Respiratory Disorders of Sleep

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Sleep Related Breathing Disorders
AASM Classification 2005

- Central Sleep Apnea Syndromes
- Obstructive Sleep Apnea Syndromes
- Sleep Related Hypoventilation/Hypoxemic Syndromes
  - Sleep Related Nonobstructive Alveolar Hypoventilation, Idiopathic
  - Congenital Central Alveolar Hypoventilation Syndrome
- Sleep Related Hypoventilation/Hypoxemia Due to Medical Condition
  - Sleep Related Hypoventilation/Hypoxemia Due to Pulmonary Parenchymal or Vascular Pathology
  - Sleep Related Hypoventilation/Hypoxemia Due to Lower Airways Obstruction
  - Sleep Related Hypoventilation/Hypoxemia Due to Neuromuscular and Chest Wall Disorders
- Other Sleep Related Breathing Disorder eg. Sleep-related Asthma, Sleep Choking Syndrome, Sleep-related Abnormal Swallowing, Sleep-related Laryngospasm
Normal Sleep

How much is normal?

- Babies under 1: 14-18 hours throughout the day and night
- Toddlers: 12-14 hours per 24 hour period
- Primary school: 10-12 hours per day
- High school: 8-10 hours per day
- Adults: 7-9 hours per day

*Divided into typical number of naps per day. Length of naps may vary quite widely.
Sleep architecture

- Regular sleep cycles of REM and NREM sleep
- Arousals/awakenings between each sleep cycle

**REM Sleep**
- rapid eye movements
- low muscle tone (esp. upper airway muscles & accessory muscles of respiration)
- dulled airway reflexes
- irregular breathing
- reduction in tidal volume
- Dreaming!

**NREM Sleep**
- stages 1-4 (light to deep)
- regular breathing
- slower respiratory rate
- better muscular tone & upper airway reflexes
Neonatal Hypnogram

- 40 min sleep cycles
- Sleep entered through “active” sleep (REM precursor)
- Cycles of active/quiet sleep – no change in pattern
Hypnogram - child to adult

- Infants/young children – 50-60 min cycles
- Older children/adults – 90 min cycles
  - Sleep entered through NREM Stage1/2
  - Patterns change – more SWS in first half, REM in second half

Eg. Sleep architecture of 3 yr old child
Case 1 – 5 yr old boy

- Snoring for 2 yrs, worse the past 6 months
- Restless sleeper, waking unrefreshed
- Tired at school, prep teacher worried about concentration & learning
- Grumpy behaviour
- Poor appetite, hard to keep weight on

What’s the diagnosis?
Sleep-disordered breathing

- A continuum from primary snoring to severe obstructive sleep apnoea

**Primary Snoring**

- UARS (Upper airways resistance syndrome)

**Mild OSA**

**Mod OSA**

**Severe OSA**

- Clinical diagnosis
- OR
- A diagnosis of exclusion on a sleep study

- Can’t diagnose without oesophageal pressure catheter on a sleep study

- Severity stratification is a sleep study diagnosis
- BUT
- OSA can be a clinical diagnosis
Obstructive Sleep apnoea

“episodes of partial or complete upper airways obstruction that occur during sleep, usually associated with a reduction in oxyhaemoglobin saturation and/or hypercarbia”

Charles Dickens, 1836
Joe the “fat boy” who consumes great quantities of food and constantly falls asleep in any situation at any time of day
History/examination

- **History**
  - Snoring or heavy breathing
  - Pauses in breathing, gasps, snorts, chokes
  - Mouth-breathing (nasal obstruction, adenoids),
  - Restlessness, sweating
  - Work of breathing, posture of neck hyperextension
  - Daytime symptoms - sleepiness, poor school performance, failure to thrive, behaviour difficulties
  - Family history of snoring/sleep apnoea

- **Examination**
  - “adenoid facies”
  - Airway assessment
  - Tonsil size
  - Nasal turbinate swelling, polyps, airflow
  - Chest wall deformity
  - Growth parameters
  - Blood pressure
  - Signs of pulmonary hypertension
Modified Mallampati Scoring of airway

Class I: Full visibility of tonsils, uvula and soft palate
Class II: Visibility of hard and soft palate, upper portion of tonsils and uvula
Class III: Soft and hard palate and base of the uvula are visible
Class IV: Only Hard Palate visible
Brodsky’s classification of tonsillar size

- grade 0, tonsils limited to tonsillar fossa
- grade 1+, tonsils occupy less than 25% of oropharynx
- grade 2+, tonsils occupy 25% to 50% of oropharynx
- grade 3+, tonsils occupy 50% to 75% of oropharynx
- grade 4+, tonsils occupy more than 75% of oropharynx
Causes of OSA in childhood

- Adeno-tonsillar hypertrophy
  - Maximal enlargement - 2-7 yrs
  - Adenoidal regrowth
- Other
  - Chronic rhinitis/hayfever
  - Laryngomalacia (usually < 1 yr)
  - Obesity
  - Anatomical abnormalities of jaw, maxilla, uvula, palate
  - Syndromes eg. Down Syndrome, Pierre-Robin Syndrome
  - Abnormal muscular tone eg. Cerebral palsy, hypotonia
  - Mucopolysaccharidoses, Achondroplasia
Adeno-tonsillar hypertrophy in children
High risk conditions

- Syndromes with anatomical variation
- Abnormal neuromuscular tone
Diagnostic Tests

- History/clinical examination are poor predictors of the OSA group
- 15-22% of children snore, but only 3% have obstructive sleep apnoea (OSA)

Which tests are helpful?

- **Overnight Oximetry**
  - useful if positive and can assist early referral to ENT
  - if negative, test is inconclusive

- **Polysomnography (PSG) = Sleep Study**
  - For all complex children and negative oximetry
  - saves some children from unnecessary surgery (if negative)
  - stratifies risk in others
Overnight Oximetry

- **McGill score** (Nixon et al, 2004)
  - A validated scoring system for overnight oximetry against routine PSG
  - Tool to prioritize the T&A waiting list
  - 22% go directly to T&A
  - Increase in positives under 5 yrs
  - Some inadequate traces

- Overall, a useful screening tool, but to rule OSA in, not rule out!

  i.e. a negative study is inconclusive and does not exclude a diagnosis of OSA

  (PPV 97%; NPV 47% - Brouillette et al (2000))
Overnight oximetry trace

- Clusters of desaturations associated with accelerations in heart rate
- Satisfies McGill’s criteria\(^1\) for mild obstructive sleep apnoea
- PPV 97\%; NPV 47\%\(^2\)

2. Brouilette et al, 2000
Polysomnography

- a painless, non-invasive test
- **In paediatrics, all done in sleep units**
- **no item number for home paediatric sleep studies yet**
- can simultaneously measure multiple channels
  (incl. breathing, heart rate, oximetry, CO2, sleep stage, muscle activity)
- the child stays overnight with 1 parent in the sleep unit
- Currently performed at
  - **Public – Melbourne Children’s Sleep Unit (Monash Medical Centre)**
    - Children 0-18 years
    - waiting list 3-6 months
    - Best for complex or difficult kids
  - **Privately**
    - Cabrini Brighton Sleep Unit (3yrs to adult)
    - Waiting list 2-4 weeks
    - Best for “normal” kids

NB. Unlike in adults, all patients must first see a paediatric Sleep accredited physician
Two patterns of severe obstructive sleep apnoea

Indication for Study: OSA, hypoventilation

Position: FLBR

Arousals:

SaO2

TcCO2

Exp CO2

Cn.A

Ob.A

Mx.A

Hyp

Uns

Sound: Not assessed in this study.

PLMs: +10

RDI ≥ 5 = 66.2 / hr  CnAI ≥ 5 = 1.8 / hr  SpO2 nadir = 90%  PLM I = 0.0 / hr

RDI ≥ 10 = 56.3 / hr  CnAI ≥ 10 = 0.4 / hr  SpO2 < 90% = 0.0 / hr  Arousal I = 33.3 / hr

OAHI ≥ 5 = 64.4 / hr  REM RDI ≥ 5 = 12.9 / hr  SpO2 ≥ 4% drop = 50.0 / hr  % resp ar = 56%

OAHI ≥ 10 = 55.9 / hr  % PLM ar = 0%

No. REM sleep periods including time supine or semi-supine: 3

Mild hypoxemia & frequent hypopnoeas in NREM with severe sleep fragmentation, but no significant CO2 rise

Severe REM-related hypoxemia, hypercapnia & cyclic hypopnoeas, but sleep architecture relatively well-preserved
Management of OSA in children

- Mild or moderate OSA (without significant gas exchange abnormality)
  - Medication - Intranasal steroids, singulair
  - Weight Management
  - Allergy management
  - Positional therapy
  - Nothing!! (CHAT Study)
Management of OSA in children

Moderate to severe OSA

- Adeno-tonsillectomy
  - Risks
    - Haemorrhage (up to 10%), anaesthetic complications, respiratory distress, velopharyngeal incompetence, stricture, mortality estimated 1/16,000

- Redo-adenoidectomy

- Other ENT procedures eg. Turbinectomy, septoplasty

- Alternative surgery - Craniofacial abnormalities
  - Micro/retrognathia – mandibular distraction osteogenesis (young patients) vs “adult-type” distraction (teenagers)
  - Midfacial hypoplasia – maxillary distraction

- CPAP
Nasal CPAP

- First reported use in childhood OSA in 1981 (Sullivan)
- acts as a pneumatic splint to the upper airway
  - maintains airway patency
  - prevents airway collapse
  - reduces the inspiratory work of breathing
- Titration in sleep unit (determine optimal pressure)
- Follow up sleep studies to monitor CPAP requirements with growth
- Side Effects
  - Generally safe and well tolerated
  - Nasal Symptoms
  - dryness, congestion, rhinorrhea, epistaxis
  - Skin ulceration, facial dermatitis
  - Conjunctivitis and eye irritation
  - Mid-facial hypoplasia with longer term use
# Intranasal steroids

<table>
<thead>
<tr>
<th>Name</th>
<th>Mode (OTC or script)</th>
<th>Medication</th>
<th>Spray s/pk</th>
<th>Dose (per nostril)</th>
<th>Dose/day</th>
<th>Price – Wood s</th>
<th>Price – Chemist Warehouse</th>
<th>Price per spray</th>
<th>Price per day</th>
<th>Comments</th>
</tr>
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<tr>
<td>Beconase Allergy/Hayfever ORANGE</td>
<td>OTC</td>
<td>Fluticasone 50mcg</td>
<td>60</td>
<td>2 daily</td>
<td>200mcg</td>
<td>$18.95</td>
<td>$14.99</td>
<td>25c (32c)</td>
<td>$1.00 (1.28)</td>
<td>Low systemic bioavailability (1%)</td>
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<tr>
<td>Beconase Allergy and Hayfever Blue</td>
<td>OTC</td>
<td>Beclomethasone 50mcg</td>
<td>200</td>
<td>2 BD</td>
<td>400mcg</td>
<td>$15.95</td>
<td>$10.99</td>
<td>5c (8c)</td>
<td>44c</td>
<td>Systemic bioavailability 44%</td>
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<td>Telnase</td>
<td>OTC</td>
<td>Triamcinolone 55mcg</td>
<td>120</td>
<td>2 daily</td>
<td>220mcg</td>
<td>$17.95</td>
<td>$7.99</td>
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<td>27c</td>
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<tr>
<td>Rhinocort</td>
<td>OTC</td>
<td>Budesonide 32mcg</td>
<td>120</td>
<td>2 BD</td>
<td>248mcg</td>
<td>$23.95</td>
<td>16.99</td>
<td>14c (20c)</td>
<td>$1.13 (1.60)</td>
<td>Systemic bioavailability 20-35%</td>
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<td>Rhinocort</td>
<td>Script</td>
<td>Budesonide 64mcg</td>
<td>240</td>
<td>2 daily</td>
<td>248mcg</td>
<td>$58.95</td>
<td>49.99</td>
<td>20c (25c)</td>
<td>$0.80 ($1.00)</td>
<td>Systemic bioavailability 20-35%</td>
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<td>Nasonex</td>
<td>Script</td>
<td>Mometasone 50mcg</td>
<td>140</td>
<td>1 daily</td>
<td>100mcg</td>
<td>$48.95</td>
<td>39.99</td>
<td>29c (35c)</td>
<td>$0.59 (0.70)</td>
<td>Low systemic bioavailability (0.1% &gt;3yo)</td>
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<td>Avamys</td>
<td>Script</td>
<td>Fluticasone 27.5mcg</td>
<td>120</td>
<td>2 daily</td>
<td>100mcg</td>
<td>$45.95</td>
<td>38.99</td>
<td>32c (38c)</td>
<td>$1.28 ($1.52)</td>
<td>Low systemic bioavailability (1%)</td>
</tr>
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</table>
• T&A provides significant improvements in SDB
  • Cure – 27.2%
  • Residual disease 72.8%
    • Significant risk factors for residual disease
      • age >7y (P<0.001)
      • Obese (P<0.001)
      • Asthma (P<0.05)
      • High AHI on pre-op sleep study (P<0.05)
Case 2

- 15 yr old male – Duchenne’s Muscular Dystrophy (wheelchair bound)
- Morning headache and daytime somnolence
- Worsening school performance
- Lung function – severe restrictive ventilatory defect (vital capacity 35% predicted)

? What’s going on
Symptoms of Hypoventilation

- Fatigue/Daytime Sleepiness
- Morning headache
- Irritability
- Hyperactivity
- Impaired learning
- Frequent waking at night or insomnia
- None!
“At Risk” Neuromuscular Disease

- Muscular dystrophies
  - Duchenne’s, Becker
- Congenital and metabolic myopathies
- Neuromuscular Junction
  - Myasthenia Gravis
- Nerve
  - Polyneuropathies, HMSN (CMT)
- Anterior Horn Cell
  - SMA
Daytime predictors of sleep hypoventilation in NMD

- Not well characterised esp in kids with DMD, mixed study populations, small numbers

- FVC of < 1 L predictive of poor outcome, 5-year survival rate 8% without assisted ventilation (Simonds, 2006)

- Daytime respiratory failure (raised awake CO2) predicts life expectancy of approx. 9 - 10 months without nocturnal respiratory support. (Simonds, 2006)

- Daytime PFTs and respiratory muscle parameters correlate poorly with nocturnal hypoxaemia and hypercapnia in children with NMD (Faroux et al)
  - FVC < 40% high risk nocturnal hypoventilation

- Nocturnal hypoxaemia and hypercapnia should be diagnosed early to prevent neurocognitive and cardiac consequences as well as the risk of acute respiratory failure. (Faroux et al)
Figure 2. Natural history of the evolution of respiratory insufficiency in patients with neuromuscular disease. NREM = non-REM; pred = predicted. Simonds, Chest 2006
Diagnostic sleep study - hypoventilation

- Indication for Study: Hypoventilation
- Associated Medical Conditions: Guillain-Barre Syndrome

- Position:
- Lights:
- Arousal:

- SaO2
- TcCO2
- Exp CO2
- Cn.A
- Ob.A
- Mx.A
- Hyp
- Cn Hyp
- RERA

- PLMs:

<table>
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<tr>
<th>Time</th>
<th>11PM</th>
<th>12AM</th>
<th>1AM</th>
<th>2AM</th>
<th>3AM</th>
<th>4AM</th>
<th>5AM</th>
<th>6AM</th>
<th>7AM</th>
<th>8AM</th>
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<tr>
<td>RDI</td>
<td>16.2/hr</td>
<td>SpO2 nadir</td>
<td>74%</td>
<td>Arousal I</td>
<td>27.6/hr</td>
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<td></td>
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</tr>
<tr>
<td>OAH1</td>
<td>0.0/hr</td>
<td>Avg SpO2 drop</td>
<td>7%</td>
<td>% Resp Ar</td>
<td>52%</td>
<td></td>
<td></td>
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<tr>
<td>CnAHL</td>
<td>0.0/hr</td>
<td>SpO2 &lt; 90%</td>
<td>11.0/hr</td>
<td>PLMI (TST)</td>
<td>0.0/hr</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>REM RDI</td>
<td>63.7/hr</td>
<td>SpO2 ≥ 4% drop</td>
<td>12.4/hr</td>
<td>% PLMAp</td>
<td>0.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CnPause</td>
<td>0.0/hr</td>
<td>Avg TcCO2↑ REM</td>
<td>&lt;5 mmHg</td>
<td>Avg TcCO2 TST</td>
<td>66.6 mmHg</td>
<td></td>
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</tbody>
</table>

Minimum duration of respiratory events: 2 resp cycles or ≥ 10 sec
No. supine or semi-supine REM sleep: 2/2
Bilevel non-invasive ventilation (NIV)

- BIPAP (Respironics) and VPAP (ResMed)
- Provides pressure support ventilation non-invasively via mask interface
  - Re-expands collapsed/poorly ventilated alveoli
  - Decreases the work of breathing
  - Improves oxygenation and CO2 elimination
  - May reset respiratory centre chemoreceptor sensitivity
- Differs from CPAP – continuous pressure
- Settings
  - IPAP = inspiratory positive airway pressure (assists ventilation)
  - EPAP = expiratory positive airway pressure (maintains airway patency / splints airway open)
  - Mode - spontaneous, timed, spontaneous/timed
    - In S or ST mode
      - Patient inhales – machine triggered to IPAP level (volume activated)
      - Patient exhales – pressure drops to EPAP level (flow activated)
  - Timed modes (S/T and T)
    - Preset rate for backup breaths
    - Max/min duration of backup breaths (IPAP max and min)
Does NIV in NMD help?

- When applied nocturnally improves
  - nocturnal and diurnal gas exchange
  - Daytime Symptoms
  - Neurocognitive function
  - Quality of life
  - Survival

- Prevents
  - respiratory exacerbations
  - Progression of cardiomyopathy
A rare autosomal dominant condition of primary alveolar hypoventilation

Mutations in PHOX2B gene at 4p12

All subjects heterozygous for a mutation

92% of cases accounted for by polyalanine repeat expansions of 25-33 repeats on the affected allele (PCR-based assay)

8% non expansion mutations (gene sequencing)

Ventilatory response to hypercapnia is absent, and response to hypoxemia is variable to absent

Autonomic abnormality in respiratory control centre in the brainstem at the cellular level
Clinical Presentation

- **Severe forms**
  - may present in the first few hours of life
  - hypoventilate awake as well as asleep

- **Typical presentation**
  - Adequate ventilation awake, hypoventilate asleep
  - Present in infancy with protracted lower respiratory tract infection when unable to be weaned from the ventilator

- **In sleep ventilation is worse in NREM than REM**

- **During exercise there is a risk of hypercapnia & hypoxemia**
Sleep Study of a patient with CCHS

Arousal
Heart Rate
180
0
TcCO2
80
20
BIPAP
IPAP
EPAP
20
0
Ch.A
Cob.A
Mx.A
Hyp
Uns
+5
+5
+5
+5
+5
NPB SaO2
100
50
SaO2 awake average = 97 %
SaO2 asleep average = 92 %
SaO2 sleep average desaturation = 3 %
SaO2 worst case = 65 %
SaO2 Total time 60-89% = 2:38:16
Associated conditions

- Hirschsprung’s disease (16-20% - 20/27 up)
- Tumors of neural crest cell origin - ganglioneuroma, neuroblastoma etc
- Pupillary abnormalities
- Eesophageal dysmotility
- Poor temperature regulation
- Lack of heart rate variability, arrhythmias (pacemakers may be required)
Management

- Ventilation
  - Tracheostomy/IPV
  - Negative pressure ventilation
  - NIV – mask bilevel
  - Phrenic nerve/Diaphragmatic pacing
    - daytime common with night trache ventilation
    - night time possible as alternative to NIV
    - Pacing wires attached to both phrenic nerves, connected to a subcutaneous unit
Ongoing monitoring

- Guidelines for management exist (ATS etc)
- Oximetry+/-Capnography at home
- Blood gases
- Sleep studies
- Echo (6-12 monthly - for pulmonary hypertension due to unrecognised hypoxemia)
- Developmental assessments
- Complications (eg. Pacemakers)
Outcome

- Diagnosis is life long
- Potential for normal lifespan, but increased risk of sudden death
- Requirement for ventilatory support is life long
- Exercise restriction - non contact sports, no swimming without supervision (will not perceive physiological compromise)
- If death occurs, autopsy by guidelines of International Registry for CCAHS
Thank you

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