# NOTES
## PNS DEMYELINATING DISORDERS

## GENERALLY, WHAT ARE THEY?

### PATHOLOGY & CAUSES

- Progressive peripheral nervous system (PNS) disorders; destruction of myelin, disruption of motor, sensory function

### TYPES

**Charcot–Marie–Tooth disease**

- Genetic mutations → defective myelin sheath, impaired neuronal mitochondrial function

**Guillain–Barré syndrome**

- Acute triggering event (e.g. infection) → aberrant autoimmune response → myelin sheath destruction

### COMPLICATIONS

**Charcot–Marie–Tooth disease**

- Muscle atrophy, impaired ambulation, foot irregularities

**Guillain–Barré syndrome**

- Respiratory failure, cardiac arrhythmias, quadriplegia

### SIGNS & SYMPTOMS

- ↓/absent deep tendon reflexes, paresthesia, muscle weakness, ↓ touch sensation

### DIAGNOSIS

#### DIAGNOSTIC IMAGING

**Gadolinium-enhanced MRI**

- Guillain–Barré
  - Intrathecal spinal nerve root thickening

#### LAB RESULTS

- Guillain–Barré
  - Albuminocytologic dissociation in cerebrospinal fluid (CSF)

#### OTHER DIAGNOSTICS

- Electromyography (EMG), nerve conduction studies (NCS)
  - ↓/blocked nerve conduction velocity
- History, physical examination

### TREATMENT

#### MEDICATIONS

- Guillain–Barré
  - Intravenous immunoglobulin (IVIG)

#### SURGERY

- Charcot–Marie–Tooth
  - Correction of severe skeletal irregularities

#### OTHER INTERVENTIONS

- Charcot–Marie–Tooth
  - Genetic testing, orthotics, physical/occupational therapy
- Guillain–Barré
  - Plasmapheresis; supportive care (e.g. respiratory/hemodynamic support)
- Pain management
  - Acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentin, carbamazepine

# CHARCOT–MARIE–TOOTH DISEASE

osms.it/Charcot-Marie-Tooth

## PATHOLOGY & CAUSES

- Group of hereditary, progressive neurological disorders; disruption of PNS processes, impaired sensory/motor function
- Genetic mutations → defective structure, function of proteins in myelin sheath/neuron's axon
- *Classification:* Types I-VII; Type X (X-linked)
  - Subtypes based on associated genes and phenotypes

## TYPES

### Charcot–Marie–Tooth I (CMT1)

- Demyelinating form
  - Caused by mutations in *PMP22*, *MPZ* genes (encode for myelin sheath proteins) → ↓ nerve conduction velocity
  - Autosomal dominant/sporadic inheritance

### CMT2

- Axonal form
  - Caused by mutations in *MFN2* gene (encodes for mitofusin-2 protein in neuronal mitochondria) → neuronal death
  - Autosomal dominant/recessive inheritance

## RISK FACTORS

- Inheritance of defective gene(s)

## COMPLICATIONS

- Muscle atrophy, loss of ambulation; deafness, intellectual disability, optic neuropathy, feeding difficulties, hip dysplasia

## SIGNS & SYMPTOMS

- Onset in first to third decade of life, depending on type
- Progressive distal muscle weakness; atrophy of hands, feet
- Distal sensory loss, paresthesias, loss of proprioception
- ↓ deep tendon reflexes, areflexia
- Foot irregularities
  - Foot drop, high arches (pes cavus), hammer toes, flail foot, cavovarus foot
- Unsteady gait, toe-walking

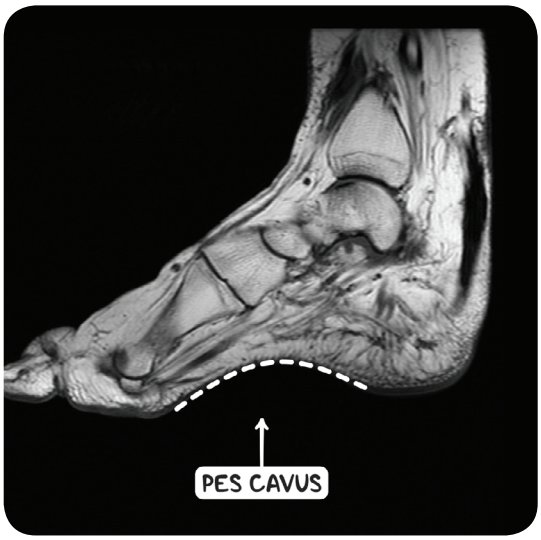


**Figure 87.1** An MRI scan of the foot of an individual with Charcot-Marie-Tooth disease. There is wasting of the plantar muscles and prominent pes cavus as well as a hammer irregularity of the great toe.

## DIAGNOSIS

### OTHER DIAGNOSTICS

- NCS, EMG
  - ↓ nerve conduction velocity
- History, physical examination (e.g. age of onset)
- Genetic testing

## TREATMENT

### MEDICATIONS

- Pain management
  - Acetaminophen, NSAIDs, gabapentin, carbamazepine

### SURGERY

- Correction of severe skeletal irregularities

### OTHER INTERVENTIONS

- Physical/occupational therapy
  - Strengthening, range of motion, balance, maintenance of mobility, activities of daily living
- Orthotics

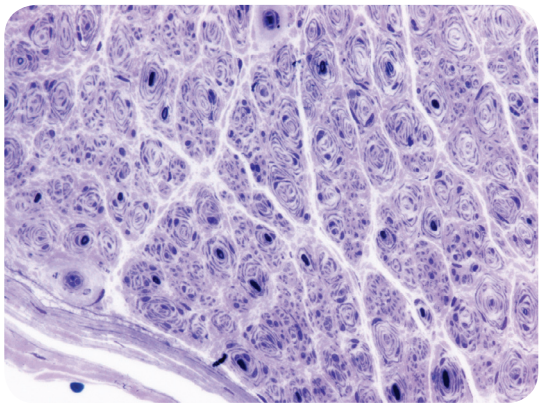

**Figure 87.2** A section of a peripheral nerve from an individual with Charcot–Marie–Tooth disease.

# GUILLAIN–BARRÉ SYNDROME

**osms.it/guillain-barre-syndrome**

## PATHOLOGY & CAUSES

- Acute, progressive demyelinating PNS disease; sensory, motor, cognitive deficits
- AKA acute inflammatory demyelinating polyneuropathy
- Abnormal autoimmune response
  - Myelin autoantigen picked up by antigen-presenting cells (e.g. dendritic) → antigen presented to helper T-cells → production of cytokines → activation of B-cells and macrophages → B-cells make antibodies, mark autoantigens; macrophages use antibody markers to attack myelin sheath on peripheral neurons → ↓/blocked nerve conduction velocity; axonal degeneration

**Variants**

- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
- Miller–Fisher syndrome
  - Affects cranial nerves (CN) III, IV, VI
- Acute motor axonal neuropathy (AMAN)
- Acute sensorimotor axonal neuropathy (AMSAN)

### CAUSES

- Molecular mimicry between microbe, nerve antigens
  - Most commonly associated with *Campylobacter jejuni*, *Mycoplasma pneumoniae*, cytomegalovirus, Epstein–Barr, influenza A, Zika, HIV

### RISK FACTORS

- Acute infection
- ↑ age
- More common in individuals who are biologically male

### COMPLICATIONS

- Acute
  - Ileus, urinary retention, cardiac arrhythmias, pneumonia, respiratory failure, quadriplegia
- Long-term
  - Chronic fatigue, chronic pain, relapses

## SIGNS & SYMPTOMS

- Variable presentation, depending on affected nerve
- Bilateral, flaccid, ascending weakness of limbs, peaking ≤ four weeks
- ↓ deep tendon reflexes, areflexia, touch sensation
- Paresthesia
- Diaphragmatic weakness → breathing difficulties (e.g. hypoventilation, requires mechanical ventilation)
- Autonomic involvement
  - Hypertension/hypotension/postural hypotension, bradycardia
- CN involvement
  - Blurred vision, dysarthria, abnormal pupillary response to light

## DIAGNOSIS

### DIAGNOSTIC IMAGING

**Gadolinium-enhanced MRI (spine)**

- T1-weighted images
  - Thickening of intrathecal spinal nerve roots

### LAB RESULTS

- CSF
  - Albuminocytologic dissociation (high levels of protein without increase in cell counts)
- Serum immunoglobulin G (IgG) antibodies to ganglioside Q1b (GQ1b)
  - Miller–Fisher

### OTHER DIAGNOSTICS

- EMG, NCS
  - ↓/blocked nerve conduction velocity
- History, physical examination

## TREATMENT

### MEDICATIONS

- IVIG
- Gabapentin/carbamazepine
  - Pain management

### OTHER INTERVENTIONS

- Plasmapheresis
- Respiratory/hemodynamic support