



# Sleep Related Hypoventilation in Children

Dr. Arun Pugalenti

MBBS, FRCPCH, RPSGT, RST

Senior Consultant in Paediatric Respiratory & Sleep Medicine

KK Women's & Children's Hospital

Singapore

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# Outline

- Hypoventilation
- AASM - scoring
- Disorders associated with sleep related hypoventilation
- Assessment
- Individual disorder - Management

# Hypoventilation

- Hypoventilation occurs when the level of alveolar ventilation is insufficient to meet metabolic needs
- 3 main factors:
  - The capacity of the respiratory muscles
  - Load that is placed on these muscles and
  - Adequacy of the central drive to breathe
- Imbalance of the above → Risk of hypoventilation

# Nocturnal Hypoventilation

- All individuals – relative hypoventilation occurs during sleep
- Blunting of hypoxic & hypercapnic drive to breathe
- 25% reduction in tidal volume
- Rise in arterial partial pressure of CO<sub>2</sub> of 3-4 mm Hg and reduction of arterial partial pressure of oxygen of similar magnitude <sup>1</sup>
- More exacerbated in REM sleep – muscle hypotonia

1. Lumb AB. *Nunn's Applied Physiology*, 2000

# American Academy of Sleep Medicine (AASM) 2018 Scoring manual - Scoring of hypoventilation

- When >25% of the total sleep time as measured by either the arterial PCO<sub>2</sub> or surrogate is spent with a PCO<sub>2</sub> >50mm Hg
- For detection of hypoventilation during the diagnostic study use arterial PCO<sub>2</sub> , transcutaneous PCO<sub>2</sub> or end tidal PCO<sub>2</sub>
- For detection of hypoventilation during Positive Airway Pressure (PAP) titration, use arterial PCO<sub>2</sub> or use transcutaneous PCO<sub>2</sub>
- Clinical judgment is essential - Assessing the accuracy of end-tidal PCO<sub>2</sub> and transcutaneous PCO<sub>2</sub> readings
- Values should not be assumed surrogates of the arterial PCO<sub>2</sub> when values does not fit the clinical picture
- Continuous arterial blood gas monitoring during PSG is not practical (or well tolerated)

# Causes of Sleep Related Hypoventilation

- Neuromuscular Disorders
- Central Hypoventilation
- Skeletal/Thoracic Cage abnormalities
- Lung and Airway diseases

# Neuromuscular Disorders

- Congenital neuropathies

e.g. Spinal muscular atrophy types I, II, III

- Acquired Neuropathies

- Secondary to trauma, infection, immune and post infectious diseases
- Metabolic diseases

- Congenital Myopathies

- Duchenne (DMD) and Becker muscular dystrophy, myotonic dystrophy, metabolic diseases

- Acquired Myopathies

# Neuromuscular disorders

- Factors affecting the pathophysiology:
  - Nature and severity of the underlying disorder
  - Age
  - Progression
  - Type and the extent of the muscle involvement
- Atonia associated with REM sleep further accentuates the muscular weakness associated with neuromuscular disorder
- Intercostal muscle weakness, loss of FRC augmented by the supine position → reduced O<sub>2</sub> reserves and increased predisposition to CO<sub>2</sub> retention



# Neuromuscular disorders

- Sleep Disordered Breathing (SDB) - major cause of morbidity & mortality in children with neuromuscular disorders
- Prevalence of >40%<sup>1</sup>, 10 fold greater occurrence in the general population
- Nocturnal respiratory problems: OSA & Nocturnal hypoventilation
- Major cause of death: Respiratory failure

1.Labanowski et al, *Neurology* 1996;47(5): 1173 - 1180

# Assessment of SDB in Neuromuscular disorders

- Daytime tests
- Nocturnal tests

# Assessment of SDB in Neuromuscular disorders

## Daytime tests:

- Daytime symptoms are vague and may include morning lethargy, headaches, anorexia and poor growth (1)
- Severe cases the clinical features are evident but in many the onset is insidious with the slow disease progression

Prospective study of 60 adults and children with various neuromuscular diseases, all were evaluated for SDB (2)

- Majority of subjects had symptoms of SDB, including disturbed sleep, snoring, and restless legs
- Despite the high prevalence of moderate-to-severe SDB (42%), symptoms were not predictive of its presence

(1) Perrin et al, *Muscle Nerve*. 2004;29(1):5–27,

(2) Labanowski et al, *Neurology*. 1996; 47 (5): 1173 - 1180

# Assessment of SDB in Neuromuscular disorders

- Clinical signs of SDB can difficult to recognize
- Snoring and obstructed breathing - may be suggestive of OSA
- Hypoventilation and apneas may be more difficult to detect
- Adeno-tonsillar hypertrophy, mouth breathing, nasal obstruction, and hypo nasal speech - may suggest the presence of OSA
- Clinical diagnosis correlates poorly with PSG and is correct for only 30% to 56% of patients. (1)

(1) Messner et al, Arch Otolaryngol Head Neck Surg. 1999;125(3):353–356

# Assessment of SDB in Neuromuscular disorders

- Pediatric questionnaires aimed at diagnosis of OSA: Indeterminate in almost half (1), (2)
- Parents are often unable to predict the severity of OSA on the basis of their observations (3)
- Even more difficult to predict hypoventilation given the vague symptoms and clinical signs

(1) Brouillette et al, *J Pediatr.* 1984;105(1):10–14

(2) Carroll et al, *Chest.* 1995;108(3):610–618

(3) Preuthippan et al, *Acta Paediatr.* 2000;89(6):708–712

# Assessment of SDB in Neuromuscular disorders

- Pulmonary function tests - better clinical predictors of nocturnal hypoventilation

## Hukins et al :

- A prospective study of 19 subjects >12 years with Duchenne muscular dystrophy
- FEV1 <40% predicted was sensitive for the presence of SDB (91%) but not specific
- An FEV1 <20% predicted is associated with daytime CO<sub>2</sub> retention

(1) Hukins et al, *Am J Respir Crit Care Med.* 2000;161(1):166–170

# Assessment of SDB in Neuromuscular disorders

- Blood gas:
  - Day time capillary / Arterial blood gas can reliably predict nocturnal hypoventilation if  $\text{CO}_2 >45$  mm Hg on a daytime sample. (1)
  - If evidence of daytime hypercapnia, then nocturnal hypercarbia is almost certainly present (earlier intervention – might be missed)

(1) Hukins et al, Am J Respir Crit Care Med 2000; 161 (1): 166-170

# Assessment of SDB in Neuromuscular Disorders

## Nocturnal Tests:

- PSG - The gold standard for assessment of SDB (1) (2)
- Comprehensive non invasive monitoring of both cardiorespiratory function and sleep
- Robust test for assessment of SDB: No significant variability in respiratory parameters from night to night
- Downside: Expensive, Labour intensive, Not readily available in all centers, Long waiting times

(1) American Thoracic Society. Standards and indications for cardiopulmonary sleep studies in children. *Am J Respir Crit Care Med.* 1996;153(2):866–878

(2) Messner AH. Evaluation of obstructive sleep apnea by polysomnography prior to pediatric adenotonsillectomy. *Arch Otolaryngol Head Neck Surg.* 1999;125(3):353–356



# Assessment of SDB in Neuromuscular Disorders

## Alternative methods of assessment

- Homemade audiotapes, videotapes – lack sensitivity and specificity for diagnosis (1) (2)
- Nap study
  - Unlikely to capture REM sleep
  - Low sensitivity
  - Risk of underestimating the severity of SDB (3)

(1) Lamm et al. *Pediatr Pulmonol.* 1999; 27 (4): 267-272

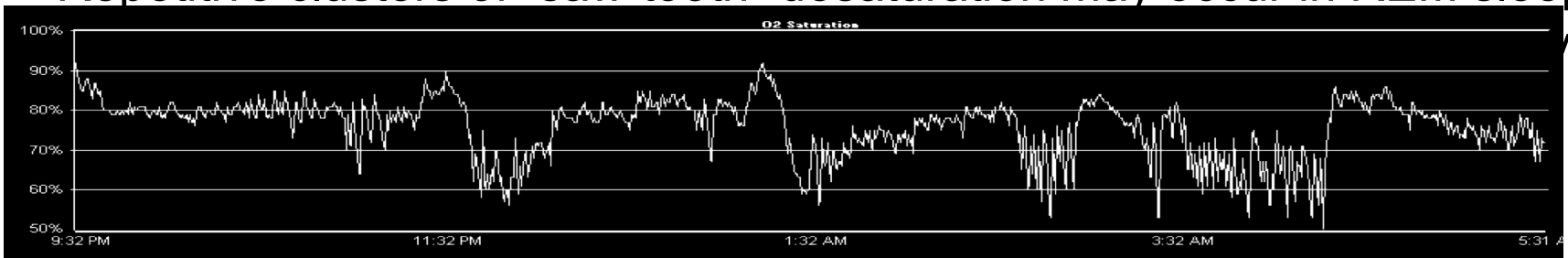
(2) Sivan et al. *Eur Respir J.* 1996;9 (10): 2127 – 2131

(3) Saeed et al, *Chest* 2000;118 (2): 360-365

# Assessment of SDB in Neuromuscular Disorders

## Overnight oximetry:

- More widely available test
- Patterns of desaturation on oximetry may be suggestive of SDB
- Repetitive clusters of “saw-tooth” desaturation may occur in REM sleep



(1) Perrin et al. *Muscle Nerve*. 2004; 29 (1); 5-27

# Assessment of SDB in Neuromuscular Disorders

## Overnight oximetry:

Cross-sectional study of 349 “healthy” children referred to a sleep laboratory for possible OSA (1)

- Positive predictive value of 97%, the severity of SDB was not discernible
- Oximetry - did not distinguish between hypoventilation and OSA
- “Normal” pulse oximetry reading did not rule out SDB
- Technical problems: motion artifact, long built-in averaging time of the device

(1) Brouillette et al. *Pediatrics*. 2000; 105 (2): 405 - 412

# Indications for PSG

- Symptoms of OSA / Hypoventilation
- Loss of ambulation due to progressive weakness or who can never ambulate
- $FVC/FEV1 < 40\%$
- Diaphragm weakness
- Infantile onset muscle weakness
- Recurrent chest infections
- Assessment for surgery

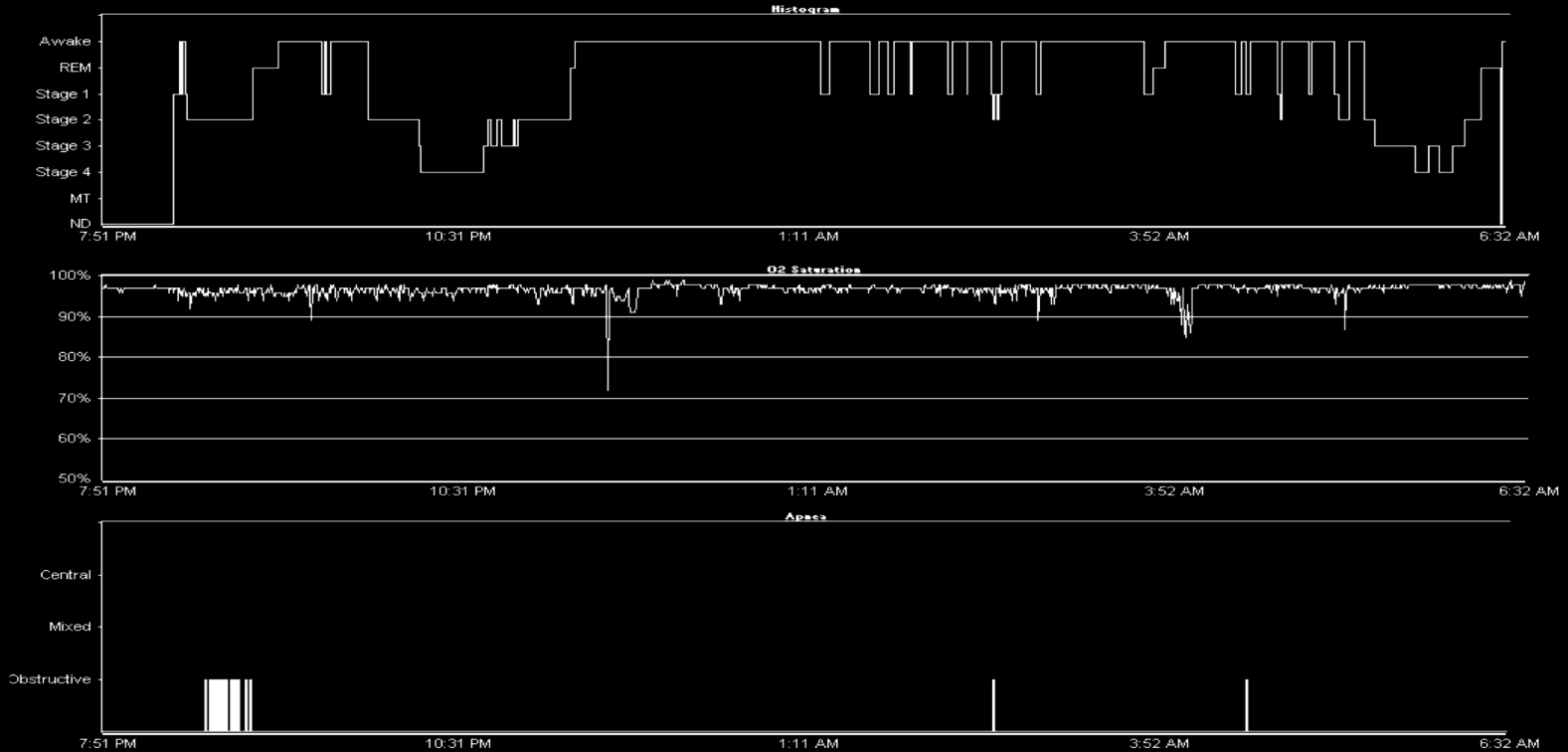
# Neuromuscular Disorders

## Initial stages:

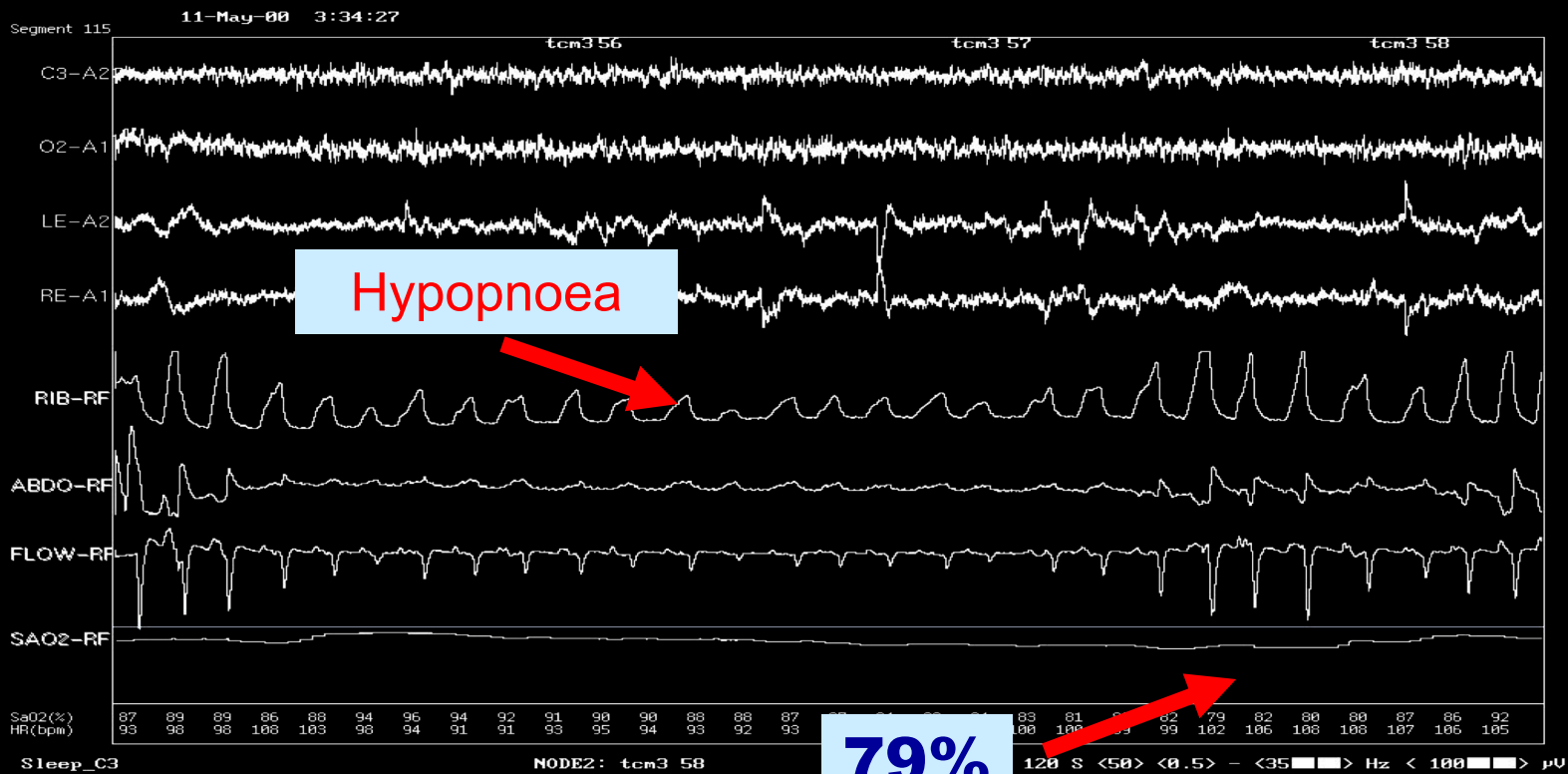
- Compensation occurs with arousal response to prevent prolonged oxygen desaturation or hypercapnia
- Sleep fragmentation
- Daytime fatigue/hypersomnolence
- Overtime – reset of ventilatory chemoreceptor sensitivity and the arousal response becomes blunted

# Myopathy - Early Respiratory Failure

## Multiple Awakenings - Minimal Oxygen Desaturation



# Hypoventilation in REM



# Management

- Ventilation:
  - Non invasive ventilation – Bi-level
  - Invasive ventilation – Bi-level
- Oxygen supplementation
- Other supportive management



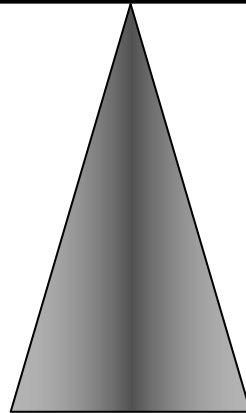
# Advantages of NIV

- Relative simplicity
- No intubation
- Speech maintained
- Less morbidity

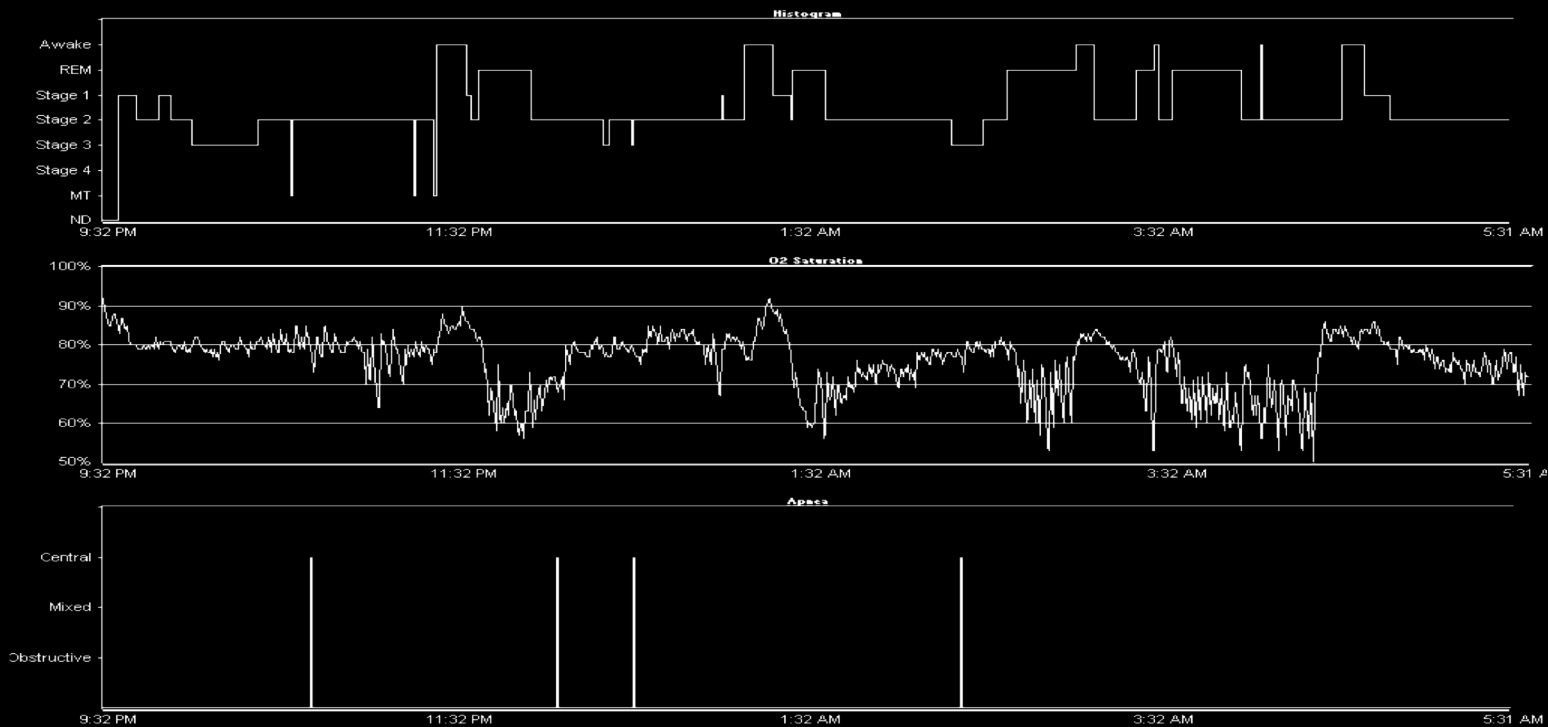
# NIV unloads the respiratory muscles

Respiratory load

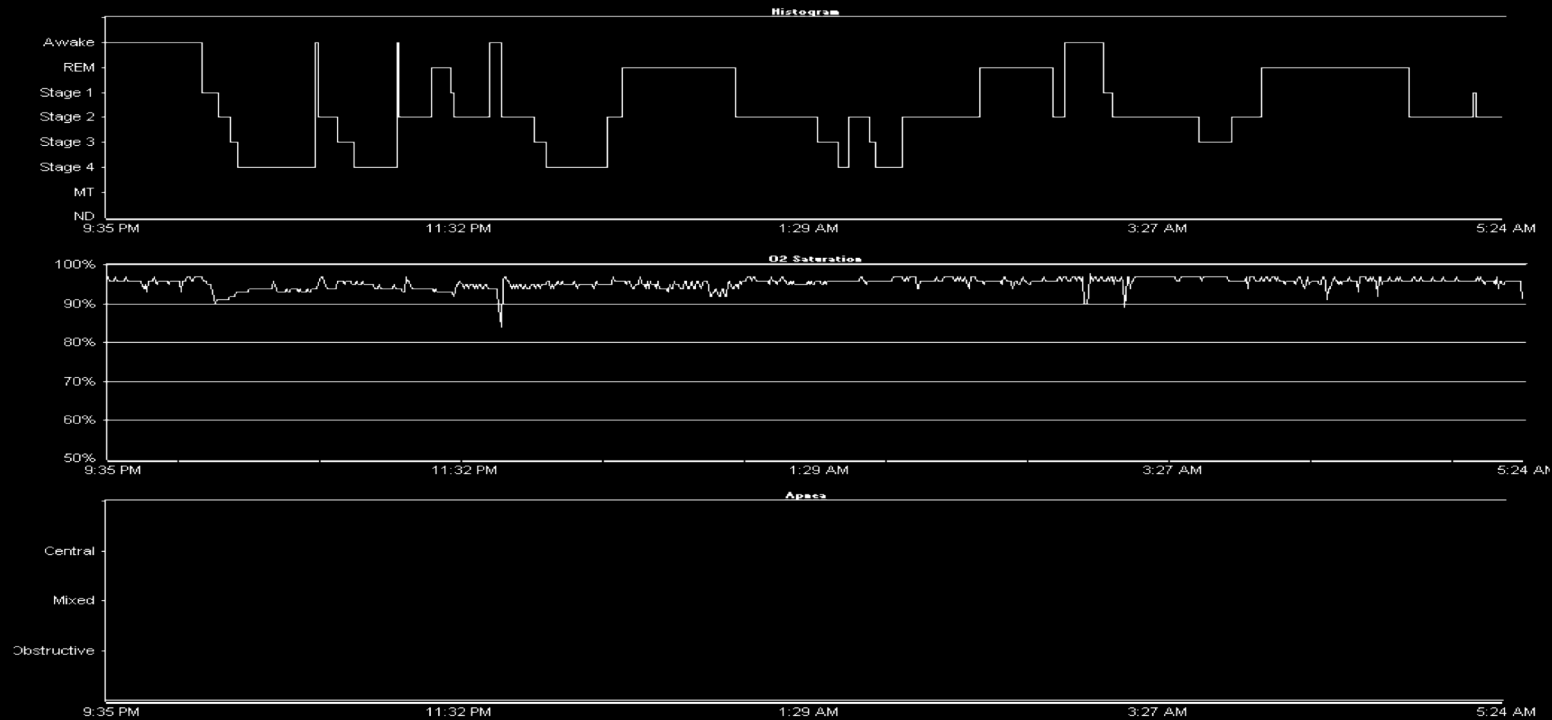
Respiratory muscles



# Myopathy - Advanced Respiratory Failure



# Bi-level Pressure support



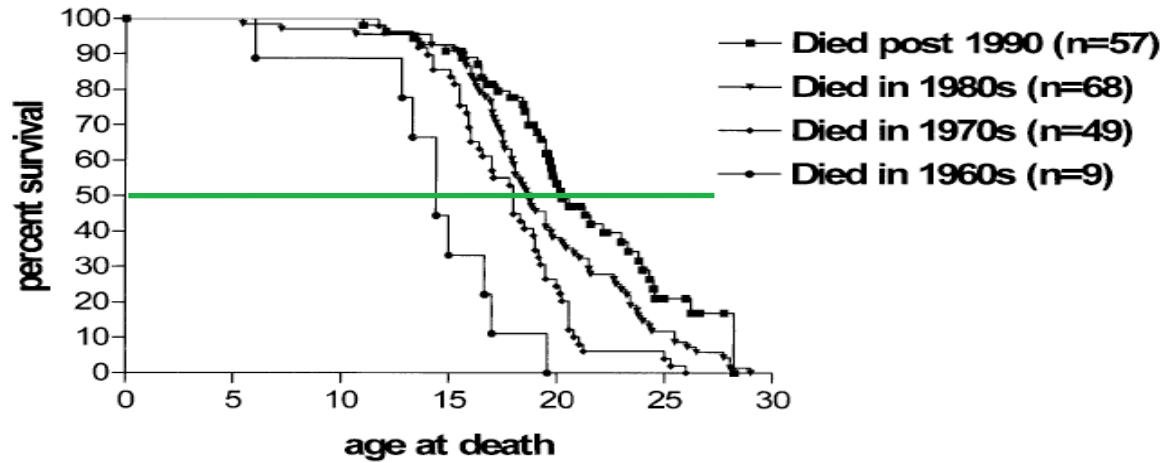


Fig. 1. Survival curves (Kaplan Meier), showing comparison in percentage survival decade on decade from the 1960s to 2002. The post-1990s cohort includes all boys, ventilated or not. If the ventilated group is removed from the post-1990s cohort, the 1980s and 1990s cohorts are not significantly different as shown in Fig. 2 ( $P = 0.82$ , log rank test, data not shown). Legend: Log rank tests for successive decades 1960s vs. 1970s,  $P = 0.002$ ; 1970s vs. 1980s,  $P = 0.007$ ; 1980s vs. 1990s,  $P = 0.03$ .

*M. Eagle et al. / Neuromuscular Disorders 12 (2002) 926–929*

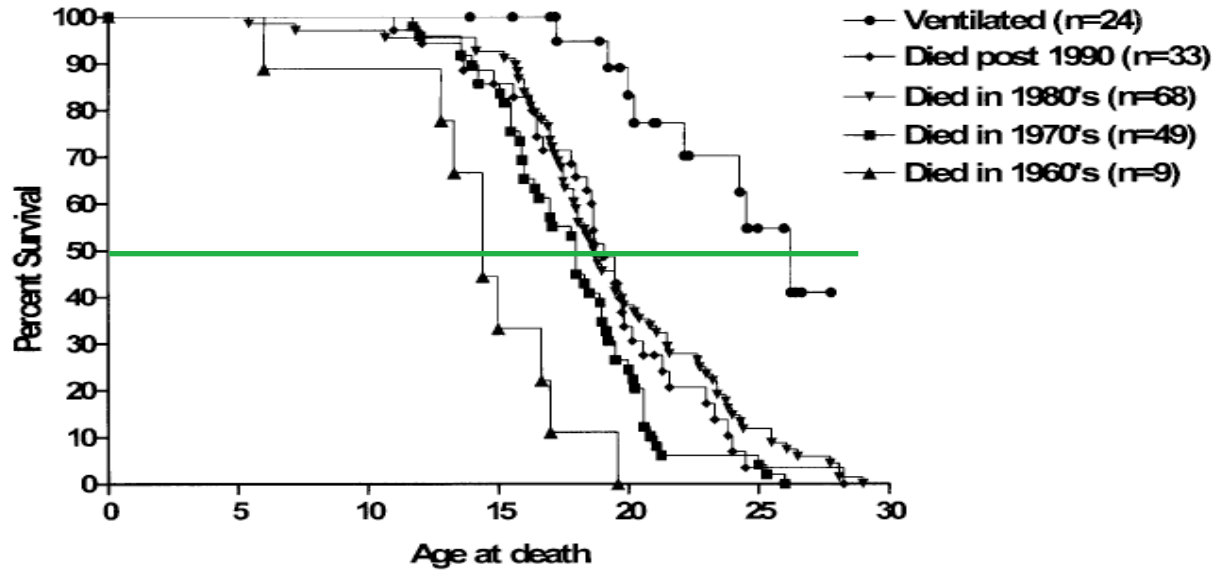


Fig. 2. Survival curves (Kaplan Meier) showing percentage survival of ventilated versus non-ventilated patients 1967–2002. (Includes live patients censored on 28th February 2002.) Legend; Log rank test for non-ventilated vs. ventilated patients post-1990 ( $P = 0.0001$ ).

M. Eagle et al. / *Neuromuscular Disorders* 12 (2002) 926–929

# Oxygen Supplementation

- Not advocated to use oxygen alone
- Combined with NIV
- Correct hypoxia
- If high pressures are not tolerated
- Admixing O<sub>2</sub> in the circuit: FiO<sub>2</sub> generated is generally unknown and potentially variable
- To monitor with pulse oximetry

# Causes of sleep related hypoventilation

- Neuromuscular disorders
- Central Hypoventilation
- Skeletal/Thoracic cage abnormalities
- Lung and Airway diseases



# Central Hypoventilation

- Congenital central hypoventilation syndrome (CCHS)
  - Neonatal/early-onset
  - Late-onset
- (ROHHAD) - Rapid-onset obesity, hypoventilation, hypothalamic dysfunction, and autonomic deregulation
- Central nervous system (CNS) structural anomalies: Chiari malformation type I and type II, hydrocephalus, syringomyelia
- CNS injury: Severe asphyxia, CNS hemorrhage/stroke
- Others: Prader-Willi syndrome, Rett syndrome, Familial dysautonomia, Joubert syndrome

# Congenital Central Hypoventilation Syndrome (CCHS)

SingHealth Academic Healthcare Cluster



Singapore General Hospital



KK Women's and Children's Hospital



National Cancer Centre Singapore



National Dental Centre Singapore



National Heart Centre Singapore



National Neuroscience Institute



Singapore National Eye Centre



Polyclinics SingHealth



Bright Vision Hospital

Sengkang Health

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# CCHS - Pathophysiology

- Abnormality of Autonomic nervous system
- Integration of chemoreceptor input to central ventilatory controllers
- Absent or negligible ventilatory sensitivity to hypercapnia and hypoxemia -  
Sleep and Wakefulness
- NREM (Non–Rapid eye movement) sleep affected – Primarily under chemoreceptor control
- Progressive hypercapnia and hypoxemia
- Children do not exhibit signs of respiratory distress when challenged with hypercarbia or hypoxia

# CCHS - Incidence & Genetics

- 1/100-200,000 live births
- Polyalanine repeat mutation in the Paired like Homeobox (PHOX2B) gene 4p12
- Key in the formation of Autonomic reflex pathways
- >90% have increased repeat expansion sequence in the PHOX2B gene ranging from 24-33 alanine's (Normal : 20 alanine sequence)
-  Ventilatory support time - increasing alanine sequencing

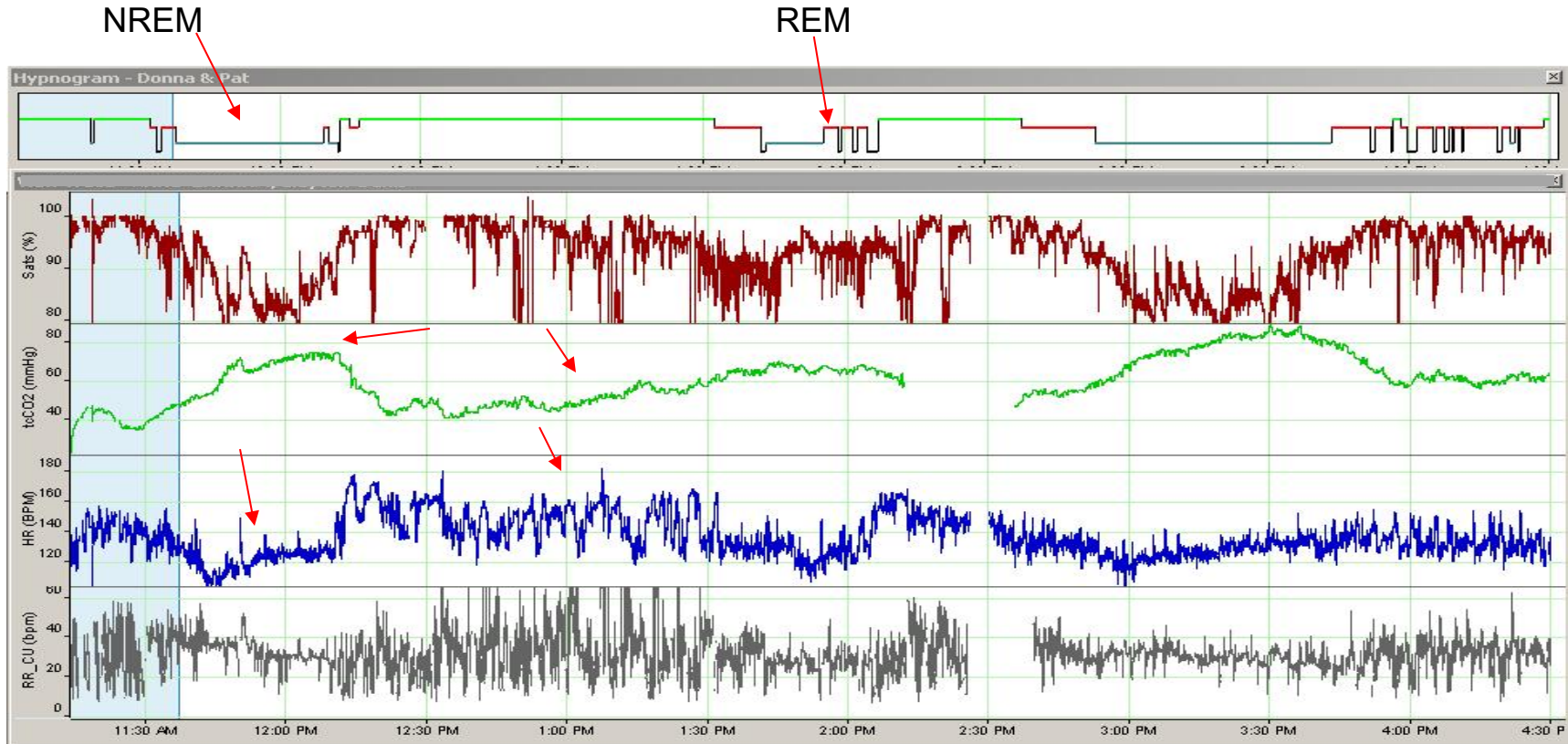
# CCHS - Genetics

- 20/24 genotype – present with respiratory illness
- 20/25 genotype – rarely require 24hr ventilation
- 20/26 genotype – variable depending on activity
- 20/27 – 20/33 genotype – continuous ventilatory support

# CCHS - Clinical Presentation

- Newborn period: Chronic intermittent duskiess, cyanosis and measurable hypercapnia
- Some infants present with frank apnoea and respiratory arrest upon falling asleep
- No respiratory distress with these episodes
- If undetected or misdiagnosed, will present later with: pulmonary hypertension and Right heart failure

# CCHS – Diagnostic Overnight PSG



# CCHS Management

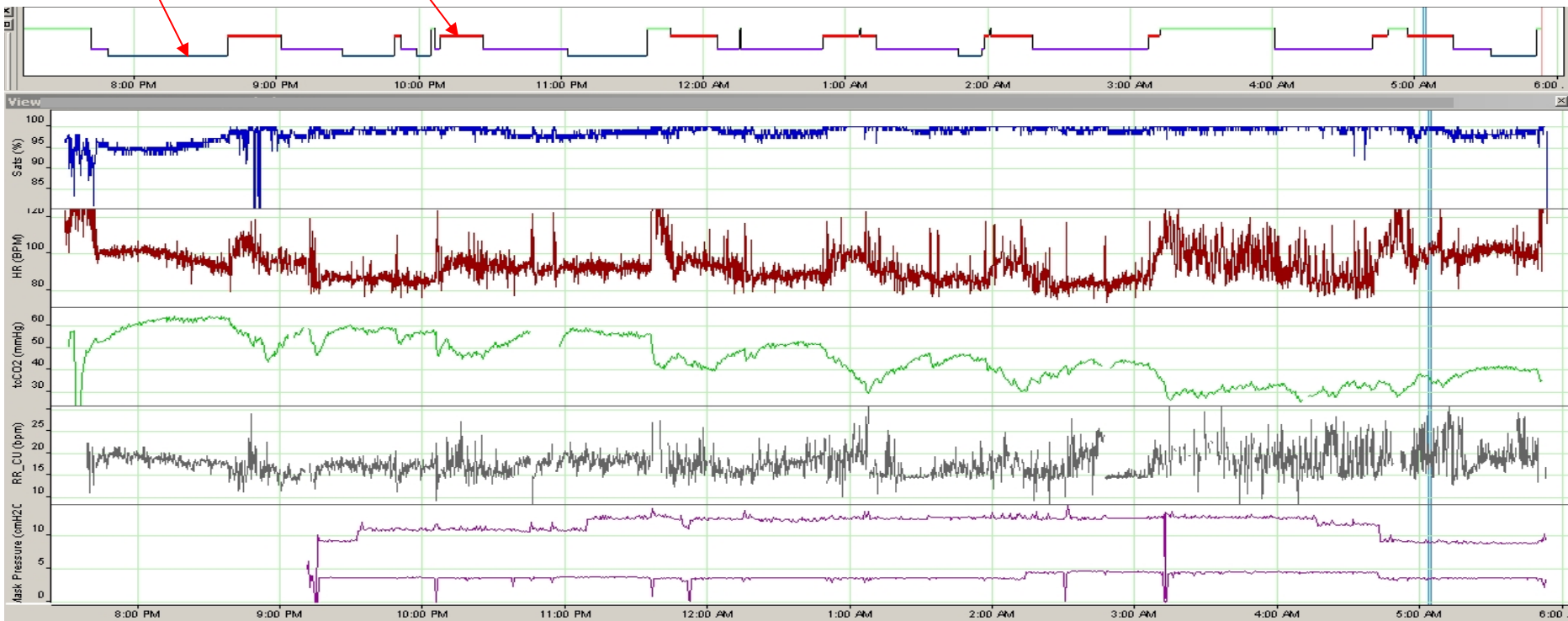
- Ventilatory support during sleep - Lifelong
- Pharmacological respiratory stimulants – Not effective
- Adequate ventilation : Bi-level support, majority via tracheostomy and later stage nasal mask >6 years age
- Continuous ventilation: wake and sleep and then weaning to all sleep



# CCHS - Overnight PSG during Bi-level titration

NREM

REM



# Rx of CCHS Children is Different

- Lack of objective or subjective response to hypoxaemia and hypercapnia while awake & asleep
- Do not mount fever or tachypnea response when unwell
- Minor respiratory infection – may cause apnoea
- Complete absence of subjective or objective response to hypoxia and hypercapnia while awake or asleep
- CCHS patients are NOT like other children on home mechanical ventilation
- Requires diligence and vigilance – parents and care givers

# Associated Abnormalities

- Anomalies of the Autonomic nervous system:
  - Hirschsprung's disease
  - Cardiac arrhythmias
  - Pupillary abnormalities
  - Neural crest tumours

# CCHS - Prognosis

- Early diagnosis and treatment & MDT
- 65% attend mainstream school
- Good quality of life
- Overall mortality 10-40%
- Most deaths in the first 2 years
- Lifelong optimal ventilatory support

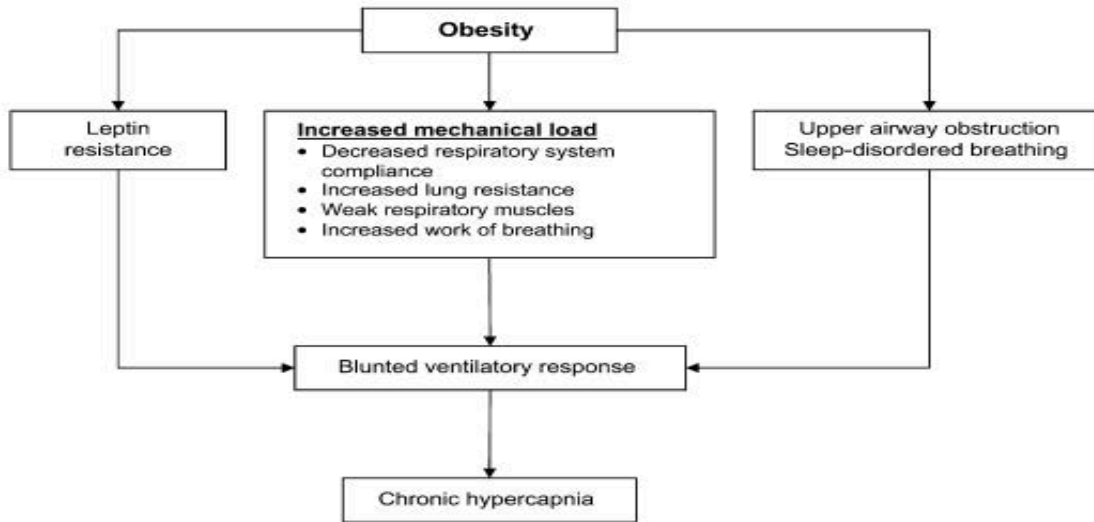
# Overview

- Neuromuscular disorders
- Central control hypoventilation
- Skeletal/Thoracic cage abnormalities, Obesity hypoventilation
- Lung and airway diseases

# Skeletal/Thoracic cage abnormalities, Obesity Hypoventilation

- Most common disorder – Scoliosis and Kyphoscoliosis
- Idiopathic or secondary to variety of other causes e.g., neuromuscular disorder
- Restrictive pattern
- Airway obstruction from breathing at low volume/displacement of intrathoracic trachea, main stem bronchi

# Obesity Hypoventilation (OHS)



*Figure 2.* Mechanisms by which obesity can lead to chronic daytime hypercapnia.

# Management

- Weight reduction measures/Bariatric surgery
- Surgery – Kyphoscoliosis
- Non-invasive: Bi-level ventilation



# Causes of Sleep Related Hypoventilation

- Neuromuscular disorders
- Central control hypoventilation
- Skeletal/Thoracic cage abnormalities
- Lung and airway diseases

# Lung and Airway diseases

- Chronic lung disease – various causes eg; cystic fibrosis, diffuse lung diseases
- Airway abnormalities
- Cause hypoxemia, hypercarbia

# Lung and Airway Diseases Management

- Management of underlying disorder
- Nutrition
- Airway clearance
- Rx of infections
- Supplemental oxygen
- Non – invasive ventilation

# Ventilation

- Improve gas exchange
- Optimize lung volumes
- Reduce the work of breathing
- Reverse atelectasis
- Stabilize chest wall

# Modes of ventilation

## Bi-level

### • Non-invasive:

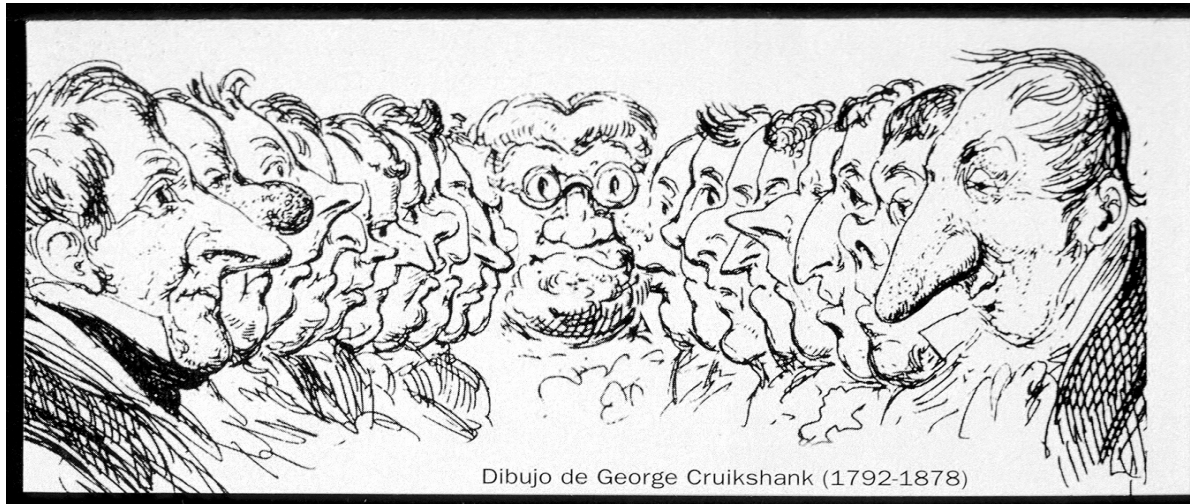
- Nasal mask
- Oro-nasal mask
- Face mask
- Nasal pillows

### • Invasive:

- Tracheostomy

# Interface

- Different size, shape
- Mask choice



# Summary

- Sleep history & assessment in children is important
- SDB is common, insidious onset of symptoms
- Diagnosis of SDB remains challenging
- Pulmonary function tests (FEV1 or FVC of 40% predicted), reliable to predict SDB
- Sleep oximetry may be helpful for screening, If normal does not exclude SDB

# Summary

- Polysomnography remains the gold standard for diagnosis of SDB
- Appropriate Rx of SDB – NIV, has significant impact on morbidity and mortality
- CCHS – mandatory ventilation during sleep, close monitoring, good prognosis