Obstructive sleep apnoea in children

Educational aims

- To understand the aetiology and pathophysiology of obstructive sleep apnoea in childhood.
- To recognise sleep apnoea-related morbidity from the cardiovascular and central nervous systems.
- To get familiar with treatment indications and available therapeutic modalities for obstructive sleep apnoea in childhood.

Summary

Adenotonsillar hypertrophy, obesity, craniofacial anomalies and abnormal neuromotor tone are the main conditions predisposing to obstructive sleep apnoea (OSA) in childhood. Overnight polysomnography is the gold standard for diagnosis of the disorder. Sleep apnoeic children experience increased prevalence of enuresis, elevated blood pressure, excessive daytime sleepiness, hyperactivity, learning problems and neurocognitive dysfunction. Successful treatment of paediatric OSA requires a multifaceted approach which will address all the different conditions related to dysfunctional upper airway during sleep.

Definition, aetiology and pathophysiology

Obstructive sleep apnoea (OSA) is a respiratory disorder characterised by intermittent partial and/or complete upper airway obstruction during sleep (hypopnoea or obstructive apnoea, respectively) that may impair normal ventilation and sleep pattern. Snoring, witnessed apnoeas, laboured breathing and restless sleep are the most common clinical manifestations. Reduction or cessation of airflow are frequently accompanied by episodic hypoxia, hypercapnia, arousal from sleep and exaggerated intrathoracic pressure swings.

Children with OSA suffer from functional impairment of the upper airway while asleep, which results from the presence of several different disease entities or conditions: 1) adenotonsillar hypertrophy; 2) obesity; 3) subtle craniofacial abnormalities or profound craniofacial anomalies; 4) abnormal neuromotor tone and/or abnormal control of breathing; and 5) combinations of the previous disorders or conditions (table 1).

In particular, patency of the upper airway during sleep results from complex interactions between upper airway resistance, pharyngeal collapsibility and tone of the pharyngeal dilator muscles and negative intraluminal pressure generated by the inspiratory muscles. In some children, this fine balance of mechanical forces is disturbed. For example, enlarged tonsils and adenoid or obesity may increase resistance to airflow and the tendency of the pharynx to collapse during inspiration (pharyngeal collapsibility).

It has been speculated that inspiratory intraluminal pressure becomes more negative than usual to compensate for increased upper airway resistance and to maintain normal airflow and alveolar ventilation. However,
during sleep, when the neuromotor tone of the pharyngeal dilator muscles decreases, negative intraluminal pressure cannot be balanced, leading to intermittent partial or complete pharyngeal airway collapse. Studies in children with OSA have confirmed a higher tendency of the upper airway to collapse compared to age-matched controls [1, 2]. This tendency is complicated by the fact that sleep apnoeic children are less likely to arouse in response to upper airway obstruction or to the apnoea-associated hypercapnia [2, 3].

**Epidemiology**

Nocturnal polysomnography is the gold standard for the diagnosis of upper airway obstruction during sleep and the mean number of apnoeas and hypopnoeas per hour of sleep time (apnoea–hypopnea index (AHI)) is the most frequently used index of OSA severity [4]. Two population-based studies from the USA (TuCASA and Penn State University Study) have determined OSA prevalence in childhood by overnight polysomnography [5, 6]. Approximately 25% and 1% of 5–12 yr-old children were found to have AHI >1 episode·h⁻¹ and >5 episodes·h⁻¹, respectively [5, 6].

Other studies of children recruited from the general population have estimated the frequency of OSA symptoms, and their results have been summarised in a recent review article [7]. The calculated prevalence of snoring by parental report is 7.45% (95% CI: 5.75–9.61) and that of parent-witnessed apnoeas ranges 0.2–4% [7]. In general, parental report of OSA symptoms underestimates the problem. In the Pennsylvania State University (PA, USA) study, presence of snoring was recalled by parents in 14.9% of children but the frequency of the same symptom was identified by polysomnography in 26.1% of subjects [8].

**Diagnosis**

Most frequent nocturnal symptoms associated with OSA include snoring and difficult breathing during sleep. Other commonly reported nocturnal symptoms include chest retractions, restless sleep, nocturnal sweating, nocturnal enuresis and a higher frequency of various parasomnias. Typical daytime symptoms are usually related to the presence of adenotonsillar hypertrophy and include frequent upper respiratory tract infections, chronic mouth breathing, hearing and eating problems. The classical daytime symptom of OSA in adults, excessive daytime sleepiness, is less commonly reported in children. Many sleep-apnoeic children can present with behavioral and neurocognitive symptoms including hyperactivity, aggressive behavior and poor school performance.

Physical examination of the child with suspected OSA should include visual assessment of the upper airway patency using scoring systems like the Brodsky and Mallampati [9]. Other upper airway-related signs that need to be documented are adenoidal facies, mouth breathing, nasal voice tone, retrognathia, micrognathia or midfacial hypoplasia. Furthermore, the nose and palate also need to be assessed. A neurological examination is also necessary to identify any neurological impairment, since abnormal neuromotor tone contributes to upper airway dysfunction during sleep. Blood pressure measurement should also be performed. Finally, since paediatric OSA can be either a cause of growth delay or it can be related to obesity, it is important to document the growth pattern in children with suspected sleep apnoea.

Polysomnography remains the gold standard in the diagnosis of paediatric OSA. Although it is an expensive and time-consuming diagnostic tool, no other study has been shown to be sensitive and specific enough to diagnose OSA in children. It is important to note that scoring of respiratory events during sleep in children differs from definitions used in adults. For a detailed overview of these definitions and technical prerequisites, we refer to the recently published guidelines of the American Academy of Sleep Medicine [4]. These guidelines can be used to

---

**Table 1. Characteristic examples of disorders or conditions predisposing to obstructive sleep apnoea in children**

| Disorder or Condition                                      |
|------------------------------------------------------------|
| Adenotonsilar hypertrophy                                   |
| Obesity                                                    |
| Subtle craniofacial abnormalities or profound craniofacial anomalies |
| Mild mandibular retrognathia                                |
| Marked midfacial hypoplasia (e.g. Apert syndrome, Crouzon syndrome) |
| Marked mandibular hypoplasia (e.g. Pierre Robin sequence, Treacher Collins syndrome, Stickler syndrome) |
| Mucopolysacharidoses                                       |
| Abnormal neuromotor tone and/or control of breathing       |
| Cerebral palsy                                             |
| Duchenne muscular dystrophy                                |
| Combinations of the above disorders or conditions          |
| Down’s syndrome                                            |
| Achondroplasia                                             |
| Prader-Willi syndrome                                      |
score respiratory events for adolescents up to the age of 18 yrs. However, an individual sleep specialist can choose to score polysomnography recordings from children ≥13 yrs of age using the adult criteria.

Thresholds of polysomnography indices for the diagnosis of OSA in childhood are based on normative polysomnographic values derived from healthy children [5, 10–13]. However, it is important to note that these studies differ in terms of subjects’ recruitment criteria and in some cases they have used slightly different definitions for the various respiratory events during sleep. In spite of these methodological differences, it is clear that obstructive events in normal children are rare. Moreover, the distribution of respiratory events seems not to be influenced by Tanner stage [14]. Therefore, OSA in children is commonly diagnosed with an apnoea-hypopnoea index ≥1 episode·h⁻¹ [15].

Finally, several studies have shown that a single-night polysomnography is sufficient to diagnose sleep apnoea in children. However, in a child with a normal sleep study but with a very suggestive history and physical examination, a second night might be warranted.

**OSA-related morbidity**

The main consequence of repetitive apnoeas and hypopnoeas during sleep is intermittent hypoxia, which is a potent trigger of oxidative stress and inflammation [16]. Indeed, several studies have documented increased markers of oxidative stress and inflammation in children who exhibit sleep apnoea [17-20]. Other mechanisms by which OSA may cause complications include increased sympathetic activity [21, 22], increased serum cortisol [23], and hormonal changes resulting from hypoxia, arousal from sleep and secondary sleep debt [24-26].

**Neurocognitive and behavioural complications**

In spite of major differences in study design, population sample and definitions of OSA and outcome measures, most studies have described an increase in subjective sleepiness, mood disturbance, behaviour problems and deficits in attention, memory and executive functions [27]. Other studies have also demonstrated an association between OSA and lower academic achievement which might persist into adolescence [28, 29]. HALLSEW et al. [30] have reported signs of neuronal damage in children with OSA. Since this is a cross-sectional study, it is not clear whether the neuronal injury would be fully reversible after appropriate treatment.

Another interesting fact is that the prevalence of snoring and OSA is significantly increased in children with attention deficit hyperactivity disorder, and that a clear improvement is seen after adenotonsillectomy [31]. Not all studies have reported a dose-response relationship between severity of OSA and neurobehavioural morbidity. Additional factors such as genetic susceptibility, exposure to passive smoking, obesity, short sleep duration and other sleep disorders may also affect neurocognitive outcomes [27].

**Cardiovascular complications**

Cardiovascular complications of OSA might be of particular clinical importance to obese children and teenagers because it could augment the many obesity-related cardiovascular consequences. Cross-sectional studies indicate that increasing severity of OSA in obese children and adolescents is associated with increasing risk for the metabolic syndrome [32, 33]. Moreover, several studies reveal a positive correlation between sleep apnoea and insulin resistance and dyslipidaemia in children [25, 26, 34, 35]. However, it must be noted that other studies have failed to find a similar relationship [36–38], possibly due to variations in the magnitude of obesity and the ages of study subjects, reflecting varying severity and/or duration of disease and pubertal status. Cross-sectional studies of patients prior to and following treatment have yielded conflicting results [39–41]. Overall, OSA appears to have modest effects on metabolic function in children, and the long-term consequences of childhood sleep apnoea on metabolic morbidity in early adulthood remain to be demonstrated in longitudinal investigations. Nevertheless, it should also be noted that OSA in childhood is associated with cardiovascular complications, including increase in diastolic blood pressure, blunting of the nocturnal fall in blood pressure [42, 43] and increase in left ventricular mass and reduction in systolic and diastolic cardiac function [44–46].

**Effects on growth**

Although obesity becomes more and more an important risk factor of childhood OSA, early studies reported growth failure in children with sleep apnoea [47, 48]. Although full-blown failure to thrive is nowadays rarely seen, it is...
well known that most children gain weight after adenotonsillectomy [49, 50]. Possible mechanisms for growth impairment include increased energy expenditure during sleep, altered production of growth hormone and increased peripheral resistance to growth factors [51–53].

**Treatment**

There are no long-term, follow-up studies clarifying whether OSA symptoms, abnormal polysomnography findings, OSA-related morbidity or any of their potential combinations are indications for treatment. For many years, \( \text{AHI} > 5 \text{ episodes}\cdot\text{h}^{-1} \) in children with adenotonsillar hypertrophy has been an indication for adenotonsillectomy [54]. However, recent evidence suggests that even the presence of snoring without apnoeas (\( \text{AHI} < 1 \text{ episode}\cdot\text{h}^{-1} \)) is associated with elevated blood pressure [55]. Even an \( \text{AHI} \) as low as 1 episode\cdot\text{h}^{-1} \) is related to excessive daytime sleepiness or learning problems [15]. Although sleep apnoea can be accompanied by morbidity, it should be taken under consideration that OSA resolves spontaneously in many children; 70% of preadolescent subjects with \( \text{AHI} \geq 1 \text{ episode}\cdot\text{h}^{-1} \) will have an \( \text{AHI} < 1 \text{ episode}\cdot\text{h}^{-1} \) in adolescence [56].

Despite the absence of controlled trials on the value of OSA treatment, some indications for therapeutic intervention can be summarised as follows:

1. **Children with OSA of moderate or higher severity** (\( \text{AHI} > 5 \text{ episode}\cdot\text{h}^{-1} \)) should receive some form of treatment, irrespective to the presence of morbidity.

2. **Subjects with \( \text{AHI} 1–5 \text{ episodes}\cdot\text{h}^{-1} \), but with OSA-related morbidity (e.g. enuresis, inadequate somatic growth, poor academic performance, excessive daytime sleepiness, systolic or diastolic blood pressure >95th, pulmonary hypertension) are candidates for treatment.**

3. **Increasing body mass index percentile and male gender are risk factors for persistent OSA and they should be taken under consideration when treatment decisions are made.**

4. **Subjects with neuromuscular disorders and craniofacial anomalies frequently have moderate-to-severe OSA and they are at risk for development of pulmonary hypertension [57, 58].** Thus, treatment of OSA is indicated and it may reduce pulmonary artery pressure [59].

The available treatment options for OSA include: administration of anti-inflammatory medications, adenotonsillectomy, weight loss, use of orthodontic appliances, nasal continuous positive airway pressure (nCPAP), midface and mandibular distraction osteogenesis and tracheostomy. If it is determined that a child is a candidate for treatment, then the applied therapeutic modalities should address the specific abnormality or abnormalities causing upper airway dysfunction [57, 60]. For example, a child with adenotonsillar hypertrophy and hypoplastic mandible or midfacial hypoplasia should be treated with the combination of adenotonsillectomy and use of an orthodontic appliance or craniofacial surgery [61, 62].

The need for a multifaceted treatment approach is emphasised by the finding that approximately 20% of patients do not achieve \( \text{AHI} < 5 \text{ episode}\cdot\text{h}^{-1} \) with adenotonsillectomy alone [63]. Obesity is a significant predictor for persistence of OSA postoperatively, indicating that supplemental treatment options such as weight loss and nCPAP have to be used [63, 64]. In addition, children with cerebral palsy and OSA can improve with adenotonsillectomy although their main abnormality (abnormal neuromotor tone) may ultimately require use of nCPAP [65].

Successful treatment of OSA is accompanied by improvement in quality of life [66, 67], significant increase in weight and height [47], resolution or decrease in the frequency of enuresis [68–70], reduction in diastolic blood pressure [39, 71] and reversal of cor pulmonale [72]. Furthermore, children have less daytime sleepiness, hyperactivity and aggression [31, 73–75] and less health care utilisation [76], post-treatment.

One randomised controlled trial supports the administration of intranasal corticosteroids for 6 weeks to children with OSA and adenoidal hypertrophy, which results in improvement in polysomnography indices [77]. Similarly, in a non-randomised, open-label study of children with mild OSA who received montelukast for 16 weeks, both \( \text{AHI} \) and adenoidal tissue size decreased [78]. Of note, no randomised, controlled trials on the efficacy of adenotonsillectomy have been published [79]. In a retrospective, multicentre study, polysomnography indices have been used as primary outcome measures for evaluating the efficacy of adenotonsillectomy [63]. Postoperatively, significant improvements in \( \text{AHI} \), respiratory arousal index and oxygen saturation of haemoglobin nadir have been identified.
In a recent nonrandomised investigation, weight loss by ~35% in children with OSA and a mean body mass index z-score of 2.4–2.8 was related to a significant decrease in the severity of intermittent upper airway obstruction during sleep [80]. However, in children with OSA and obesity who do not respond to weight loss, those with residual disease after adenotonsillectomy or in sleep apnoeic children with neuromuscular disorders or craniofacial abnormalities, nCPAP may be effective in ameliorating apnoeas and hypopneas [81, 82].

A single randomised, controlled investigation has revealed that application of orthodontic appliances in children with dental malocclusion and OSA is associated with reduced AHI and diminished daytime and nighttime symptoms [61, 83]. Mandibular distraction osteogenesis can be effective in the relief of upper airway obstruction affecting children with mandibular hypoplasia [84]. Midfacial distraction osteogenesis has been used in cases of midfacial hypoplasia [85].

**Conclusion**

OSA is a frequent condition in childhood with recognised morbidity from the cardiovascular and central nervous systems. A combination of different treatment modalities is necessary for the successful alleviation of upper airway dysfunction during sleep.

**Questions**

1. Adenotonsillectomy in children with obstructive sleep apnoea
   a) Consistently results in cure of OSA
   b) May not have an initial benefit, but results in improvement in OSA over time
   c) Is frequently associated with weight gain
   d) Is more effective for obese children than for normal weight children.

2. The respiratory events of a sleep study in a 15-year-old obese adolescent must be scored
   a) By pediatric rules
   b) By adult rules
   c) By either pediatric or adult definitions.
   d) There is no consensus whether it should be scored by pediatric or adult rules.

3. The first treatment option for a normal-weight child with moderate-to-severe OSA is
   a) Nasal CPAP
   b) Intranasal steroids
   c) Adenotonsillectomy
   d) Orthodontic treatment

**References**

1. Isono S, Shindama A, Utsugi M, et al. Comparison of static mechanical properties of the passive pharynx between normal children and children with sleep-disordered breathing. *Am J Respir Crit Care Med* 1998; 157: 1204–1212.
2. Marcus CL, Katz ES, Lutz J, et al. Upper airway dynamic responses in children with the obstructive sleep apnoea syndrome. *Pediatr Res* 2005; 57: 99–107.
3. Marcus CL, Moreira GA, Bamford O, et al. Response to inspiratory resistive loading during sleep in normal children and children with obstructive apnoea. *J Appl Physiol* 1999; 87: 1448–1454.
4. Vgontzas AN, Lin HM, et al. Blood pressure associated with sleep-disordered breathing in a population sample of children. *Hypertension* 2006; 52: 841–846.
5. Daya T, Kheirollash-Gozal L, Sans Capdevila O, et al. Obstructive sleep apnoea in children: relative contributions of body mass index and adenotonsillar hypertrophy. *Chest* 2009; 136: 137–144.
6. Marcus CL, Omlin KJ, Basinki DJ, et al. Normal polysomnographic values for children and adolescents. *Am Rev Respir Dis* 1992; 146: 1235–1239.
7. American Thoracic Society. Cardiorespiratory sleep studies in children. Establishment of normative data and polysomnographic predictors of morbidity. *Am J Respir Crit Care Med* 1999; 160: 1381–1387.
8. Montgomery-Downs HE, O’Brien LM, et al. Polysomnographic characteristics in normal preschool and early school-aged children. *Pediatrics* 2006; 117: 741–753.
9. Verhulst SL, Schrauwen N, Haentjens D, et al. Reference values for sleep-related respiratory variables in asymptomatic European children and adolescents. *Pediatr Pulmonol* 2007; 42: 159–167.
10. Tapia IE, Karamessinis L, Bandia P, et al. Polysomnographic values in children undergoing puberty: pediatric vs. adult respiratory rules in adolescents. *Sleep* 2008; 31: 1737–1744.
11. Goodwin JL, Kaemingk KL, Fregosi RF, et al. Clinical outcomes associated with sleep-disordered breathing in Caucasian and Hispanic children – the Tucson Children’s Assessment of Sleep Apnoea study (TuCASA). *Sleep 2003; 26: 587–591.
12. Larkin EK, Rosen CL, Kirchner HL, et al. Variation of C-reactive protein levels in adolescents: association with sleep-disordered breathing and sleep duration. *Circulation* 2005; 111: 1978–1984.
13. Tauman R, O’Brien LM, Gozal D, Hysopemia and obesity modulate plasma C-reactive protein and interleukin-6 levels in sleep-disordered breathing. *Sleep Breath* 2007; 11: 77–84.
14. Kadiotis G, Gozal D, Snow AB, et al. Uric acid excretion in North American and Southeast European children with obstructive sleep apnoea. *Sleep Med* 2010; 11: 489–493.
15. Aljadeff G, Gozal D, Schechtman VL, et al. Heart rate variability in children with obstructive sleep apnoea. *Sleep* 1997; 20: 151–157.
16. Bratel T, Wennliund A, Carlstrom K. Pituitary reactivity, androgens and catecholamines in obstructive sleep apnoea. Effects of continuous positive airway pressure treatment (CPAP). *Respir Med* 1999; 93: 1–7.
OSA in children

24. Spiegel K, Knutson K, Leproult R, et al. Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes. J Appl Physiol 2005; 99: 2008–2019.

25. Flint J, Kothare SW, Zihlif M, et al. Association between inadequate sleep and insulin resistance in obese children. J Pediatr 2007; 150: 364–369.

26. Verhulst SL, Schrauwen N, Haentjens D, et al. Sleep duration and metabolic dysregulation in overweight children and adolescents. Arch Dis Child 2008; 93: 89–90.

27. Owens JA. Neurocognitive and behavioral impact of sleep disordered breathing in children. Pediatr Pulmonol 2009; 44: 417–422.

28. Gozal D, Pope DW Jr. Snoring during early childhood and academic performance at ages thirteen to fourteen years. Pediatrics 2001; 107: 1394–1399.

29. Gozal D. Sleep-disordered breathing and school performance in children. Pediatrics 1998; 102: 616–620.

30. Halbower AC, Degaonkar M, Barker PB, et al. Childhood obstructive sleep apnoea associates with neuropsychological deficits and neuronal brain injury. PLoS Med 2006; 3: e301.

31. Chervin RD, Ruzicka DL, Giordani BJ, et al. Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. Pediatrics 2006; 117: e769–e778.

32. Redline S, Storfer-Isser A, Rosen CL, et al. Association between metabolic syndrome and sleep disordered breathing in adolescents. Am J Respir Crit Care Med 2007; 176: 401–408.

33. Verhulst SL, Schrauwen N, Haentjens D, et al. Sleep-disordered breathing and the metabolic syndrome in overweight and obese children and adolescents. J Pediatr 2007; 150: 608–612.

34. Waters KA, Mast BT, Vella S, et al. Structural equation modeling of sleep apnoea, inflammation, and metabolic dysfunction in children. J Sleep Res 2007; 16: 388–395.

35. Alexopoulos EI, Gletsou E, Kostadima E, et al. Effects of obstructive sleep apnoea on serum lipid levels in Greek children with snoring. Sleep Breath 2010; 10(1): 10.1007/s11325-010-0410-z.

36. Tauman R, O’Brien LM, Ivanenko A, et al. Obesity rather than severity of sleep-disordered breathing as the major determinant of insulin resistance and altered lipidemia in snoring children. Pediatrics 2005; 116: e66–e73.

37. Dubem B, Tounian P, Medjadhi N, et al. Pulmonary function and sleep-related breathing disorders in severely obese children. Clin Nutr 2006; 25: 803–809.

38. Kaditis AG, Alexopoulos EI, Damani E, et al. Obstructive sleep-disordered breathing and fasting insulin levels in nonobese children. Pediatr Pulmonol 2005; 40: 515–523.

39. Apostolidou MT, Alexopoulos EI, Damani E, et al. Absence of blood pressure, metabolic, and inflammatory marker changes after adenotonsillectomy for sleep apnoea in Greek children. Pediatr Pulmonol 2008; 43: 550–560.

40. Waters KA, Sitha S, O’Brien L M, et al. Follow-up on metabolic markers in children treated for obstructive sleep apnoea. Am J Respir Crit Care Med 2006; 174: 455–460.

41. Gozal D, Capdevila OS, Kheirandish-Gozal L. Metabolic alterations and systemic inflammation in obstructive sleep apnoea among nonobese and obese prepubertal children. Am J Respir Crit Care Med 2008; 177: 1142–1149.

42. Marcus CL, Greene MG, Carroll JL. Blood pressure in children with obstructive sleep apnoea. Am J Respir Crit Care Med 1998; 157: 1098–1103.

43. Amin RS, Somers VK, McConnell K, et al. Activity-adjusted 24-hour ambulatory blood pressure and cardiac remodeling in children with sleep disordered breathing. Hypertension 2008; 51: 84–91.

44. Amin RS, Kimball TR, Bean JA, et al. Left ventricular hypertrophy and abnormal ventricular geometry in children and adolescents with obstructive sleep apnea. Am J Respir Crit Care Med 2002; 165: 1395–1399.

45. Kaditis AG, Alexopoulos EI, Dalapashia M, et al. Cardiac systolic function in Greek children with obstructive sleep-disordered breathing. Sleep Med 2010; 11: 406–412.

46. Amin RS, Kimball TR, Kaira M, et al. Left ventricular function in children with sleep-disordered breathing. Am J Cardiol 2005; 95: 801–804.

47. Bonuck KA, Freeman K, Henderson J. Growth and growth biomarker changes after adenotonsillectomy: systematic review and meta-analysis. Arch Dis Child 2009; 94: 83–91.

48. Brouillette RT, Fernbach SK, Hunt CE. Obstructive sleep apnoea in infants and children. J Pediatr 1982; 100: 31–40.

49. Soultan Z, Wadowski S, Rao M, et al. Effect of treating obstructive sleep apnoea by tonsillectomy and/or adenoidectomy on obesity in children. Arch Pediatr Adolesc Med 1999; 153: 33–37.

50. Wilja AH, Scholtens S, Wieringa MH, et al. Adenotonsillectomy and the development of overweight. Pediatrics 2009; 123: 1095–1101.

51. Bar A, Tarasuk A, Segev Y, et al. The effect of adenotonsillectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnoea syndrome. J Pediatr 1999; 135: 76–80.

52. Nieminen P, Lopponen T, Tolonen U, et al. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnoea. Pediatrics 2002; 109: e55.

53. Marcus CL, Carroll JL, Koerner CB, et al. Determinants of growth in children with the obstructive sleep apnoea syndrome. J Pediatr 1994; 125: 556–562.

54. Suen JS, Arnold JE, Brooks LJ. Adenotonsillectomy for treatment of obstructive sleep apnoea in children. Arch Otolaryngol Head Neck Surg 1995; 121: 525–530.

55. Li AM, Au CT, Ho C, et al. Blood pressure is elevated in children with primary snoring. J Pediatr 2009; 155: 362–368.

56. Goodwin JL, Vasquez MM, Silva GE, et al. Incidence and remission of sleep-disordered breathing and related symptoms in 6- to 17-year old children—the Tucson Children’s Assessment of Sleep Apnoea Study. J Pediatr 2010; 157: 57–61.

57. Bower CM, Richmond D. Tonsillectomy and adenoidectomy in patients with Down syndrome. Int J Pediatr Otorhinolaryngol 1995; 33: 141–148.

58. Melacini P, Vianello A, Villanova C, et al. Cardiac and respiratory involvement in advanced stage Duchenne muscular dystrophy. Neuromuscul Disord 1996; 6: 367–376.

59. Jacobs IN, Teague WG, Bland JW Jr. Pulmonary vascular complications of chronic airway obstruction in children. Arch Otolaryngol Head Neck Surg 1997; 123: 700–704.

60. Jacobs IN, Gray RF, Todd NW. Upper airway obstruction in children with Down syndrome. Arch Otolaryngol Head Neck Surg 1996; 122: 945–950.

61. Villa MP, Bernkopf E, Pagan J, et al. Randomized controlled study of an oral jaw-positioning appliance for the treatment of obstructive sleep apnoea in children with malocclusion. Am J Respir Crit Care Med 2002; 165: 123–127.
62. Amonoo-Kuofi K, Phillips SP, Randhawa PS, et al. Adenotonsillectomy for sleep-disordered breathing in children with syndromic craniosynostosis. J Craniofac Surg 2009; 20: 1978–1980.
63. Bhattacharjee R, Khairandish-Gozal L, Spruyt K, et al. Adenotonsillectomy outcomes in treatment of obstructive sleep apnoea in children: a multicenter retrospective study. Am J Respir Crit Care Med 2010; 182: 676–683.
64. Costa DJ, Mitchell R. Adenotonsillectomy for obstructive sleep apnoea in obese children: a meta-analysis. Otolaryngol Head Neck Surg 2009; 140: 435–460.
65. Magardino YM, Tom LW. Surgical management of obstructive sleep apnoea in children with cerebral palsy. Laryngoscope 1999; 109: 1611–1615.
66. Mitchell RB, Boss EF. Pediatric obstructive sleep apnoea in obese and normal-weight children: impact of adenotonsillectomy on quality-of-life and behavior. Dev Neuropsychol 2009; 34: 650–661.
67. Powell SM, Tremlett M, Bosman DA. Quality of life of children with sleep-disordered breathing treated with adenotonsillectomy. J Laryngol Otol 2010; 27: 1–6.
68. Alexopoulos E KA, Kalampouka E, Kostadima E, et al. Nasal budesonide ameliorates symptoms and polysomnography findings in children with chronic nasal obstruction and mild sleep-disordered breathing. Eur Respir J 2003; 22: 391S.
69. Basha S, Bialowas C, Ende K, et al. Effectiveness of adenotonsillectomy in the resolution of nocturnal enuresis secondary to obstructive sleep apnoea. Laryngoscope 2005; 115: 1101–1103.
70. Weissbach A, Leiberman A, Tarasiuk A, et al. Adenotonsillectomy improves enuresis in children with obstructive sleep apnoea syndrome. Int J Pediatr Otorhinolaryngol 2006; 70: 1351–1356.
71. Ng DK, Wong JC, Chan CH, et al. Ambulatory blood pressure before and after adenotonsillectomy in children with obstructive sleep apnoea. Sleep Med 2010; 11: 721–725.
72. Mucklow ES. Obstructive sleep apnoea causing severe pulmonary hypertension reversed by emergency tonsillectomy. Br J Clin Pract 1989; 43: 260–263.
73. Mitchell RB, Kelly J. Child behavior after adenotonsillectomy for obstructive sleep apnoea syndrome. Laryngoscope 2005; 115: 2051–2055.
74. Friedman BC, Hendeles-Amitai A, Kozinsky E, et al. Adenotonsillectomy improves neurocognitive function in children with obstructive sleep apnoea syndrome. Sleep 2003; 26: 999–1005.
75. Montgomery-Dowis HL, Crabtree VM, et al. Cognition, sleep and respiration in at-risk children treated for obstructive sleep apnoea. Eur Respir J 2005; 25: 336–342.
76. Tarasiuk A, Simon T, Tal A, et al. Adenotonsillectomy in children with obstructive sleep apnoea syndrome reduces health care utilization. Pediatrics 2004; 113: 351–356.
77. Brouillette RT, Manoukian JJ, Ducharme FM, et al. Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnoea. J Pediatr 2001; 138: 838–844.
78. Goldbart AD, Goldman JL, Veling MC, et al. Leukotriene modifier therapy for mild sleep-disordered breathing in children. Am J Respir Crit Care Med 2005; 172: 364–370.
79. Lim J, McKeen M. Adenotonsillectomy for obstructive sleep apnoea in children. Cochrane Database Syst Rev 2003; CD003136.
80. Verhulst SL, Franckx H, Van Gaal L, et al. The effect of weight loss on sleep-disordered breathing in obese teenagers. Obesity 2009; 17: 1178–1183.
81. Waters KA, Everett FM, Bruderer JW, et al. Obstructive sleep apnoea: the use of nasal CPAP in 80 children. Am J Respir Crit Care Med 1995; 152: 780–785.
82. Marcus CL, Rosen G, Ward SL, et al. Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnoea. Pediatrics 2006; 117: e442–e451.
83. Carvalho FR, Lentini-Oliveira D, Machado MA, et al. Oral appliances and functional orthopaedic appliances for obstructive sleep apnoea in children. Cochrane Database Syst Rev 2007; CD005520.
84. Steinbacher DM, Kaban LB, Troulis MJ. Mandibular advancement by distraction osteogenesis for tracheostomy-dependent children with severe micrognathia. J Oral Maxillofac Surg 2005; 63: 1072–1079.
85. Mathijsen I, Arnaud E, Marchac D, et al. Respiratory outcome of mid-face advancement with distraction: a comparison between Le Fort III and frontofacial monobloc. J Craniofac Surg 2006; 17: 880–882.