

Myotonic Dystrophy

Myotonic dystrophy is the most common heritable neuromuscular disorder, inherited in an autosomal dominant manner. It is also known as Dystrophica Myotonica, DM1 or Steinert disease.

Epidemiology

- Incidence: 1/8000
- Male = Female

Genetics

- Myotonic Dystrophy is caused by CTG triplet repeat expansion in the non-coding region of the *DMPK* gene (DM1) gene on chromosome 19q13.3, encoding myotonin.
- Triplet repeat expansion is detected in 98% of patients
- Onset of symptoms is earlier in successive generations due to triplet repeat expansion (anticipation)
- As a general rule, prognosis cannot be predicted using molecular analysis alone except in congenital myotonic dystrophy when there is gross (>1000) repeat expansion.
- Normal myotonin is required for intercellular conduction.
- The effect of the CTG repeat is complex but may affect adjacent genes and RNA processing.

Clinical presentation

- Clinical presentation of myotonic dystrophy is extremely variable, even within families.
- Varies from severe respiratory insufficiency in infancy to cataracts alone in adulthood.
- Most common age of symptom onset is 20-30 years.

Physical Signs

- Frontal balding
- Myotonia: elicited by inability to rapidly relax clenched fist or by tapping thenar eminence
- Facial muscles: ptosis, inability to frown, clench teeth, smile.
- Peripheral muscles: reduced power in sternocleidomastoids, distal arm and leg, reflexes may still be present if only mild disease presentation
- Bradycardia/heart block
- Lens opacities

Diagnosis

- Molecular DNA analysis is routinely available for myotonic dystrophy. Pre-natal diagnosis is available.
- Urine dipstick for glucose
- ECG: conduction defects
- Ophthalmology assessment
- Sleep studies
- Consider EMG if there is diagnostic uncertainty and normal molecular analysis

Complications

- Myopathy: poor mobility, difficulty swallowing
- Lens opacities

- Heart conduction defects
 - Gastrointestinal dysfunction
 - Obstructive sleep apnoea and daytime hypersomnolence
 - Adverse response to general anaesthetics: (prolonged recovery, aspiration, dysrhythmias)
 - In pregnancy: higher miscarriage rate, polyhydramnios, prematurity, failure to progress in labour, post-partum haemorrhage
- Life expectancy:
- Mean age of death 60 years
 - Mortality most commonly due to pneumonia and cardiac dysrhythmias

Congenital myotonic dystrophy:

There is a risk of congenital myotonic dystrophy in babies born to affected mothers. This is due to gross triplet repeat expansion. Congenital myotonic dystrophy presents with hypotonia, respiratory and feeding difficulties and has a 20% mortality. Surviving children have learning difficulties.

Treatment

- May require pacemaker
- May require NIPPV for obstructive sleep apnoea
- Medic alert badge
- Caution with sedatives, opiates, general anaesthetics

Genetic Counselling

- Offspring risk of an affected individual is 50%.
- Predictive testing for at-risk relatives is available. Referral to clinical genetics is recommended to discuss implications including psychosocial and insurance issues.

Surveillance

- Annual ECG, urine dipstick for glucose and optician
- Ability to drive

Differential diagnosis (BOX)

- Proximal myotonic myopathy (DM2): autosomal dominant, proximal myopathy, muscle pain, mild myotonia.
- Distal myopathies: Inclusion body myositis, limb girdle myopathies
- Congenital non-progressive myotonias: improve with exercise
- Hyperkalemic periodic paralysis

ALERT BOX

Risk from general anaesthetics
May lead to malignant hyperpyrexia

Photos:
Myopathic face
Myotonia
ECG heart block