Rett syndrome
Unmasking complex cardio-respiratory dysfunction and possible treatment.

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RETT SYNDROME

- Rare
  (1:10,000 girls)
- Genetic – seldom inherited
  (> 99% sporadic)
- Neuro-developmental disorder – not progressive!
- Immature brainstem/brain
- Central control of the autonomic nervous system insufficient/deranged

- Breathing dysrhythmia
- Blood pressure & heart rate uncontrolled
- Blood circulation in tissues deranged
- Agitation and seizures
- Epilepsy
- Gastrointestinal dysfunction
- Incoordination of thoughts and movements
Brainstem features become clinically significant during stage II (regression)

This appears at variable ages
Disease-Causing Mutations in MeCP2
We are dealing with basic human physiology

We do not expect these controls to be deranged

Monitor, Interpretation, Integration

Drivers

Targets

Clinical exams must consider these functional units (autonomic nuclei)
Brainstem features

- Breathing dysrhythmia, insufficient control of blood gases, unstable blood pressure and heart rate.
- Oropharyngeal and gastrointestinal dysfunctions cause swallowing difficulties, aspiration, gastrooesophageal reflux, oesophagitis and constipation.
- Agitation, fear, mood swings, difficulty to relax and concentrate, cold and discoloured feet.
- Extrapyramidal symptom: dystonia with orthopaedic deformities, muscle wasting, incoordination of thoughts and movements.
Organisation of brainstem nuclei in adults

Schematic sagittal projection of sensory nuclei.

Schematic sagittal projection of motor nuclei.

Sensory

Motor
We require Cortico-Bulbar Neurophysiology

- EEG
- Video
- Subject
- Beat-to-beat non-invasive BP
- Breathing movement
- Transcutaneous pO₂ and pCO₂
- NeuroScope
The Frösö Declaration

Addressing the cardiorespiratory challenges posed by Rett Syndrome in Medicine.


Three cardiorespiratory phenotypes

- Forceful breathers
- Feeble breathers
- Apneustic breathers
Three cardiorespiratory phenotypes

- Nutritional needs can be doubled the normal value for forceful breathers.

- Feeble or apneustic breathers may not restart spontaneous breathing post-operatively due to artificial hyperventilation.

- Feeble breathers are sensitive to sedation (Opioids and Diazepam) and these drugs can cause apnoea.

- Valsalva's manoeuvre is a common complication in Rett syndrome.
Measurement of breathing movements:

1 s

Amplitude

Ramp inspiration

Expiration early late
Forceful Breathing

Deep Breathing

Tachypnoea

Hyperventilation
Feeble Breathing

Rapid Shallow

Shallow

Central Apnoea
Apneustic Breathin
Figure 2

Valsalva manoeuvre in girl with Rett syndrome

Some movement artefacts are present
Treatment of breathing dysfunction in Rett syndrome

- **Forceful breathers:** Rebreathing of own expired air in a rebreathing mask with adjusted dead space, when awake.

- **Feeble breathers:** Assisted breathing with CPAP or Bi-PAP, mainly at night. Sometimes using an oxygen concentrator initially.

- **Apneustic breathers:** Buspirone to shorten apneustic breaths, if not too much feeble breathing.
With the rebreathing mask Angelica gets calm and relaxed
Outcome of treatment of a forceful breather with Rett syndrome with a rebreathing mask.

- Increased attentiveness and interest at home and in school.
- Face expressive and smiling in stead of mimicless and serious.
- Muscles less tense, more relaxed.
- Increased muscle strength being able to stand up longer.
- Dramatic decrease of seizures.
- Decrease of cyanosis from several times each day to once in 4 months.
- Normal colour of lips and face.
- Normalisation of colour and temperature of feet (earlier cold and bluish).
Outcome of treatment of a feeble breather with Rett syndrome with a Bi-PAP/CPAP.

- Her face does not turn grey or blue.
- Her gross motor ability has improved.
- She is calmer and more attentive.
- She responds to people around her with a smile.
- She sleeps better at night.
- Dramatic decrease of seizures.
- Normalisation of colour and temperature of feet (earlier cold and bluish).
- Decrease of cyanosis from several times each day to once in 4 months.
- Normal colour of lips and face.
References


Tissue respiration

- Tissue respiration: Transport from blood vessels to tissue needs energy.

- Energy is made by mitochondria in the cells and needs both oxygen and carbon dioxide at right levels.

- Without adequate oxygen or carbon dioxide tissue, respiration becomes anaerobic – produces a slight amount of energy and causes pain. The body gets progressively week, stiff, ”burnt out”.

- May be understood as progression of the disorder.
General treatment

- Central autonomic control
  - Cardiovascular
  - Breathing
  - Sleep
  - Mood
  - Gastrointestinal
  - Bladder
  - Seizures
- Learning
  - Concentration
  - Motivation
  - Communication
  - Activity
- Growth and Nutrition
  - Expenses
- Muscle tone
  - Dystonia
  - Contractures
- Postural control
- Movements
  - Coordination
  - Initiation
  - Mobility
- Epilepsy