CASE 1

- Male, 50 days-old
- Weight: 2,700 g (15°); length 50 cm (50°); BMI 10,88
- During the second day of life, it was noted that the patient had distended abdomen and was unable to pass meconium without rectal stimulation → diagnosis of Hirschsprung's disease
- For the next few days recurrent apnea and hypercarbia leading to the clinical suspicious of Congenital Central Hypoventilation Syndrome (CCHS)
- Baby had mutations in the PHOX2B gene (alanine repeat expansion number 20/26), confirming the diagnosis.

Congenital Central Hypoventilation Syndrome (CCHS)

- Rare life-threatening disorder of autonomic dysregulation with hypoventilation during sleep so lifelong ventilatory assistance is necessary.
- PHOX2B is the only gene in which mutation is known to cause CCHS
- The most frequently found mutation is a polyalanine expansion in exon 3. The normal genotype has a sequence of 20 alanines (20/20 genotype). CCHS occurs from four extra alanines in one of the alleles (20/24 genotype).
- There is a correlation between genotype and phenotype: the higher the number of alanines, the greater the severity of clinical findings.
- In 1978, Gabriel Haddad was the first author to describe the association between CCHS, Hirschsprung's disease (HSCR)

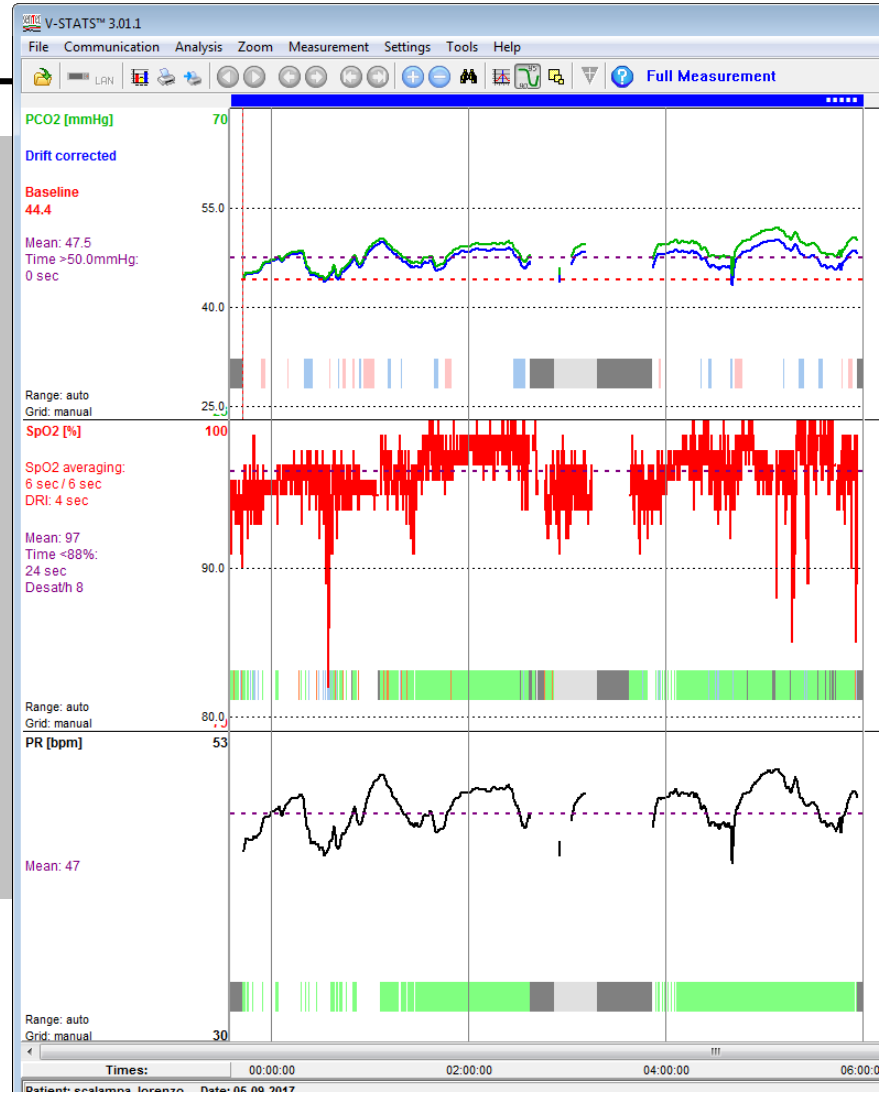
Weese-Mayer DE, et al 2010

POLYGRAPHY STUDY

Central apnea and periodic breathing

POLYGRAPHY STUDY

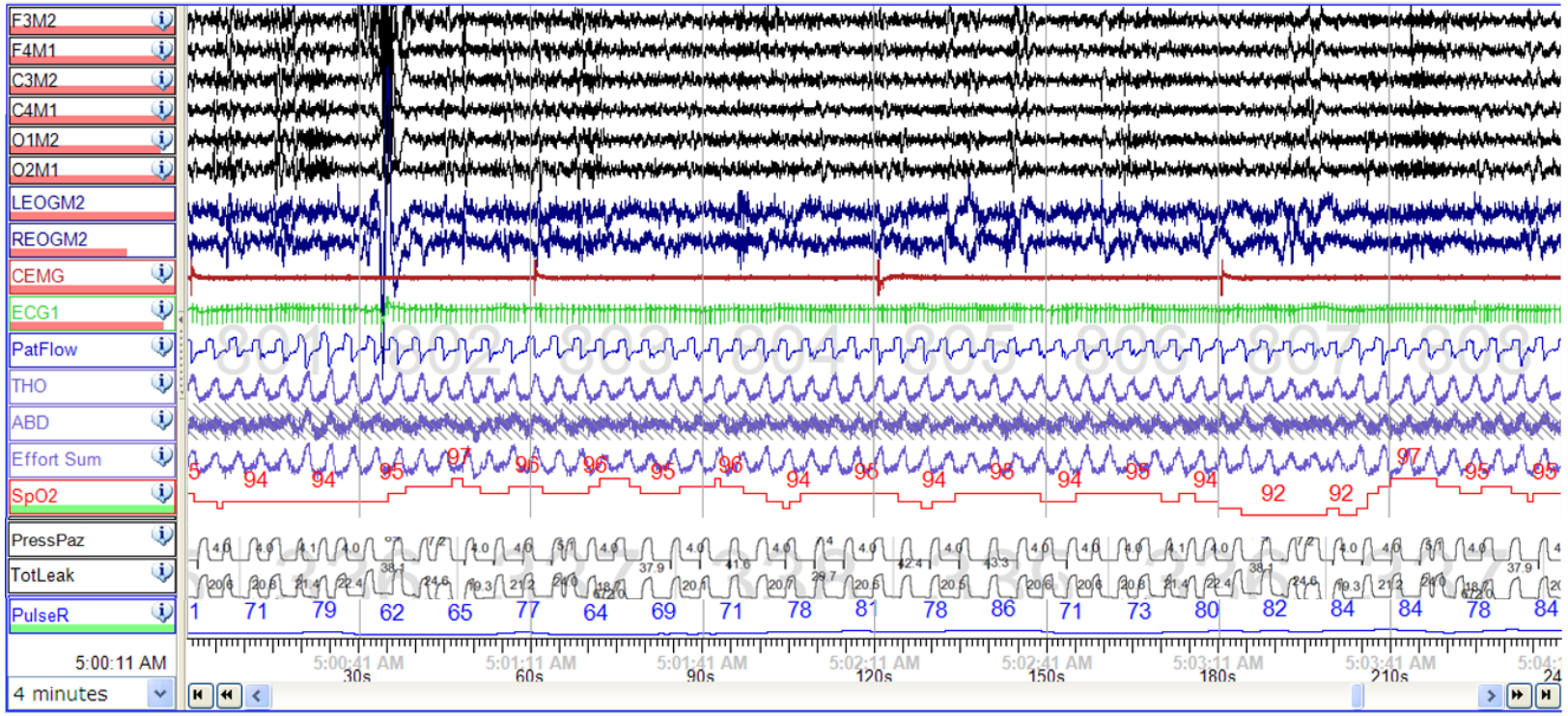
PARAMETERS	BASELINE
Mean SaO2 (%)	93
Minimal SaO2 (%)	77
SaO2 < 90% (%TST)	7
Desaturation Index (n° desat >4%/h)	31,4
AHI (n° obstructive/mixed apneas hypopneas/h)	0,9
Central Apnea Index (n° central apneas/h)	4,9
Periodic breathing (% time)	35
Mean tcCO2 (mmHg)	48
Maximal tcCO2 (mmHg)	58
Time spent tcCO2 > 50 mmHg (%TST)	56



Nocturnal hypoventilation

WICH VENTILATION MODE?

APCV: IPAP 14cmH2O-EPAP 4 cmH2O, RR 25/min



PG in NIV

Mean SaO2 (%)	98,8
Minimal SaO2 (%)	86
SaO2 <90% (%TST)	0,1
ODI (n° desat >4%/h)	1,5
AHI (n° /h)	2
Central Apnea Index	0,8
Periodic Breathing (% time)	9
mean tcCO2 (mmHg)	44
maximal tcCO2 (mmHg)	52
Time >50 mmHg(%TST)	11

CCHS - NIV

- Technological advances allow patients with mild to moderate phenotypes to receive adequate support by non-invasive ventilation (NIV), or diaphragm pacing (or combination of the two) avoiding the need for long-term ventilation by tracheostomy
- Nasal BiPAP ventilation is a safe, well-tolerated, and noninvasive means of providing ventilatory support that is suitable in the first year of life. The equipment is simple to use, and acceptance of this mode of ventilatory support was excellent in the 9-month-old infant
- CCHS provides an unusual insight into medical decision-making around long-term ventilator support of children as the organ damage or disabilities associated with the usual situations of long-term ventilation use are stripped away.

Weese-Mayer DE, et al 2010

CASE 2

- Male, 3 months-old
- Weight: 5,45 g (15°); length 65 cm (85°); BMI 12,9
- 10 days of life: diagnosis of Congenital muscular dystrophy with absent merosin (Laminin 2) on skeletal muscle biopsy, confirmed by mutation analysis.
- 2 months of life: night desaturations, intercostal retractions, poor suction and swallow

Merosin deficient congenital muscular dystrophy 1A (MDC1A)

- Results from mutations in the /react-text *LAMA2* react-text: 230 gene
- The phenotype includes elevated serum creatine kinase levels >1000 U/l, onset of severe weakness within the first six months of life and proximal joint contractures
- Patients with absent merosin staining were more likely to require ventilatory support in comparison with those who have residual staining.

Genotype–phenotype correlation in a large population of muscular dystrophy patients with *LAMA2* mutations. Geranmayeh, Fatemeh et al. Neuromuscular Disorders , Volume 20 , Issue 4 , 241 - 250

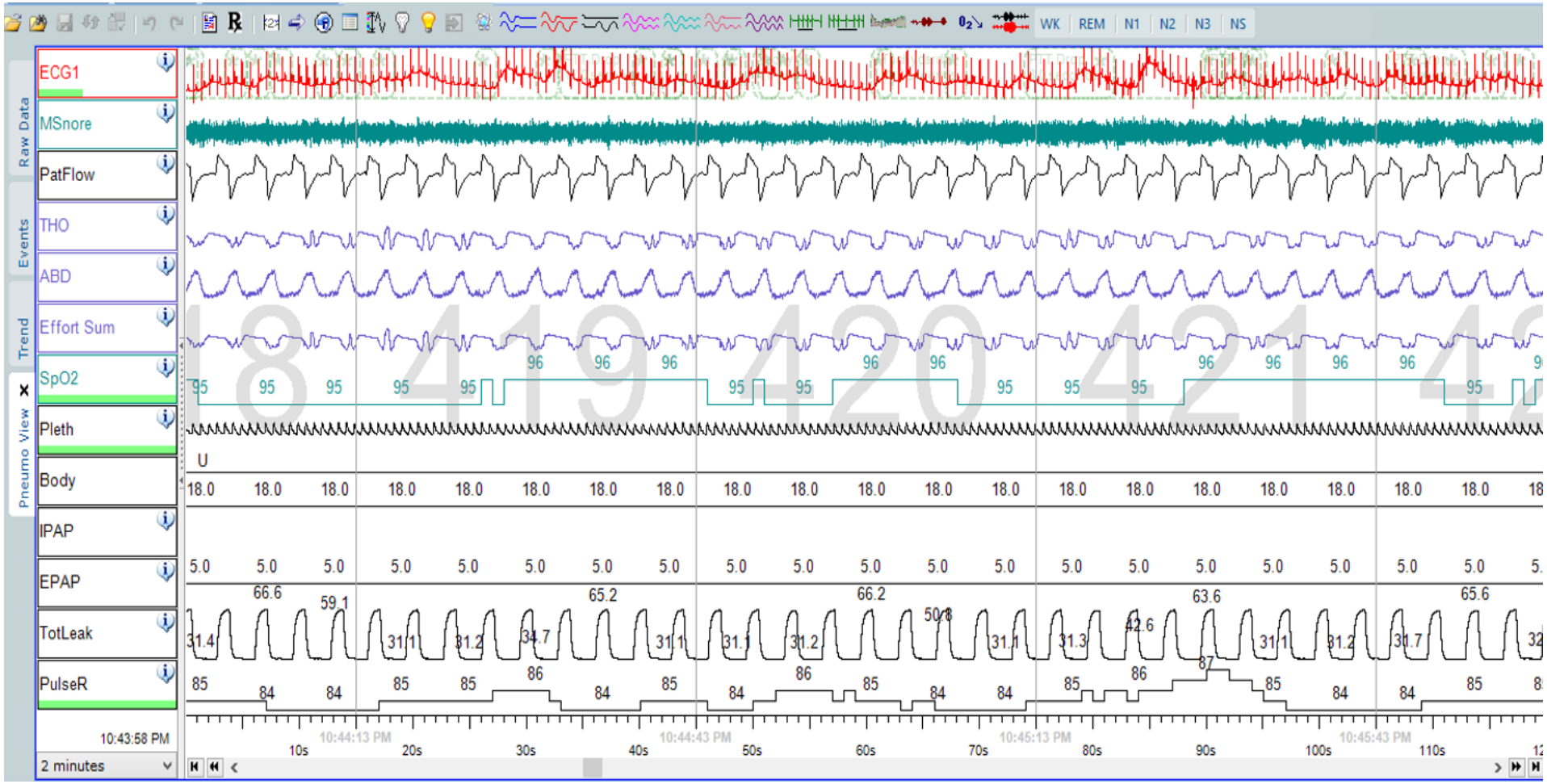
POLYGRAPHY STUDY

PARAMETERS	BASELINE	NIV (7 days)
Mean SaO2 (%)	89	93
Minimal SaO2 (%)	75	0,0
SaO2 < 90% (%TST)	64,1	0,0
Desaturation Index (n° desat >4%/h)	21,2	0,0
AHI (n° obstructive/mixed apneas hypopneas/h)	13,7	0,0
Central Apnea Index (n° central apneas/h)	0,2	0.1
Mean tcCO2 (mmHg)	50	47.5
Maximal tcCO2 (mmH)	55	49
Time spent tcCO2 > 50 mmHg (%TST)	21	0

NOCTURNAL POLYGRAPHY → **Severe Obstructive Sleep Apneas**

WICH MODE OF VENTILATION?

PSV: IPAP of 18 cmH2O and EPAP of 5 cmH2O



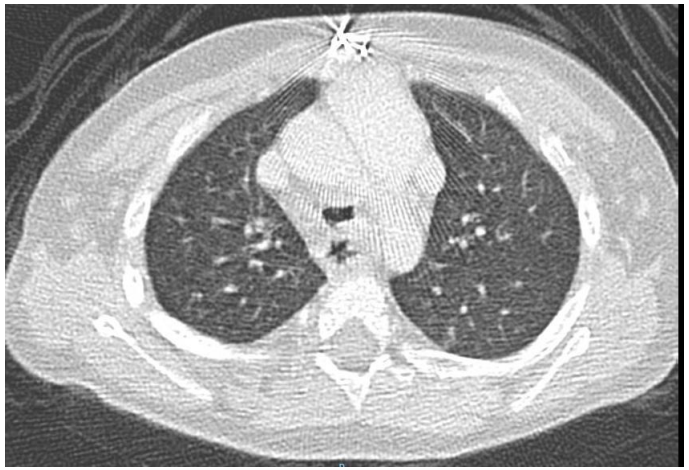
CASE 3

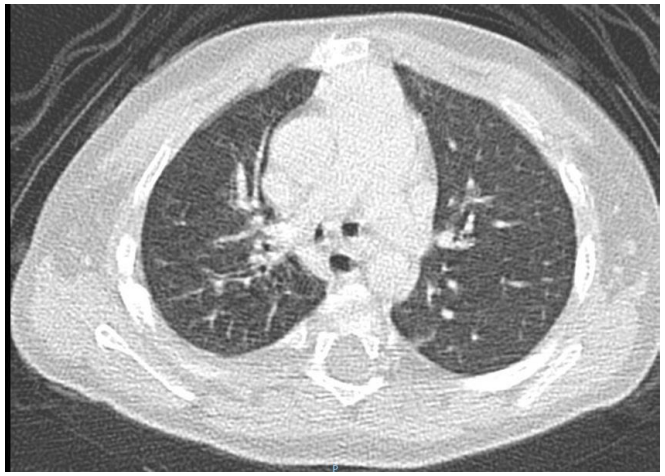
- Male, 3/12 months-old
- Weight: Kg 5,380
- Length 59 cm
- CC 40 cm

- Acute dyspnea
- Stridor
- Hypercapnia
- Bronchoscopy: Tracheomalacia
- Normal bronchoalveolar lavage fluid culture, viral analysis, differential cells count and lipid-laden index

Dynamic CT scan

Expiratory deformation of the main airways with a significant caliber reduction of the main left bronchus (3.5x2 mm), carina and upper lobar right bronchus consistent with a *Tracheobroncomalacia* diagnosis.





Baseline Psg + CO_2+ ABG

Parameters	Values
pH	7,39
PaCO2 (mmHg)	58,1
PaO2 (mmHg)	101,2
HCO3- (mmol/L)	35
BE (mmol/L)	10,2

Parameters	Values
TST (hh.min)	06.42
Mean SaO2 (%)	99,6
Minimal SaO2 (%)	80
SaO2 < 90% (%TST)	0,2
Desaturation Index (n° desat >4%/h)	8,7
AHI (n° obstructive/mixed apneas hypopneas/h)	19
Central Apnea Index (n° central apneas/h)	2,1
Mean tcCO2 (mmHg)	61
Maximal tcCO2 (mmHg)	66
Time spent tcCO2 > 50 mmHg (%TST)	97,3

Diurnal hypercapnia

Severe Obstructive Sleep Apneas

Nocturnal hypoventilation

Tracheobroncomalacia

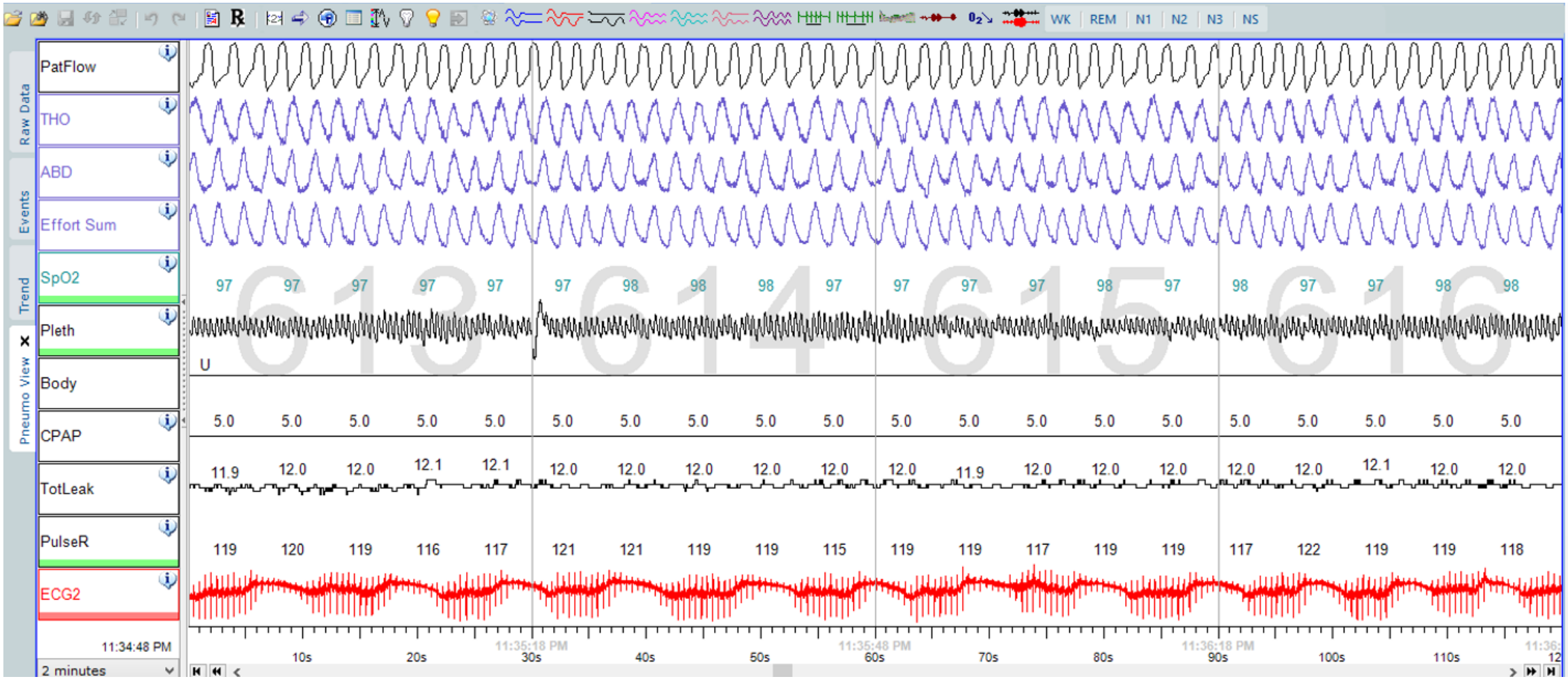
- Tracheomalacia (TM) refers to diffuse or segmental tracheal weakness.
- Tracheobronchomalacia (TBM) exists when the weakness extends into one or both main stem bronchi.
- Both conditions result in exaggerated luminal narrowing during expiration and widening during inspiration
- CPAP can be use as a bridge-treatment waiting for an increased rigidity of the bronchial cartilage with growth
- CPAP delivers a continuous distending pressure throughout the respiratory cycle that reduce the work of breathing
- Surgical therapy is preferred in very severe cases

Austin J, Ali T. Paediatr Anaesth. 2003;13(1):3
Carden KA, Boiselle PM, Waltz DA, Ernst A. Chest. 2005;127(3):984.

HELMET-CPAP → Nasal-cpap

- He started a trial of non-invasive respiratory support with Helmet-CPAP (5 cmH_2O)
- After 2 weeks training period, good compliance with nasal-CPAP (5 cmH_20)
- Improvement of dyspnea and stridor
- Further reduction of $tcpCO_2$ and of obstructive sleep apneas

Psg in CPAP 5 cmH_2O



Psg+CO_2+ ABG

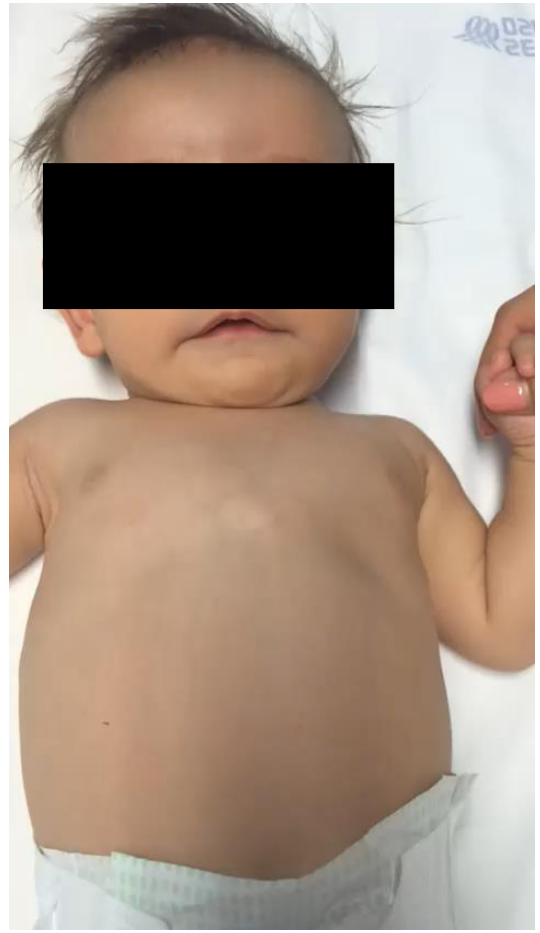
Parameters	Helmet-CPAP (2 days)	Nasal-CPAP (15 days)
pH	7,37	7,43
PaCO2 (mmHg)	53	44,2
PaO2 (mmHg)	98	108
HCO3- (mmol/L)	33	28,7

Parameters	Helmet-CPAP (2 days)	Nasal-CPAP (15 days)
TST (hh:mm)	7:21	7.45
Mean SaO2 (%)	96.2	99,1
Minimal SaO2 (%)	82	93
SaO2 < 90% (%TST)	5,4	0
Desaturation Index (n° desat >4%/h)	12,3	1,5
AHI (n° obstructive/mixed apneas hypopneas/h)	8	2
Central Apnea Index (n° central apneas/h)	1,1	0,8
Mean tcCO2 (mmHg)	54	45
Maximal tcCO2 (mmHg)	63	50
Time spent tcCO2 > 50 mmHg (%TST)	23	11

CASE 4

- Male, 3/12 months-old
- Weight: Kg 4,820
- Length 57 cm
- CC 39 cm

- Inspiratory stridor since second day of life
- Intercostal retractions
- Failure-to-thrive
- No neonatal or perinatal issues

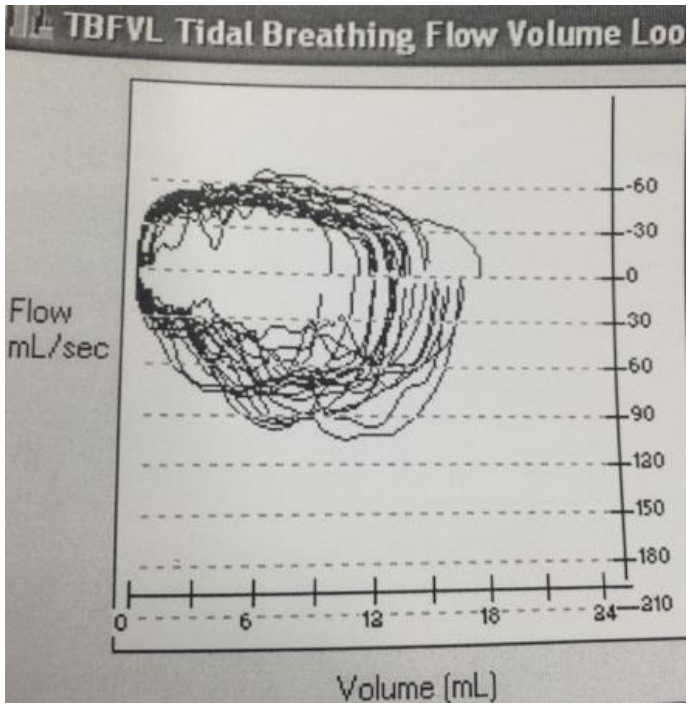


SpO_2/CO_2 sleep STUDY

Parameters	Values
TST (hh:min)	9.31
Mean tcCO2 (mmHg)	45,7
Maximal tcCO2 (mmHg)	52,1
Time spent tcCO2 > 50 mmHg (%TST)	1
Mean SaO2 (%)	97,7
Minimal SaO2 (%)	87
SaO2 < 90% (%TST)	0,1
Desaturation Index (n° desat >4%/h)	6,6

Lung function tests

- Inspiratory obstruction
- Vt 2,7 mL/kg
- RR 85 b/min
- PTIF 80mL/s
- PTEF 57 mL/s
- TPTEF/Te 0.43
- TEF50/TIF50 0.8



CPAP 6 cm H_2O

- Weight gain
- Good adherence
- No stridor or intercostal retractions

Laryngomalacia

- Laryngomalacia refers to collapse of the supraglottic structures during inspiration
- Laryngomalacia manifests with inspiratory stridor, usually in the neonatal period.
- The diagnosis of laryngomalacia is usually suspected based upon the history and physical examination. It is confirmed with flexible fiberoptic laryngoscopy
- CPAP or BIPAP may be indicated in infants with comorbidities, failure to respond to surgery or as a bridge to surgical intervention
- Infants with moderate or severe laryngomalacia (stridor with feeding difficulty, dyspnea, tachypnea, cyanosis, apnea) should be referred to an otolaryngologist for full endoscopic evaluation and intervention

Ayari S.Eur Ann Otorhinolaryngol Head Neck Dis. 2013 Feb;130(1):15-21.

EPIGLOTTOPLASTY