep apnea. *Acta Endocrinol* 1987;116:95-101.
- 19 Levy AM, Tabakin BS, Hanson JS, Narkewick RM. Hypertrophied adenoids causing pulmonary hypertension and severe congestive heart failure. *N Engl J Med* 1967;397:506-11.
- 20 Sofer S, Weinhouse E, Tal A, Wanderman KL, Margulis G, Leiberman A, et al. Cor pulmonale due to adenoidal or tonsillar hypertrophy or both in children: non-invasive diagnosis and follow-up. *Chest* 1988;93:119-22.
- 21 Messer J. Mort subite par apnées obstructives chez l'enfant. *Arch Fr Pediatr* 1984;41:333-6.
- 22 Wilkinson AR, McCormick MS, Freeland AP, Pickering D. Electrocardiographic signs of pulmonary hypertension in children who snore. *BMJ* 1981;282:1579-81.
- 23 Hunt CE, Brouillette RT. Abnormalities of breathing control and airway maintenance in infants and children as a cause of cor pulmonale. *Pediatr Cardiol* 1982;3:249-56.
- 24 Tal A, Leiberman A, Margulis G, Sofer S. Ventricular dysfunction in children with obstructive sleep apnea: radionuclide assessment. *Pediatr Pulmonol* 1988;4:139-43.
- 25 Guilleminault C, Shiomi T, Stoohs R, Schnitzger I. Echocardiographic studies in adults and children presenting with obstructive sleep apnea or heavy snoring. In: Gaultier C, Escourrou P, Curzi-Dascalova L, eds. *Sleep and cardio-respiratory control*. Colloque INSERM/John Libbey Eurotext Ltd, 1991:95-103.
- 26 Wadowski SJ, Shatila AF, Singh S, Rao M. Failure of history, physical, laboratory or nap studies to predict pulmonary hypertension in children with obstructive sleep apnea. *Am J Respir Crit Care Med* 1994;149:A885.
- 27 Kunzman LA, Keens TG, Davidson Ward SL. Incidence of systemic hypertension in children with obstructive sleep apnea syndrome. *Am Rev Respir Dis* 1991;141:A808.
- 28 D'Andrea LA, Rosen CL, Haddad GG. Severe hypoxemia in children with upper airway obstruction during sleep does not lead to significant changes in heart rate. *Pediatr Pulmonol* 1993;16:362-9.
- 29 Guilleminault C, Connolly S, Winkle R, Melvin K, Tilkian A. Cyclical variation of heart rate in sleep apnea syndrome. Mechanisms and usefulness of 24th electrocardiography as a screening technique. *Lancet* 1984;i:126-31.
- 30 Baharav A, Kotagal S, Rubin BK, Gibbons V, Pratt J, Karim J, et al. Obstructive sleep apnea and the autonomic cardiovascular control: an investigation by power spectrum analysis of heart rate variability. *Am J Respir Crit Care Med* 1994;149:A558.
- 31 Brouillette R, Hanson D, David R, Klemka L, Szatkowski A, Ferbach S, et al. A diagnostic approach to children with suspected obstructive sleep apnea. *J Pediatr* 1984;105:10-14.
- 32 Carroll JL, McColley SA, Marcus CL, Curtis S, Pysik P, Loughlin GM. Reported symptoms of childhood obstructive sleep apnea syndrome vs primary snoring. *Am Rev Respir Dis* 1992;145:A177.
- 33 Kahn A, Groswasser J, Sottiaux M, Rebuffat E, Sunseri M, Franco P, et al. Clinical symptoms associated with brief obstructive sleep apnea in normal infants. *Sleep* 1993;16:409-13.
- 34 Marcus CL, Keens TG, Ward SL. Comparison of nap and overnight polysomnography in children. *Pediatr Pulmonol* 1992;13:16-21.
- 35 Canet E, Gaultier C, D'Allest AM, Dehan M. Effects of sleep deprivation on respiratory events during sleep in healthy infants. *J Appl Physiol* 1989;66:1158-63.
- 36 Hershenson M, Brouillette RT, Olsen E, Hunt CE. The effect of chloral hydrate on genioglossus and diaphragmatic activity. *Pediatr Res* 1984;18:516-9.
- 37 Biban P, Baraldi E, Pettenazzo A. The adverse effect of chloral hydrate in children with OSA. *Pediatrics* 1993;92:461-3.
- 38 Potts WP. Comparison of polysomnography and sonography for assessing regularity of respiration during sleep in adenotonsillar hypertrophy. *Laryngoscope* 1987;97:1430-7.
- 39 Stradling JR, Thomas G, Warley AR, Williams P, Freeland A. Effect of adenotonsillectomy on nocturnal hypoxemia, sleep disturbances, and symptoms in snoring children. *Lancet* 1990;335:249-53.
- 40 Sivan Y, Schonfeld T. Polygraphic sleep study may fail to identify obstructive apnea syndrome in children. *Am J Respir Crit Care Med* 1994;149:A886.
- 41 Guilleminault C, Ariagno R, Korobkin R, Nagel L, Baldwin R, Coons S, et al. Mixed and obstructive sleep apnea and near miss for sudden infant death syndrome; 2. Comparison of near miss and normal control infants by age. *Pediatrics* 1979;64:882.
- 42 Hoppenbrouwers T, Hodgman JE, Cabal L. Obstructive apnea, associated patterns of movement, heart rate, and oxygenation in infants at low and increased risk for SIDS. *Pediatr Pulmonol* 1993;15:1-12.
- 43 Carskadon MA, Harvey K, Dement WC, Guilleminault C, Simmons B, Anders TF. Respiration during sleep in children. *West J Med* 1979;128:477-81.
- 44 Tabachnick E, Muller NL, Bryan AC, Levison H. Changes in ventilation and chest wall mechanics during sleep in normal adolescents. *J Appl Physiol* 1981;51:557-64.
- 45 Marcus CL, Omlin KJ, Basinski DJ, Bailey SL, Rachal AB, Von Pechmann WS, et al. Normal polysomnographic values for children and adolescents. *Am Rev Respir Dis* 1992;146:1235-9.
- 46 Praud JP, Gaultier C, Buvry M, Boule M, Girard F. Lung mechanics and breathing pattern during wakefulness and sleep in children with enlarged tonsils. *Sleep* 1984;7:304-12.
- 47 Miyazaki S, Itasaka Y, Yamakawa K, Okawa M, Togawa K. Respiratory disturbance during sleep due to adenotonsillar hypertrophy. *Am J Otolaryngol* 1989;10:143-9.
- 48 Gaultier C, Robin S, Praud JP, Delaperche MF. Syndrome d'apnées obstructives du sommeil du nourrisson et de l'enfant. In: Gaultier C, ed. *Pathologie respiratoire du sommeil du nourrisson et de l'enfant*. Paris: Vigot, 1989:70-7.
- 49 Praud JP, D'Allest AM, Nedelcoux H, Curzi-Dascalova

- L, Guilleminault C, Gaultier C. Sleep-related abdominal muscle behavior during partial or complete obstructed breathing in prepubertal children. *Pediatr Res* 1989;26:347-50.
- 50 Gould GA, Whyte KF, Rhind GB, Airlie MA, Catterall JR, Shapiro CM, et al. The sleep hypopnea syndrome. *Am Rev Respir Dis* 1988;137:895-8.
- 51 McGrath SA, Carroll JL, McColley SA, Marcus C, Pyzik P, Loughlin GM. Normal sleep structure found in children with obstructive sleep apnea. *Am Rev Respir Dis* 1992;145:A176.
- 52 Rechtschaffen A, Kales A. *A manual of standardized technology, techniques, and scoring for sleep stages of human subjects*. Brain Information Service, Brain Research Institute, University of California Los Angeles BRI, UCLA (Publ 204). NIH, Bethesda, MD: 1968.
- 53 Thoppil CK, Belan MA, Cowen CP, Mathew OP. Behavioral arousal in newborn infants and its association with termination of apnea. *J Appl Physiol* 1991;70:2479-84.
- 54 Guilleminault C, Stoohs R, Skrobal A, Labanowski M, Simmons J. Upper airway resistance in infants at risk for sudden infant death syndrome. *J Pediatr* 1993;122:881-6.
- 55 McGrath-Morrow SA, Carroll JL, McColley SA, Pysik P, Loughlin GM. Termination of obstructive apnea in children is not associated with arousal. *Am Rev Respir Dis* 1990;141:A195.
- 56 Ahlquist-Rastad J, Hultcrantz Z, Svanholm H. Children with tonsillar obstruction: indications for and efficacy of tonsillectomy. *Acta Paediatr Scand* 1988;77:831-5.
- 57 Croft CB, Brockbank MJ, Wright A, Swanson AR. Obstructive sleep apnoea in children undergoing routine tonsillectomy and adenoidectomy. *Clin Otolaryngol* 1990;15:307-14.
- 58 Ingram RH, Bishop JB. Ventilatory response to carbon dioxide after removal of chronic upper airway obstruction. *Am Rev Respir Dis* 1970;102:645-7.
- 59 Marcus CL, Gozol D, Arens R, Basinski DJ, Omlin KJ, Keens TG, et al. Ventilatory responses during wakefulness in children with obstructive sleep apnea. *Am J Respir Crit Care Med* 1994;149:715-21.
- 60 Jeffries B, Brouillette RT, Hunt CE. Electromyographic study of some accessory muscles of respiration in children with obstructive sleep apnea. *Am Rev Respir Dis* 1984;129:696-702.
- 61 Onal E, Lopata D, O'Connor T. Pathogenesis of apneas in hypersomnia-sleep apnea syndrome. *Am Rev Respir Dis* 1982;125:167-74.
- 62 Praud JP, D'Allest AM, Delaperche MF, Robin S, Gaultier C. Diaphragmatic and genioglossus electromyographic activity at the onset and at the end of obstructive apnea in children with obstructive sleep apnea syndrome. *Pediatr Res* 1988;23:1-4.
- 63 Leland LF. Transnasal fiberoptic endoscopy in children with obstructive apnea. *Crit Care Med* 1984;12:590-1.
- 64 Fernach SK, Brouillette RT, Riggs TW, Hunt CE. Radiologic evaluation of adenoids and tonsils in children with obstructive sleep apnea: plain films and fluoroscopy. *Pediatr Radiol* 1983;13:258-65.
- 65 Shintani T, Asakura K, Kataura A. Obstructive sleep apnea in children. In: Galio G, ed. *Tonsils, a clinically oriented update*. Adv Otorhinolaryngol 1992;47:267-70.
- 66 Marcus CL, McColley SA, Carroll JL, Loughlin GM, Smith PL, Schwartz AR. Upper airway collapsibility in children with the obstructive sleep apnea syndrome. *J Appl Physiol* 1994;77:918-24.
- 67 Morrisson DL, Launois SH, Isono S, Fereaoah TR, White-law WA, Remmers JE. Pharyngeal narrowing and closing pressures in patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993;148:606-11.
- 68 Roberts JL, Reed WR, Mathew OP, Menon AA, Thach BT. Assessment of pharyngeal airway stability in normal and micrognathic infants. *J Appl Physiol* 1985;58:290-9.
- 69 Vargervik K, Harvold EP. Experiments on the interaction between orofacial function and morphology. *Ear Nose Throat J* 1987;66:201-8.
- 70 Guilleminault C. Obstructive sleep apnea syndrome and its treatment in children: areas of agreement and controversy. *Pediatr Pulmonol* 1987;3:429-36.
- 71 Guilleminault C, Partinen M, Praud JP, Quera-Salva MA, Powell N, Riley R. Morphometric facial changes and obstructive sleep apnea in adolescents. *J Pediatr* 1989;114:997-9.
- 72 Redline S, Hans M, Prachartam N, Krejci P, Nelson S, Tishler PV, et al. Differences in the age distribution and risk factors for sleep disordered breathing in black and whites. *Am J Respir Crit Care Med* 1994;149:A576.
- 73 Chabbert-Broue A, Trang TTH, Curzi-Dascalova L, D'Allest AM, Gaultier C. Sleep-related breathing abnormalities in infants with Pierre Robin syndrome. *Eur Respir J* 1993;17:583.
- 74 Sher AE. Mechanisms of airway obstruction in Robin sequence: implications for treatment. *Cleft Palate Craniofac J* 1992;29:224-31.
- 75 Roberts JL, Reed WR, Mathew OP, Thach BT. Control of respiratory activity of the genioglossus muscle in micrognathic infants. *J Appl Physiol* 1986;61:1523-33.
- 76 Sher AE, Shprinzen RJ, Thorpy MJ. Endoscopic observations of obstructive sleep apnea in children with anomalous upper airways: predictive and therapeutic value. *Int J Pediatr Otorhinolaryngol* 1989;17:1-11.
- 77 Marcus CL, Keens TG, Bautista DB, Von Pechmann WS, Davidson-Ward SL. Obstructive sleep apnea in children with Down syndrome. *Pediatrics* 1991;88:132-9.
- 78 Davies SC, Stebbens VA, Samuels MP, Southall DP. Upper-airway obstruction and cerebrovascular accident in children with sickle cell anemia. *Lancet* 1989;ii:283-4.
- 79 Dure LS, Percy AK, Cheek WR, Laurent JP. Chiari type I malformation in children. *J Pediatr* 1989;115:273-576.
- 80 Waters KA, Morielli A, Brouillette RT. Obstructive sleep apnea in children with myelomeningocele. *Am J Respir Crit Care Med* 1994;149:A883.
- 81 Waters KA, Everett F, Silience D, Fagan E, Sullivan CE. Breathing abnormalities in sleep in achondroplasia. *Arch Dis Child* 1993;69:191-6.
- 82 Trang TTH, Desguerre I, Goldman M, Delaperche MF, Gaultier C. Sleep-related breathing pattern in young children with neuromuscular disorders. *Am Rev Respir Dis* 1993;147:A760.
- 83 Hertz G, Cataletto M, Feinsilver SH, Angulo M. Sleep and breathing patterns in patients with Prader Willi syndrome: effects of age and gender. *Sleep* 1993;16:366-71.
- 84 Marcus CL, Crockett DM, Davidson-Ward SL. Evaluation of epiglottoplasty as treatment for severe laryngomalacia. *J Pediatr* 1990;117:706-10.
- 85 Redline S, Tosteson T, Tishler PV, Carskadon MA, Millman RP. Studies of genetics of obstructive sleep apnea: familial aggregation of symptoms associated with sleep-related breathing disturbances. *Am Rev Respir Dis* 1992;145:440-4.
- 86 Redline S, Tishler PV. Familial influences on sleep apnea. In: Saunders NA, Sullivan CE, eds. *Sleep and Breathing. Lung biology in health and disease*, Vol 71. New York: Marcel Dekker, 1994:363-77.
- 87 Douglas NJ, Luke M, Mathur R. Is the sleep apnea/hypopnea syndrome interested? *Thorax* 1993;48:719-21.
- 88 Teculescu D, Dame MC, Mauffret E, Gaultier C, Monin P. Habitual snoring prevalence and associated factors in a sample of children aged 4 to 12 in Lorraine, France. *1er Congrès international de Pneumologie Pédiatrique Nice, France*, 2-5 June 1994.
- 89 Guilleminault C, Souquet M, Ariagno RL, Korobkin R, Simmons FB. Five cases of near-miss sudden infant death syndrome and development of obstructive sleep apnea syndrome. *Pediatrics* 1984;73:71-8.
- 90 Guilleminault C, Stoohs R. From apnea of infancy to obstructive sleep apnea syndrome in the young child. *Chest* 1992;102:1065-71.
- 91 Kahn A, Grosswasser J, Rebuffat E, Sortiaux M, Blum D, Foester M, et al. Sleep and cardiorespiratory characteristics of infant victims of sudden infant death: a prospective case-control study. *Sleep* 1992;15:287-92.
- 92 Mathur R, Douglas NJ. Sudden infant death syndrome and adult sleep apnea hypopnea syndrome: is there a relationship. *Am J Respir Crit Care Med* 1994;149:A557.
- 93 Gunn R, Tonkin SL. Upper airway measurements during inspiration and expiration in infants. *Pediatrics* 1989;84:73-7.
- 94 Francois M, Elmaleh M, Garel C, Narcy P. Dimensions du pharynx en fonction de la position chez le nouveau-né et le nourrisson. *Arch Fr Pédiatr* 1992;49:23-6.
- 95 Laitinen SH, Ranta RE. Cephalometric measurements in patients with Pierre Robin syndrome and isolated cleft palate. *Scand J Plast Reconstr Hand Surg* 1992;26:177-83.
- 96 Contencin P, Nottet JB, Yacoubian K, Soussi T, Nivoche T, Narcy P. Pharyngolaryngo-fibroscopie sous anesthésie générale chez l'enfant: Techniques et indications dans les apnées-hypopnées du aommeil. *Ann Otolaryngol* 1991;108:373-7.
- 97 Guilleminault C, Nino-Murcia G, Heldt G, Baldwin R, Hutchinson D. Alternative treatment to tracheostomy in obstructive sleep apnea syndrome: nasal continuous positive airway pressure in young children. *Pediatrics* 1986;78:797-802.
- 98 Marcus CL, Brooks LJ, Ward SLD, Mallory GB, Rosen CL, Beckerman RC, et al. CPAP use for treatment of childhood obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 1994;149:A886.
- 99 Trang TTH, Gaultier C. Nocturnal nasal CPAP in young children with severe sleep-obstructive apnea syndrome. *Am J Respir Crit Care Med* 1994;149:A885.
- 100 D'Andrea LA, Traquina DN, Rosen CL. Continuous positive airway pressure (CPAP) for temporary sleep relief of obstructive sleep apnea syndrome (OSAS) in children with adenotonsillar hypertrophy awaiting surgery. *Am J Respir Crit Care Med* 1994;149:A886.
- 101 Spier S, Rivlin J, Rowe RD, Egan T. Sleep in Pierre Robin syndrome. *Chest* 1986;90:711-5.