

# General information

Record ID \_\_\_\_\_

NHC \_\_\_\_\_

Hospital \_\_\_\_\_

Date of birth \_\_\_\_\_

Place of birth \_\_\_\_\_

Sex  Male  
 Female

Ethnics  Caucasian  
 Subsaharian african  
 Southamerican  
 Asian  
 Gypsy

Affected relatives  Yes  
 No

Consanguinity  Yes  
 No

Genetic inheritance  Maternal  
 Recessive  
 Dominant  
 Unknown

Age of onset (specify months or years) \_\_\_\_\_

Death  Yes  
 No

Specify cause of death \_\_\_\_\_

# Clinical characteristics

Diagnostic

- Alpers
- Ataxia
- Barth
- Cardiomyopathy
- Carnitine disorders
- Cartilage-hair hypoplasia
- Congenital weakness
- Cramps
- Deafness
- Deafness-dystonia
- Diabetes
- DIDMOAD
- Dystonia
- Encephalopathy
- Fatigue and exercise intolerance
- Friedreich ataxia
- Gastrointestinal
- HAM ( hearing loss, ataxia, myoclonus)
- Hepatic
- Hypoglycemia
- Infantile CNS
- Kearns- Sayre
- Lebers-optic (LHON)
- Leygh syndrome
- Leukodystrophy
- Lipomatosis
- MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis, Stroke)
- MERFF (Myoclonic Epilepsy, Ragged Red Fibers)
- MILS (Leigh syndrome, maternal inheritance)
- MLASA (lactic acidosis, Sideroblastic Anemia)
- MNGIE (Myopathy and external ophtalmoplegia, Neuropathy, Gastro-Intestinal, Encephalopathy)
- Myalgias
- Myoglobinuria
- Myopathy syndrome
- NARP/MILS (Neuropathy, Ataxia, Retinitis Pigmentosa)
- Neuropathy
- Ophtalmoplegia External (PEO)
- Pancreas
- Parkinson's
- Pearson's
- Rhabdomyolysis
- SANDO (Sensory Ataxic Neuropathy Dysarthria, Ophthalmoparesis)
- Spastic Paraparesis
- Spinal muscular atrop
- Toxic (drug)
- Other
- Unknown

Mitochondrial disease criteria (Morava et al 2006)

[Attachment: "criterios clínicos Morava Neurology 2006.pdf"]

Mitochondrial disease criteria

- 1: mitochondrial disorder unlikely
- 2-4: possible mitochondrial disorder
- 5-7: probable mitochondrial disorder
- 8-12: definitive mitochondrial disorder

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**DISEASE ONSET SYMPTOMS**

Neuromuscular disorders symptoms

- Yes
- No

Neuromuscular disorders

- Cardiac arrhythmia
- cardiomyopathy
- Exercise intolerance
- Hypotonia
- Muscle wasting
- Muscle weakness
- Myalgia/muscle pain
- Myoglobinuria
- Peripheral neuropathy
- Respiratory impairment
- Other

If other neuromuscular disorder symptoms, please specify

\_\_\_\_\_

Eyes symptoms

- Yes
- No

Eyes

- Cataract
- Eyelid ptosis
- Ophthalmoparesis
- Optic neuropathy
- Retinopathy
- Visual impairment
- Other

If other eyes symptoms, please specify

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Brain and movement disorders symptoms

- Yes
- No

Brain and movement disorders

- Ataxia
- Cerebellar signs
- Consciousness disturbance
- Dementia
- Dyskinesia
- Dystonia
- Epileptic seizures
- Hearing loss
- Microcephaly
- Migraine
- Motor-neuron disease
- Myoclonus
- Nystagmus
- Parkinsonisms
- Psychiatric symptoms/abnormal behaviour
- Neurological regression
- Psychomotor retardation
- Pyramidal signs
- Status epilepticus
- Stroke-like episodes
- Tremor
- Unspecified abnormal movements
- Unspecified abnormal eye movements
- Unspecified epileptic seizures
- Dysautonomic symptoms
- Bulbar dysfunction
- Other

If other brain and movement disorders, please specify

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Gastrointestinal and endocrinopathy symptoms

- Yes
- No

Gastrointestinal and endocrinopathy

- Diabetes mellitus
- Failure to thrive
- Gastrointestinal dysmotility
- Hepatopathy
- Hypogonadism
- Hypoparathyroidism
- Hypothyroidism
- Kidney involvement
- Short stature
- Swallowing impairment
- Vomiting
- pancreatic insufficiency
- Other

If other gastrointestinal symptoms, please specify

Blood abnormalities symptoms

- Yes
- No

Blood abnormalities

- Anaemia
- Increment of ALT/AST
- Increment of CK
- Neutropenia
- Pancytopenia
- Abnormal clotting factors
- Others

If other blood abnormalities, please specify

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Cutaneous involvement symptoms

- Yes
- No

General appearance and cutaneous involvement

- Acrocyanosis
- Dysmorphic features
- Hirsutism
- Multiple lipomatosis
- Hair abnormalities
- Abnormal pigmentation
- Other

If other cutaneous symptoms, please specify

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# The Newcastle Mitochondrial Scale

Please select one of the options

- Paediatric patient  
 Adult patient

If paediatric, choose one option

- NPMDS 0-24 months  
 NPMDS 2-11 years  
 NPMDS 12-18 years

THE NEWCASTLE PAEDIATRIC MITOCHONDRIAL DISEASE SCALE

[Attachment: "NPMDS escala 0 - 24 meses.pdf"]

NPMDS date \_\_\_\_\_

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## Section I: Current Function (preceding 2 week period)

Vision

- Normal. No parental concerns  
 Mild. Limited eye or head movement to large objects or parental face in visula field  
 Moderate. No response to large objects or parental face in the visual field  
 Servere. No response to light

Hearing

- Normal  
 Mild. Body, head or eye movement only to loud noise  
 Moderate. No reaction to loud noise  
 Severe. No hearing (even with aid)

Communication (assessed with appropriate regard for age)

- Normal. Age appropriate communication  
 Mild. Delayed development of communication  
 Moderate. Communication unintelligible to parents or completely reliant on non-verbal communication  
 Severe Not communicating effectively in any form.

Feeding

- Normal  
 Mild. Difficulties in sucking/ coughing/ anorexia/wheezy with feeds or occasional choking  
 Moderate: Supplementary enteral feeding or recurrent aspiration pneumonia  
 Severe. elusive enteral feeding (gastrostomy/NG tube). Nil by mouth

Mobility

- Normal. No concerns. Age appropriate mobility  
 Mild. Clumsy age appropriate mode of mobility  
 Moderate. Mobile but through age inappropriate mode  
 Severe. Immobile

Section I score \_\_\_\_\_

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**Section II: System Specific Involvement (preceding 6 month period)**

- Seizures
- None
  - Mild. Myoclonic or absence seizures only or < 1 generalised tonic-clonic seizure/month
  - Moderate. >5 generalized tonic-clonic seizures/month or >20 absence or myoclonic seizures/month
  - Severe, Status epilepticus or intractable seizures
- Encephalopathy
- None
  - Mild. Abnormal sleepiness/lethargy. Waking only for feeds
  - Moderate. Recurrent episodes of mild encephalopathy (>2/years)
  - Severe. Life threatening encephalopathy-requires artificial ventilation
- Gastrointestinal
- Normal
  - Mild. Constipation or unexplained vomiting/diarrhoea >3 week
  - Moderate. Severe constipation (no relief with laxative treatment) or unexplained vomiting/diarrhoea every day or surgical intervention for dysmotility
  - Severe. Malabsorption/Failure to thrive
- Endocrine
- Normal
  - Mild. Biochemical evidence of impaired function
  - Moderate. Endocrine failure requiring replacement therapy
  - Severe. Endocrine decompensation (e.g. diabetic ketoacidosis, Addisonian crisis)
- Respiratory
- Mild. Abnormal respiratory pattern not requiring therapy/hospitalisation
  - Moderate. Abnormal respiration requiring oxygen flow or hospitalisation but not ventilation
  - Severe. Abnormal respiration requiring artificial ventilation
- Cardiovascular (over preceding 12 months)
- Normal
  - Mild. Asymptomatic ECG change
  - Moderate. Abnormal echocardiogram (e. g. cardiomegaly or sustained/ symptomatic arrhythmia on ECG)
  - Severe. Decompensated cardiomyopathy or requiring pacing device/defibrillator/ablation
- Renal
- Normal
  - Mild. Impaired function but no change in diet or therapy required
  - Moderate. Impaired function requiring restricted protein diet
  - Severe. Failure requiring transplant/ dialysis

- Liver
- Normal
  - Mild. Mildly impaired Liver Function Tests (LFTs). Normal albumin and coagulation. No symptoms of hepatic failure
  - Moderate. Impaired LFTs with symptoms (e.g. jaundice, coagulation anomalies, oedema)
  - Severe. Failure requiring hospitalisation and/ or transplantation
- Blood
- Normal
  - Mild. Anaemia only
  - Moderate. Asymptomatic pancytopenia
  - Severe. Pancytopenia requiring regular transfusion/ transplantation
- Section II score \_\_\_\_\_

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### Section III: Current Clinical Assessment (at the time of assessment)

- Growth (weight ) over preceding 6 months
- Normal. Following normal growth trajectory
  - Mild. Weight less than second centile but growing parallel to it
  - Moderate. Weight crossing one centile
  - Severe. Weight crossing  $\geq 2$  centiles or less than second centile with divergent trajectory
- Development over preceding 4 months \_\_\_\_\_
- Vision
- Normal
  - Mild. Impaired fixation and tracking
  - Moderate. Impaired fixation and/or tracking of familiar faces
  - Severe. No response to light or registered blind
- Ptosis and eye movement
- Normal
  - Mild. Gaze evoked nystagmus or unilateral ptosis or impaired eye movement at extremities
  - Moderate. Intermittent nystagmus at rest or bilateral ptosis not obscuring pupils or restriction of  $>50\%$  eye movement
  - Severe. Continuous nystagmus at rest or bilateral ptosis obscuring pupils or only a flicker of eye movement.
- Myopathy
- Normal
  - Mild. Mild symmetrical weakness of hip and/or shoulder girdle only
  - Moderate. Moderate symmetrical weakness (proximal  $>$  distal) limiting functional movement
  - Severe. Wheelchair/carrier dependent or respiratory compromise due to myopathy
- Pyramidal
- Normal
  - Mild. Unilateral pyramidal signs but retaining functional movement
  - Moderate. Dense hemiplegia with little movement of affected side
  - Severe. Bilateral pyramidal weakness with little or no movement

Extrapyramidal

- Normal  
 Mild. Unilateral extrapyramidal posturing and increased tone  
 Moderate. Bilateral extrapyramidal posturing and increased tone  
 Severe. Severe extrapyramidal posturing resulting in very little movement

Neuropathy

- Normal  
 Mild. Areflexia only  
 Moderate. Sensory ataxia or motor impairment (distal weakness) but mobile  
 Severe. RELiant on mobility aids primarily due to neuropathy

Section III score

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## Section IV: Quality of life

This survey asks for your views about your child's recent health. Please answer every question by marking an "x" in the box next to the phrase which best describes your answer

1. During the past 4 weeks, how would you rate your child's overall health?

- Very poor    Poor    Fair  
 Good    Very good

2. During the past 4 weeks, how much did your child's physical health problems limit their physical activities (such as moving or playnig)

- Very much    Quite a lot  
 Somewhat    A little  
 Not at all

3. During the past 4 weeks, how much energy did your child have?

- None    A little    Some  
 Quite a lot    Very much

4. During the past 4 weeks, how much bodily pain/ discomfort did your child have

- Very much    quite a lot  
 Some    A little    None

5. During the past 4 weeks, how would you rate your child's behaviour compared with other children his/her age?

- Very poor    Poor    Fair  
 Good    Very good

6. During the past 4 weeks, how would you rate your child's ability to interact with other people (e.g. with you, siblings or other children his/her age) compared with other children his/her age?

- Very poor    Poor    Fair  
 Good    Very good

Total score

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THE NEWCASTLE MITOCHONDRIAL DISEASE ADULT SCALE (NMDAS)

[Attachment: "The newcastle mitochondrial disease adult scale (NMDAS).pdf"]

NMDAS date

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**Section I: Current function (preceding 4 week period)**

- Vision
- Normal
  - No functional impairment but aware of worsened acuities
  - Mild- difficulty with small print or text on television
  - Moderate- difficulty outside the home (eg buns numbers, road signs or shopping)
  - Severe- difficulty recognising faces
  - Unable to navigate without help (eg carer, dog, cane)
- Hearing with our without hearing aid
- Normal
  - No communication problems but aware of tinnitus or derioration from prior "normal" hearing.
  - Mild deafness (eg missing words in presence of background noise). Fully corrected with hearing aid.
  - Moderate deafness (eg regularly requiring repetition). Not fully corrected with hearing aid.
  - Severe deafness- poor hearing even with aid (see 3 above)
  - End stage-virtually no hearing despite aid. Relies heavily on non-verbal communication (eg lip reading) or has cochlear implant.
- Speech
- Normal
  - Communication unaffected but patient or others aware of changes in speech patterns or quality
  - Mild difficulties- usually understood and rarely asked to repeat things
  - Moderate difficulties- poorly understood by strangers and frequently asked to repeat things
  - Severe difficulties- poorly undestood by family or friends.
  - Not understood by family or friends. Rquires communication aid.
- Swallowing
- Normal
  - Mild- sensation of solids "sticking" (occasional)
  - Sensation of solids "Sticking" (most meals) or need to modify diet (eg avoidance of steak/ sald).
  - Difficulty swallowing solids- a ffecting meal size or duration. Coughing, choking or nasal regurgitation infrequent (1 to 4 times per month) but more than peers.
  - Requires adapted diet- regular coughing, choking, or nasal regurgitation (more than once per week).
  - Rquiring enteral feeding (eg. PEG)

## Handwriting

- Normal
- Writing speed unaffected but aware of increasing untidiness
- Mild- Has to write slower to maintain tidiness/legibility
- Moderate- Handwriting takes at least twice as long or resorts to printing (must previously have used joined writing)
- Sever. Handwriting mostly illegible. Printing very slow and untidy
- Unable to write. No legible words

## Cutting food and handling utensils

- Normal
- Slightly slow and/or clumsy but minimal effect on meal duration.
- Slow and/or clumsy with extended meal duration, but no help required
- Difficulty cutting up food and inaccuracy of transfer pronounced. Can manage alone but avoids problem foods (eg peas) or carer typically offers minor assistance (eg cutting up steak).
- Unable to cut up food. Can pass food to mouth with great effort or inaccuracy. Resultant intake minimal. Requires major assistance
- Needs to be fed

## Dressing

- Normal
- Occasional difficulties (eg shoe laces, buttons etc) but no real impact on time or effort taken to dress.
- Mild - Dressing takes longer and requires more effort than expected at the patient's age. No help required.
- Moderate - Can dress unaided but takes at least twice as long and is a major effort. Carer typically helps with difficult tasks such as shoe laces or buttons
- Severe - Unable to dress without help but some tasks completed unaided
- Needs to be dressed

## Hygiene

- Normal
- Occasional difficulties only but no real impact on time or effort required.
- Mild - hygienic care takes longer but quality unaffected
- Moderate - bathes and showers alone with difficulty or needs bath chair / modifications. Dextrous tasks (eg brushing teeth, combing hair) performed poorly.
- Severe - unable to bathe or shower without help. Major difficulty using toilet alone. Dextrous tasks require help.
- Dependent upon carers to wash, bathe, and toilet

Exercise Tolerance

- Normal
- Unlimited on flat - symptomatic on inclines or stairs
- Able to walk < 1000m on the flat. Restricted on inclines or stairs - rest needed after 1 flight (12 steps).
- Able to walk < 500m on the flat. Rest needed after 8 steps on stairs.
- Able to walk < 100m on the flat. Rest needed after 4 steps on stairs.
- Able to walk < 25m on the flat. Unable to do stairs alone.

Gait stability

- Normal.
- Normal gait - occasional difficulties on turns, uneven ground, or if required to balance on narrow base.
- Gait reasonably steady. Aware of impaired balance. Occasionally off balance when walking.
- Unsteady gait. Always off balance when walking. Occasional falls. Gait steady with support of stick 6, or person.
- Gait grossly unsteady without support. High likelihood of falls. Can only walk short distances (< 10m) 8, without support.
- Unable to walk without support. Falls on standing.

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## Section II. System Specific Involvement (preceding 12 month period)

Psychiatric

- None
- Mild & transient (eg reactive depression) - lasting less than 3 months
- Mild & persistent (lasting more than 3 months) or recurrent. Patient has consulted GP
- Moderate & warranting specialist treatment (e.g. from a psychiatrist) - eg. bipolar disorder or depression with vegetative symptoms (insomnia, anorexia, abulia etc).
- Severe (eg self harm - psychosis etc).
- Institutionalised or suicide attempt.

Migraine Headaches during the last 3 months (how many days have headaches prevented the patient from functioning normally at school, work or in the home?)

- No past history
- Asymptomatic but past history of migraines
- One day per month
- Two days per month
- Three days per month
- Four days per month or more

Seizures

- No past history
- Asymptomatic but past history of epilepsy
- Myoclonic or simple partial seizures only
- Multiple absence, complex partial, or myoclonic seizures affecting function or single generalised seizure
- Multiple generalised seizures.
- Status epilepticus

Stroke-like-episodes (exclude focal deficits felt to be of vascular aetiology)

- None
- Transient focal sensory symptoms only (less than 24 hours).
- Transient focal motor symptoms only (less than 24 hours).
- Single stroke-like episode affecting one hemisphere (more than 24 hours).
- Single stroke-like episode affecting both hemispheres (more than 24 hours).
- Multiple stroke-like episodes (more than 24 hours each).

Encephalopathic episodes

- No past history
- Asymptomatic but past history of encephalopathy.
- Mild - single episode of personality or behavioural change but retaining orientation in time/place/person
- Moderate - single episode of confusion or disorientation in time, place or person
- Severe - multiple moderate episodes (as above) or emergency hospital admission due to encephalopathy without associated seizures or stroke-like episodes.
- Very severe - in association with seizures, strokes or gross lactic acidaemia

Gastro-intestinal symptoms

- None
- Mild constipation only or past history of bowel resection for dysmotility
- Occasional symptoms of 'irritable bowel' (pain, bloating or diarrhoea) with long spells of normality.
- Frequent symptoms (as above) most weeks or severe constipation with bowels open less than once/week or need for daily medications.
- Dysmotility requiring admission or persistent and/or recurrent anorexia/vomiting/weight loss.
- Surgical procedures or resections for gastrointestinal dysmotility

Diabetes mellitus

- None
- Past history of gestational diabetes or transient glucose intolerance related to intercurrent illness.
- Impaired glucose tolerance (in absence of intercurrent illness).
- NIDDM (diet).
- NIDDM (tablets).
- DM requiring insulin (irrespective of treatment at onset).

Respiratory muscle weakness

- FVC normal ( $\geq 85\%$  predicted).
- FVC  $< 85\%$  predicted.
- FVC  $< 75\%$  predicted.
- FVC  $< 65\%$  predicted.
- FVC  $< 55\%$  predicted.
- FVC  $< 45\%$  predicted or ventilatory support for over 6 hours per 24 hr period (not for OSA alone).

Cardiovascular system

- None
- Asymptomatic ECG change
- Asymptomatic LVH on echo or non-sustained brady/tachyarrhythmia on ECG
- Sustained or symptomatic arrhythmia, LVH or cardiomyopathy. Dilated chambers or reduced function on echo. Mobitz II AV block or greater.
- Requires pacemaker, defibrillator, arrhythmia ablation, or LVEF < 35% on echocardiogram.
- Symptoms of left ventricular failure with clinical and/or x-ray evidence of pulmonary oedema or LVEF < 30% on echocardiogram.

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### Section III. Current Clinical Assessment (at the time of assessment)

Visual acuity (with usual glasses, contact lenses or pinhole)

- CSD  $\leq$  12 (ie normal vision - 6/6, 6/6 or better).
- CSD  $\leq$  18 (eg 6/9, 6/9).
- CSD  $\leq$  36 (eg 6/12, 6/24).
- CSD  $\leq$  60 (eg 6/24, 6/36).
- CSD  $\leq$  96 (eg 6/60, 6/36).
- CSD  $\geq$  120 (eg 6/60, 6/60 or worse).

Ptosis

- None
- Mild ptosis - not obscuring either pupil.
- Unilateral ptosis obscuring < 1/3 of pupil.
- Bilateral ptosis obscuring < 1/3 or unilateral ptosis obscuring > 1/3 of pupil or prior unilateral surgery
- Bilateral ptosis obscuring > 1/3 of pupils or prior bilateral surgery
- Bilateral ptosis obscuring >2/3 of pupils or >1/3 of pupils despite prior bilateral surgery.

Chronic Progressive External Ophthalmoplegia

- None
- Some restriction of eye movement (any direction). Abduction complete.
- Abduction of worst eye incomplete.
- Abduction of worst eye below 60% of normal
- Abduction of worst eye below 30% of normal
- Abduction of worst eye minimal (flicker)

Dysphonia/Dysarthria

- None.
- Minimal - noted on examination only.
- Mild - clear impairment but easily understood.
- Moderate - some words poorly understood and infrequent repetition needed.
- Severe - many words poorly understood and frequent repetition needed.
- Not understood. Requires communication aid.

## Myopathy

- Normal.
- Minimal reduction in hip flexion and/or shoulder abduction only (eg MRC 4+/5).
- Mild but clear proximal weakness in hip flexion and shoulder abduction (MRC 4/5). Minimal weakness in elbow flexion and knee extension (MRC 4+/5 - both examined with joint at 90 degrees).
- Moderate proximal weakness including elbow flexion & knee extension (MRC 4/5 or 4-/5) or difficulty rising from a 90 degree squat.
- Waddling gait. Unable to rise from a 90 degree squat (=a chair) unaided.
- Wheelchair dependent primarily due to proximal weakness.

## Cerebellar ataxia

- None.
- Normal gait but hesitant heel-toe.
- Gait reasonably steady. Unable to maintain heel-toe walking or mild UL dysmetria.
- Ataxic gait (but walks unaided) or UL intention tremor & past-pointing. Unable to walk heel-toe - falls immediately.
- Severe - gait grossly unsteady without support or UL ataxia sufficient to affect feeding.
- Wheelchair dependent primarily due to ataxia or UL ataxia prevents feeding.

## Neuropathy

- None.
- Subtle sensory symptoms or areflexia.
- Sensory impairment only (eg glove & stocking sensory loss).
- Motor impairment (distal weakness) or sensory ataxia.
- Sensory ataxia or motor effects severely limit ambulation.
- Wheelchair bound primarily due to sensory ataxia or neurogenic weakness

## Pyramidal Involvement

- None.
- Focal or generalised increase in tone or reflexes only.
- Mild focal weakness, sensory loss or fine motor impairment (eg cortical hand).
- Moderate hemiplegia allowing unaided ambulation or dense UL monoplegia.
- Severe hemiplegia allowing ambulation with aids or moderate tetraplegia (ambulant).
- Wheelchair dependant primarily due to hemiplegia or tetraplegia.

## Extrapyramidal

- Normal.
- Mild and unilateral. Not disabling (H&Y stage 1).
- Mild and bilateral. Minimal disability. Gait affected (H&Y stage 2).
- Moderate. Significant slowing of body movements (H&Y stage 3)
- Severe. Rigidity and bradykinesia. Unable to live alone. Can walk to limited extent (H&Y stage 4).
- Cannot walk or stand unaided. Requires constant nursing care (H&Y stage 5).

Cognition (patient undergo testing using WTAR, Symbol Search and Speed of Comprehension Test

- Combined centiles 100 or more.
- Combined centiles 60 - 99
- Combined centiles 30 - 59
- Combined centiles 15 - 29
- Combined centiles 5 - 14
- Combined centiles 4 or below.

THE NEWCASTLE PAEDIATRIC MITOCHONDRIAL DISEASE SCALE (NPMDS)

[Attachment: "NPMDS escala 2 - 11 años-1.pdf"]

NPMDS date \_\_\_\_\_

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### Section I: Current Function (preceding 4 week period)

- Vision
- Normal. No parental / patient concerns
  - Mild. Inattention to small objects in visual field or parent concerned about abnormality of visual behaviour
  - Moderate. Visual impairment not fully corrected with glasses or inattention to large objects in visual field
  - Severe. Not recognising faces or registered blind or using additional visual aids
- Hearing
- Normal
  - Mild. Requires regular repetition / raised voice or not reacting to loud sounds
  - Moderate. Hearing impaired but fully corrected with hearing aid
  - Severe. Poor hearing even with aid
- Communication
- Normal. Age appropriate communication
  - Mild. Verbal communication impaired. Supplemented by alternative methods (e.g. signing, pointing)
  - Moderate. Not communicating effectively with strangers (irrespective of methods)
  - Severe. Not communicating effectively with parents (irrespective of methods)
- Feeding
- Normal
  - Mild. Choking / vomiting / anorexia resulting in reduced intake or adaptation of age appropriate diet
  - Moderate. Supplementary enteral feeding or recurrent aspiration pneumonia
  - Severe. Exclusive enteral feeding (gastrostomy / NG tube). Nil by mouth
- Self-care (personal hygiene, dressing, utensil use)
- Normal. No concerns. Age appropriately reliant on carers / parents
  - Mild. Requires help with some age appropriate tasks
  - Moderate. Requires help with all age appropriate tasks
  - Severe. Reliant on parents with no contribution to self care

- Mobility
- Normal. No concerns. Age appropriate mobility
  - Mild. Difficulty walking up stairs or inclines
  - Moderate. Requires support (stick / frame / callipers) to walk on the flat
  - Severe. Wheelchair / carrier dependent
- Educational achievement
- Normal. Academic achievement comparable to peers in mainstream school / nursery
  - Mild. Struggling to remain in mainstream school / nursery
  - Moderate. Attending special school / nursery
  - Severe. Not attending school / nursery primarily due to illness

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## Section II: System Specific Involvement (preceding 6 month period)

- Seizures
- None
  - Mild. Myoclonic or absence seizures only or < 1 generalised tonic-clonic seizure/month
  - Moderate. > 5 generalized tonic-clonic seizures/month or > 20 absence or myoclonic seizures/month
  - Severe. Status epilepticus
- Encephalopathy
- None
  - Mild. Single episode of personality change, excessive sleepiness, confusion or disorientation
  - Moderate. Obtunded or >2 encephalopathic episodes/year
  - Severe. Life-threatening encephalopathy- requires artificial ventilation
- Stroke-like Episodes
- None
  - Mild. Transient motor symptoms lasting < 24 hours
  - Moderate. Single stroke-like episode (> 24 hours)
  - Severe. Multiple stroke-like episodes (> 24 hours each)
- Gastrointestinal
- Normal
  - Mild. Mild constipation or unexplained vomiting / diarrhoea < 1/week
  - Moderate. Moderate constipation (some relief with laxative treatment) or unexplained vomiting / diarrhoea > 3/week
  - Severe. Severe constipation (no relief with laxative treatment) or unexplained vomiting / diarrhoea every day or surgical intervention for dysmotility
- Endocrine
- Normal
  - Mild. Biochemical evidence of impaired function
  - Moderate. Endocrine failure requiring replacement therapy
  - Severe. Decompensation (e.g. diabetic ketoacidosis, Addisonian crisis)

- Respiratory
- Normal
  - Mild. Abnormal respiration not requiring hospitalisation
  - Moderate. Abnormal respiration requiring hospitalisation but not ventilation
  - Severe. Abnormal respiration requiring artificial ventilation
- Cardiovascular (over preceding 12 months)
- Normal
  - Mild. Asymptomatic ECG change
  - Moderate. Abnormal echocardiogram (e.g. cardiomegaly) or sustained / symptomatic arrhythmia on ECG
  - Severe. Decompensated cardiomyopathy or requiring pacing device / defibrillator / ablation
- Renal
- Normal
  - Mild. Impaired function but no change in diet or therapy required
  - Moderate. Impaired function requiring restricted protein diet
  - Severe. Failure requiring transplant / dialysis
- Liver
- Normal
  - Mild. Impaired function but no change in diet or therapy required
  - Moderate. Impaired function requiring restricted protein diet
  - Severe. Failure requiring transplant / dialysis
- Blood
- Normal
  - Mild. Anaemia only
  - Moderate. Asymptomatic pancytopenia
  - Severe. Pancytopenia requiring regular transfusion / transplantation

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### Section III: Current Clinical Assessment (at the time of assessment)

- Growth (ht and Weight) over preceding 6 months
- Normal. Following normal growth trajectory
  - Mild. Height or weight or both less than 2nd centile but growing parallel to it
  - Moderate. Height or weight or both crossing one centile
  - Severe. Height or weight or both crossing  $\geq 2$  centiles or less than 2nd centile with divergent trajectory
- Development over preceding 6 months Score: \_\_\_\_\_
- Vision (with usual glasses in the better eye)
- Normal. Visual acuity better than or equal to 6/12 or normal fixation and tracking
  - Mild. Acuity worse than 6/12 but better than or equal to 6/18 or no fixation on small objects
  - Moderate. Acuity worse than 6/18 but better than or equal to 6/60 or impaired fixation on large, brightly coloured objects
  - Severe. Acuity worse than 6/60 or no response to light or visual threat or unable to finger count

Ptosis and eye movement

- Normal
- Mild. Gaze evoked nystagmus or unilateral ptosis or impaired eye movement at extremities
- Moderate. Intermittent nystagmus at rest or bilateral ptosis not obscuring pupils or restriction of >50% eye movement
- Severe. Continuous nystagmus at rest or bilateral ptosis obscuring pupils or only a flicker of eye movement

Myopathy

- Normal
- Mild. Mild symmetrical weakness of hip and / or shoulder girdle only
- Moderate. Moderate symmetrical weakness (proximal>distal) limiting mobility
- Severe. Wheelchair / carrier dependent or respiratory compromise due to myopathy

Ataxia

- Normal
- Mild. Ataxic gait but walks unaided or mild upper limb dysmetria
- Moderate. Gait abnormality requiring assistance or severe upper limb dysmetria
- Severe. Wheelchair dependent or unable to feed due to ataxia

Pyramidal

- Normal
- Mild. Focal dystonia or unilateral extrapyramidal tremor / bradykinesia
- Moderate. Generalised dystonia or bilateral extrapyramidal tremor / bradykinesia
- Severe. Wheelchair dependent due to extrapyramidal disorder

Neuropathy

- Normal.
- Mild. Areflexia only
- Moderate. Sensory ataxia or motor impairment (distal weakness) but mobile
- Severe. Reliant on mobility aids primarily due to neuropathy

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## Section IV: Quality of Life-Parent Completed

During the past 4 weeks, how would you rate your child's overall health?

- Very poor
- Poor
- Fair
- Good
- Very good

During the past 4 weeks, how much did your child's physical health problems limit their physical activities (such as walking or playing with friends)?

- Very much
- Quite a lot
- Some what
- A little
- Not at all

During the past 4 weeks, how much did your child's health problems limit their everyday life (such as attending school, caring for themselves) compared with a person of the same age in perfect health?

- Very much
- Quite a lot
- Somewhat
- A little
- Not at all

During the past 4 weeks, how much energy did your child have?

- None
- A little
- Some
- Quite a lot
- Very much

During the past 4 weeks, how much bodily pain/discomfort did your child have?

- Very much  Quite a lot  
 Some  A little  None

During the past 4 weeks, how much was your child bothered by emotional problems?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how satisfied did your child feel with their abilities, looks, relationships with other people and life in general?

- Very dissatisfied  Quite dissatisfied  
 Neither dissatisfied or satisfied  
 Quite satisfied  Very satisfied

During the past 4 weeks, how would you rate your child's behaviour compared with other children his / her age?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how would you rate your child's ability to interact with other people (e.g. making friends, talking to other children / strangers) compared with other children his / her age?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how much were you (the parent / carer) bothered by emotional problems (e.g. feelings of anxiety, sadness) as a result of your child's illness?

- Very  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much was your time limited as a result of your child's illness?

- Very  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much were your family's activities limited or interrupted as a result of your child's illness?

- Very  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 6 months, what has been the financial cost of your child's illness?

- Very expensive  Quite expensive  
 Moderately expensive  
 Little additional cost  
 No additional cost

During the past 4 weeks, how would you rate your family's ability to get along with one another?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how often did your child's illness have a positive effect on your child, you or your family (e.g. being treated well due to illness, meeting new people)?

- Never  Occasionally  
 Sometimes  Quite a lot  
 Most of the time

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#### Section IV: Quality of Life-Self Completed (7-11 years)

During the past 4 weeks, how would you rate your overall health?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how much did your physical health problems limit your physical activities (such as walking or playing with friends)?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much did your health problems limit your everyday life (such as going to school, caring for yourself) compared with a person of your age in perfect health?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much energy did you have?

- None  A little  Some  
 Quite a lot  Very much

During the past 4 weeks, how much pain or discomfort did you have?

- Very much  Quite a lot  
 Some  A little  None

During the past 4 weeks, how much were you bothered by emotional problems (such as feeling sad or frightened)?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how satisfied did you feel with your abilities, looks, relationships with other people and life in general?

- Very dissatisfied  Quite dissatisfied  
 Neither satisfied or dissatisfied  
 Quite satisfied  Very satisfied

During the past 4 weeks, how would you rate your behaviour compared with other children your age?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how easy did you find it to get on with other people (e.g. making friends, talking to other children / strangers) compared with other children your age?

- Very hard  Hard  
 Ok  Easy  Very easy

During the past 4 weeks, how would you rate your family's ability to get along with one another?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how often did your illness have a positive effect on you or your family (e.g. being treated well because of your illness, meeting new people)?

- Never  Occasionally  
 Sometimes  Quite a lot  
 Most of the time

#### THE NEWCASTLE PAEDIATRIC MITOCHONDRIAL DISEASE RATINGS SCALES (NPMDS)

[Attachment: "NPMDS escala 12 - 18 años-1.pdf"]

NPMDS date \_\_\_\_\_

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### Section I: Function (preceding 4 week period)

Vision (with usual glasses)

- Normal. No parental / patient concerns  
 Mild. Difficulty with small print or text on the television  
 Moderate. Difficulty outside the home (e.g. bus numbers, road signs or shopping)  
 Severe. Difficulty recognising faces or unable to navigate without help or registered blind

Hearing

- Normal  
 Mild. Mild deafness (e.g. missing words in presence of background noise)  
 Moderate. Hearing impaired but fully corrected with hearing aid  
 Severe. Poor hearing even with aid or reliant on non-verbal communication

Communication

- Normal  
 Mild. Mild speech difficulties but easily understood and rarely asked to repeat things  
 Moderate. Speech poorly understood by strangers and frequently asked to repeat things  
 Severe. Speech not understood by family or friends and / or requires communication aid

- Feeding
- Normal
  - Mild. Choking / vomiting / anorexia resulting in reduced intake or swallowing difficulties requiring dietary adaptations
  - Moderate. Supplementary enteral feeding or recurrent aspiration pneumonia
  - Severe. Exclusive enteral feeding (gastrostomy / NG tube). Nil by mouth
- Self-care (personal hygiene, dressing, utensil use)
- Normal
  - Mild. Slow and / or clumsy self-care requiring extra time or effort. Requires help with some tasks
  - Moderate. Requires help with most tasks but retains some independent self-care function
  - Severe. Requires one to one assistance
- Mobility
- Normal
  - Mild. Difficulty walking up stairs or inclines
  - Moderate. Requires support (stick / frame / callipers) to walk on the flat
  - Severe. Wheelchair dependent
- Educational achievement
- Normal. Academic achievement comparable to peers in mainstream school
  - Mild. Struggling to remain in mainstream school
  - Moderate. Attending special school
  - Severe. Not attending school primarily due to illness
- Section I score
- \_\_\_\_\_

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## Section II: System Specific Involvement (preceding 12 month period)

- Seizures
- None
  - Mild. Myoclonic or absence seizures only or < 1 generalised tonic-clonic seizure each month
  - Moderate. > 5 generalized tonic-clonic seizures/month or > 20 absence or myoclonic seizures/month
  - Severe. Status epilepticus
- Encephalopathy
- None
  - Mild. Single episode of personality change, excessive sleepiness, confusion or disorientation
  - Moderate. Obtunded or >2 encephalopathic episodes/year
  - Severe. Life-threatening encephalopathy- requires artificial ventilation
- Stroke-like episodes
- None
  - Mild. Transient motor symptoms lasting < 24 hours
  - Moderate. Single stroke-like episode (> 24 hours)
  - Severe. Multiple stroke-like episodes (> 24 hours each)

## Gastrointestinal

- Normal
- Mild. Mild constipation or unexplained vomiting / diarrhoea < 1/week
- Moderate. Moderate constipation (some relief with laxative treatment) or unexplained vomiting / diarrhoea > 3/week
- Severe. Severe constipation (no relief with laxative treatment) or unexplained vomiting / diarrhoea every day or surgical intervention for dysmotility

## Endocrine

- Normal
- Mild. Biochemical evidence of impaired function
- Moderate. Endocrine failure requiring replacement therapy
- Severe. Endocrine decompensation (e.g. diabetic ketoacidosis, Addisonian crisis)

## Respiratory

- Normal
- Mild. Abnormal respiration not requiring hospitalisation
- Moderate. Abnormal respiration requiring hospitalisation but not ventilation
- Severe. Abnormal respiration requiring artificial ventilation

## Cardiovascular

- Normal
- Mild. Asymptomatic ECG change
- Moderate. Abnormal echocardiogram (e.g. cardiomegaly) or sustained / symptomatic arrhythmia on ECG
- Severe. Decompensated cardiomyopathy or requiring pacing device / defibrillator / ablation

## Renal

- Normal
- Mild. Impaired function but no change in diet or therapy required
- Moderate. Impaired function requiring restricted protein diet
- Severe. Failure requiring transplant / dialysis

## Liver

- Normal
- Mild. Mildly impaired Liver Function Tests (LFTs). No symptoms of hepatic failure
- Moderate. Impaired LFTs with symptoms (e.g. jaundice, oedema)
- Severe. Failure requiring hospitalisation and / or transplantation

## Blood

- Normal
- Mild. Anaemia only
- Moderate. Asymptomatic pancytopenia
- Severe. Pancytopenia requiring regular transfusion / transplantation

## Section II total score

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**Section III: Current Clinical Assessment (at the time of the assessment unless otherwise stated in the question)**

Growth (ht and weight) over preceding 6 months

- Normal. Following normal growth trajectory
- Mild. Height or weight or both less than 2nd centile but growing parallel to it
- Moderate. Height or weight or both crossing one centile
- Severe. Height or weight or both crossing  $\geq 2$  centiles or less than 2nd centile with divergent trajectory

Development over preceding 12 months score

Vision (with usual glasses, better eye)

- 
- Normal. Following normal growth trajectory
  - Mild. Height or weight or both less than 2nd centile but growing parallel to it
  - Moderate. Height or weight or both crossing one centile
  - Severe. Height or weight or both crossing  $\geq 2$  centiles or less than 2nd centile with divergent trajectory

Ptosis and eye movement

- Normal
- Mild. Gaze evoked nystagmus or unilateral ptosis or impaired eye movement at extremities
- Moderate. Intermittent nystagmus at rest or bilateral ptosis not obscuring pupils or restriction of  $>50\%$  eye movement
- Severe. Continuous nystagmus at rest or bilateral ptosis obscuring pupils or only a flicker of eye movement

Myopathy

- Normal
- Mild. Mild symmetrical weakness of hip and / or shoulder girdle only
- Moderate. Moderate symmetrical weakness (proximal  $>$  distal) limiting mobility
- Severe. Wheelchair dependent or respiratory compromise due to myopathy

Ataxia

- Normal
- Mild. Ataxic gait but walks unaided or mild upper limb dysmetria
- Moderate. Gait abnormality requiring assistance or severe upper limb dysmetria
- Severe. Wheelchair dependent or unable to feed due to ataxia

Pyramidal

- Normal
- Mild. Mild hemiplegia allowing unaided ambulation
- Moderate. Moderate hemiplegia allowing ambulation with aids
- Severe. Wheelchair dependent due to hemi / tetraplegia

Extrapyramidal

- Normal  
 Mild. Focal dystonia or unilateral extrapyramidal tremor / bradykinesia  
 Moderate. Generalised dystonia or bilateral extrapyramidal tremor / bradykinesia  
 Severe. Wheelchair dependent due to extrapyramidal disorder

Neuropathy

- Normal.  
 Mild. Areflexia only  
 Moderate. Sensory ataxia or motor impairment (distal weakness) but mobile  
 Severe. Reliant on mobility aids primarily due to neuropathy

Section III score

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### Section IV: Quality of life-Parent Completed

During the past 4 weeks, how would you rate your child's overall health?

- Very poor    Poor    Fair  
 Good    Very good

During the past 4 weeks, how much did your child's physical health problems limit their physical activities (such as walking or playing with friends)?

- Very much    Quite a lot  
 Somewhat    A little  
 Not at all

During the past 4 weeks, how much did your child's health problems limit their everyday life (such as attending school, caring for themselves) compared with a person of the same age in perfect health?

- Very much    Quite a lot  
 Somewhat    A little  
 Not at all

During the past 4 weeks, how much energy did your child have?

- None    A little    Some  
 Quite a lot    Very much

During the past 4 weeks, how much bodily pain/discomfort did your child have?

- Very much    Quite a lot  
 Some    A little    None

During the past 4 weeks, how much was your child bothered by emotional problems?

- Very much    Quite a lot  
 Somewhat    A little  
 Not at all

During the past 4 weeks, how satisfied did your child feel with their abilities, looks, relationships with other people and life in general?

- Very dissatisfied    Quite dissatisfied  
 Neither dissatisfied or satisfied  
 Quite satisfied    Very satisfied

During the past 4 weeks, how would you rate your child's behaviour compared with other children his / her age?

- Very poor    Poor    Fair  
 Good    Very good

During the past 4 weeks, how would you rate your child's ability to interact with other people (e.g. making friends, talking to other children / strangers) compared with other children his / her age?

- Very poor    Poor    Fair  
 Good    Very good

During the past 4 weeks, how much were you (the parent / carer) bothered by emotional problems (e.g. feelings of anxiety, sadness) as a result of your child's illness?

- Very    Quite a lot  
 Somewhat    A little  
 Not at all

During the past 4 weeks, how much was your time limited as a result of your child's illness?

- Very  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much were your family's activities limited or interrupted as a result of your child's illness?

- Very  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 6 months, what has been the financial cost of your child's illness?

- Very expensive  Quite expensive  
 Moderately expensive  
 Little additional cost  
 No additional cost

During the past 4 weeks, how would you rate your family's ability to get along with one another?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how often did your child's illness have a positive effect on your child, you or your family (e.g. being treated well due to illness, meeting new people)?

- Never  Occasionally  
 Sometimes  Quite a lot  
 Most of the time

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## Section D: Quality of life-Self completed

During the past 4 weeks, how would you rate your overall health?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how much did your physical health problems limit your physical activities (such as walking or going out with friends)?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much did your health problems limit your everyday life (such as going to school, caring for yourself) compared with a person of your age in perfect health?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how much energy did you have?

- None  A little  Some  
 Quite a lot  Very much

During the past 4 weeks, how much pain or discomfort did you have?

- Very much  Quite a lot  
 Some  A little  None

During the past 4 weeks, how much were you bothered by emotional problems (e.g. feeling sad or frightened)?

- Very much  Quite a lot  
 Somewhat  A little  
 Not at all

During the past 4 weeks, how satisfied did you feel with their abilities, looks, relationships with other people and life in general?

- Very dissatisfied  Quite dissatisfied  
 Neither dissatisfied or satisfied  
 Quite satisfied  Very satisfied

During the past 4 weeks, how would you rate your behaviour compared with people your age?

- Very poor  Poor  Fair  
 Good  Very good

During the past 4 weeks, how easy did you find it to get on with other people (e.g. making friends, talking to friends / strangers) compared with other people your age?

- Very hard  Hard  
 Fair  Good  Very good

During the past 4 weeks, how would you rate your family's ability to get along with one another?

- Very poor
- Poor
- Fair
- Good
- Very good

During the past 4 weeks, how often did your illness have a positive effect on you or your family (e.g. being treated well because of your illness, meeting new people)?

- Never
- Occasionally
- Sometimes
- Quite a lot
- Most of the time

# Genetics

DNAMt depletion

- Yes
- No
- Untested

If yes, specify tissue studied

- Muscle
- Blood
- Urine
- Buccal mucose
- Other

If yes, specify % of heteroplasmy

\_\_\_\_\_

DNAMt deletion

- Yes
- No
- Untested

If yes, specify

- Single
- Multiple

DNAMt sequencing

- Negative
- Positive
- Untested

Molecular diagnosis

- DNAMt
- DNAn

Single deletion DNAMt

- Yes
- No

If yes specify size

\_\_\_\_\_

If yes, specify location

\_\_\_\_\_

DNAMt (select positive study)

- mtRNA Leu (MTTL2)
- mtRNA Lys (MTTK)
- mtRNA Trp (MTTW)
- mtRNA Ala (MTTA)
- mtRNAAGlu (MTTE)
- mtRNA Asp (MTTD)
- mtRNA Phe (MTTF)
- mtRNA Met (MTTM)
- mtRNA Val MTTV
- mtRNA Asp MTTN
- mtRNA Arg MTRR
- mtrRNA 12S MTRNR1
- mtrRNA 16S MTRNR2
- MTND1
- MTND3
- MTND4L
- MTND6
- MTCO2
- MT-ATP8
- mtRNA Ile (MTT1)
- mtRNA Ser (MTTS1)
- mtRNA Ser (MTTS2)
- mtRNA Gln (MTTQ)
- mtRNA Tyr (MTTY)
- mtRNA Cys (MTTC)
- mtRNA Thr (MTTT)
- mtRNA Pro (MTTP)
- mtRNA Leu 1 MTTL1
- mtRNA Gly MTTG
- mtRNA His MTTH
- MTCYB
- MTCO1
- MTCO3
- MT-ATP6

DNAMt Mutation

\_\_\_\_\_

DNAMt heteroplasmy

\_\_\_\_\_

DNAn (select positive study)

- AARS2
- AASS
- ABAT
- ABCB6
- ABCB7
- ACAD8
- ACAD9
- ACADM
- ACADS
- ACADSB
- ACADSD
- ACADVL
- ACAT1
- ACO2
- ACSL4
- ADCK1
- ADCK2
- ADCK3
- ADCK4
- ADCK5
- AFG3L2
- AGK
- AGXT
- AIFM1
- AK2
- ALAS2
- ALDH18A1
- ALDH2
- ALDH4A1
- ALDH5A1
- ALDH6A1
- AMACR
- AMT
- APEX1
- APEX2
- ATAD3A
- ATAD3B
- ATP5A1
- ATP5B
- ATP5C1
- ATP5D
- ATP5E
- ATP5F1
- ATP5G1
- ATP5G2
- ATP5G3
- ATP5H
- ATP5I
- ATP5J
- ATP5J2
- ATP5L
- ATP5L2
- ATP5O
- ATP7B
- ATPAF1
- ATPAF2
- ATPIF1
- AUH
- BCKDHA
- BCKDHB
- BCL2
- BCS1L
- BOLA1
- BOLA2
- BOLA3
- BRIP1
- C10ORF2
- C12ORF65
- CARS2
- CBR4

- CIAPIN1
- CLPB
- CLPX
- COA5
- COQ10A
- COQ10B
- COQ2
- COQ3
- COQ4
- COQ5
- COQ6
- COQ7
- COQ9
- COX10
- COX11
- COX14
- COX15
- COX16
- COX17
- COX18
- COX19
- COX20
- COX4I1
- COX4I2
- COX5A
- COX5B
- COX6A1
- COX6A2
- COX6B1
- COX6B2
- COX6C
- COX7A1
- COX7A2L
- COX7A2P2
- COX7B
- COX7C
- COX8
- CPOX
- CPS1
- CPT1A
- CPT2
- CRBN
- CYC1
- CYCS
- CYP11A1
- CYP11B1
- CYP11B2
- CYP24A1
- CYP27A1
- CYP27B1
- DARS2
- DBT
- DDX28
- DGUOK
- DHODH
- DHX30
- DIABLO
- DLAT
- DLD
- DMGDH
- DNA2
- DNAJC19
- DNM1L
- DUT
- EARS2
- ECHS1
- ECSIT
- ELAC2
- EMC8
- ENDOG
- ERCC6

- ERCC8
- ETFA
- ETFB
- ETFDH
- ETHE1
- FARS2
- FASN
- FASTKD2
- FBXL4
- FDX1
- FDX1L
- FDXR
- FECH
- FEN1
- FH
- FOXRED1
- FXN
- GARS
- GATM
- GCDH
- GCSH
- GFER
- GFM1
- GFM2
- GK
- GLDC
- GLRX5
- GLUD1
- GRPEL1
- GRPEL2
- GSH
- GSR
- HADH
- HADHA
- HADHB
- HADHSC
- HARS2
- HAX1
- HCCS
- HIBCH
- HIGD1A
- HK1
- HLCS
- HMGCL
- HMGCS2
- HSCA
- HSCB
- HSD17B8
- HSD3B2
- HSPA1A
- HSPA9
- HSPD1
- HTRA2
- IARS2
- IBA57
- IBA57-HOMOLOG
- IDH2
- IDH3B
- ISCA1
- ISCA2
- ISCA2-HOMOLOG
- ISCU
- IVD
- KARS
- KIF1B
- LARS2
- LIAS
- LIG3
- LIPT1
- LIPT2
- LONP1

- LRPPRC
- LYRM4
- LYRM7
- MAOA
- MARS2
- MCCC1
- MCCC2
- MCEE
- MDP1
- MECR
- MFF
- MFN2
- MGME1
- MIP
- MLYCD
- MMAA
- MMAB
- MME4
- MME6
- MPC1
- MPG
- MPV17
- MRPL12
- MRPL3
- MRPL44
- MRPL48
- MRPS16
- MRPS22
- MRRF
- MSH2
- MT-ATP6
- MT-ATP8
- MT-CO2
- MT-CO3
- MT-COI
- MT-CYB
- MTERF
- MTFMT
- MTIF2
- MTIF3
- MT-ND1
- MT-ND2
- MT-ND3
- MT-ND4
- MT-ND4L
- MT-ND5
- MT-ND6
- MTO1
- MTPAP
- MTRF1
- MTRF1L
- MTRR
- MUT
- MUTYH
- NADK2
- NARS2
- NDUFA1
- NDUFA10
- NDUFA11
- NDUFA12
- NDUFA13
- NDUFA2
- NDUFA3
- NDUFA4
- NDUFA4L2
- NDUFA5
- NDUFA6
- NDUFA7
- NDUFA8
- NDUFA9
- NDUFAB1

- NDUFAF1
- NDUFAF2
- NDUFAF3
- NDUFAF4
- NDUFAF5
- NDUFAF6
- NDUFB1
- NDUFB10
- NDUFB11
- NDUFB2
- NDUFB3
- NDUFB4
- NDUFB5
- NDUFB6
- NDUFB7
- NDUFB8
- NDUFB9
- NDUFC1
- NDUFC2
- NDUFS1
- NDUFS2
- NDUFS3
- NDUFS4
- NDUFS5
- NDUFS6
- NDUFS7
- NDUFS8
- NDUFV1
- NDUFV2
- NDUFV3
- NEIL1
- NFS1
- NFU1
- NMT1
- NT5M
- NTHL1
- NUBPL
- NUDT1
- OAT
- OGG1
- OPA1
- OPA3
- OTC
- OXA1L
- OXCT1
- PANK2
- PARK7
- PARP1
- PARS2
- PC
- PCCA
- PCCB
- PCK2
- PDHA1
- PDHA2
- PDHB
- PDHX
- PDK1
- PDK2
- PDK3
- PDP1
- PDP2
- PDSS1
- PDSS2
- PDX1
- PET100
- PHB
- PHB2
- PIF1
- PINK1
- PNPT1

- POLDIP2
- POLG
- POLG2
- POLRMT
- PPOX
- PRODH
- PTRF
- PUS1
- RAD51
- RARS2
- RFT1
- RMND1
- RMRP
- RNASEL
- RPP14
- RRM2B
- SARDH
- SARS2
- SCO1
- SCO2
- SCP2
- SDHA
- SDHAF1
- SDHAF2
- SDHB
- SDHC
- SDHD
- SERAC1
- SHMT2
- SLC19A2
- SLC19A3
- SLC25A12
- SLC25A13
- SLC25A15
- SLC25A19
- SLC25A20
- SLC25A22
- SLC25A28
- SLC25A3
- SLC25A37
- SLC25A4
- SLC25A5
- SLC46A1
- SLC52A2
- SLC52A3
- SLC9A6
- SOD2
- SPG7
- SSBP1
- STAR
- SUCLA2
- SUCLG1
- SUCLG2
- SUOX
- SUPV3L1
- SURF1
- TACO1
- TARS2
- TAZ
- TFAM
- TFB1M
- TFB2M
- TIMM44
- TIMM50
- TIMM8A
- TK2
- TMEM70
- TMLHE
- TOP1MT
- TP53
- TPK1

- TRMU
- TSFM
- TTC19
- TUFM
- TXN2
- TYMP
- UNG
- UQCC1
- UQCC2
- UQCR10
- UQCR11
- UQCRB
- UQCRC1
- UQCRC2
- UQCRFS1
- UQCRH
- UQCRHL
- UQCRQ
- VARS2
- VDAC1
- VDAC2
- WARS2
- YARS2

Other genes

Mode of inheritance

- 
- Autosomic recessive
  - Autosomic dominant
  - X-linked recessive
  - X-linked- dominant

Mutation 1

- Homozygous
- Heterozygous
- Hemizygous

cDNA change

Protein change

Pathogenicity

- Reported
- Not reported

Mutation 2

- Homozygous
- Heterozygous
- No second mutation

cDNA change

Protein change

Pathogenicity

- Reported
- Not reported

If new mutation, specify

- Family segregation
- Isolated fiber study (only in DNAMt mutation)
- Pathogenical based in bioinformatic analysis
- Other

## Complementary Tests

- Neurophtalmological tests  Yes  
 No
- Electroretinography  Normal  
 Abnormal  
 Not performed
- Visual evoked potentials  Normal  
 Abnormal  
 Not performed
- Visual field  Normal  
 Abnormal  
 Not performed
- Fundus oculi  Normal  
 Abnormal  
 Not performed
- Optical Coherence Tomography  Normal  
 Abnormal  
 Not performed
- Other paediatric tests  Yes  
 No
- Brainstem auditory evoked potencial  Normal  
 Abnormal  
 Not performed
- Nerve conduction studies and electromyographic  Normal  
 Abnormal  
 Not performed
- Electroencephalogram  Normal  
 Abnormal  
 Not performed
- Muscle biopsy  Yes  
 No
- Histological findings  Normal muscular biopsy  
 Inepespecific abnormalities in muscular biopsy  
 Ragged red fibers  
 COX negative fibers  
 Subsarcolemmal deposits of SDH  
 Fiber atrophy  
 Fiber prevalence  
 Dystrophic features  
 Total or total depletion of oxidative enzymes  
 Lipid storage  
 Aspecific myopathic changesçNeurogenic changes  
 Glycogen accumulation  
 Subsarcolemmal rims  
 Strongly succinate dehydrogenase-reactie blood vessels

If ragged red fibers, please specify

- >5  
 5-10  
 10-20  
 < 20

If COX negative fibers, please specify

- Isolated COX negatives fibers  
 All FRR are COX negatives  
 All muscular fibers are COX negative

Respiratory chain

- Normal  
 Abnormal

If abnormal please specify

- Complex I deficiency  
 Complex III deficiency  
 Complex IV deficiency  
 Complex V deficiency  
 Complex I+III+IV deficiency

Biomarkers tested

- Yes  
 No

### Plasma/serum

Lactic (Highest value in mmol/L)

- Normal  
 Abnormal

If abnormal, specify value

\_\_\_\_\_

Lactate/Pyruvate ratio

- Normal  
 Abnormal

Alanine

- Normal  
 Abnormal

FGF21

- Normal  
 Abnormal

GDF15

- Normal  
 Abnormal

Others

\_\_\_\_\_

### Urine

Lactic

- Normal  
 Abnormal

If abnormal, specify value

\_\_\_\_\_

Krebs cycle metabolites

- Normal  
 Abnormal

3-methylglutaconic

- Normal  
 Abnormal

Others

\_\_\_\_\_

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**Cerebrospinal fluid**

Proteins

- Normal  
 Abnormal

Lactic (Highest value)

- Normal  
 Abnormal

If abnormal specify value

---

Other

---

Other complementary test

---

Neuroradiological features

- Yes  
 No

Please specify

- Normal  
 Cortical atrophy  
 Cortical malformations  
 Subcortical atrophy  
 White matter abnormalities  
 Stroke-like lesions  
 Laminar necrosis  
 Basal Nuclei involvement  
 Dentate nuclei involvement  
 Thalami / Subthalamic involvement  
 Pontine / mesencephalic tegmentum involvement  
 periaqueductal region involvement  
 Bulbar involvement  
 Cerebellar atrophy  
 Cysts or vacuolated lesions  
 Calcifications  
 Corpus callosum agenesis

# Treatment

- Coenzima Q10 (CoQ10), Ubiquinona  Yes  
 No
- Ubiquinol  Yes  
 No
- Ibedenona  Yes  
 No
- L-carnitine  Yes  
 No
- Bicarbonato sódico/citrato sódico  Yes  
 No
- B1 Vitamine or tiamine  Yes  
 No
- C Vitamine or Ascorbat  Yes  
 No
- B2 vitamine or Riboflavine  Yes  
 No
- Biotine  Yes  
 No
- Folinic acid  Yes  
 No
- L-arginine  Yes  
 No
- L-citruline  Yes  
 No
- Creatine  Yes  
 No
- Cisteine  Yes  
 No
- E Vitamine  Yes  
 No
- Lipoic acid  Yes  
 No
- Timidine and citidine nucleosides  Yes  
 No
- Other treatments
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