DISTAL WEAKNESS

MK Baker

Patterns of Weakness

- Overlap/Combinations
- Unusual presentations
- Associations:
  - Sensory loss
  - Ataxia
  - Dysarthria, etc
  - Hemiplegia – strokes, etc
  - Paraplegia – spinal lesion
  - Proximal weakness – Myopathy
  - Distal weakness – Neuropathy

Lower Motor Neuron vs Upper

UMN = brain (esp pyramidal tracts), spine
- spasticity/DTR signs, clonus
- Pathological reflexes
LMN = anterior horn cell (or brainstem nuclei)
- Axons and myelin: (roots/plexuses peripheral nerves)
- Neuromuscular junction, muscle
  - Tone/DTRs/atrophy/ Fasciculations
LMN Conditions
- Motorneuron disease (also UMN)
- Spinal muscular atrophy
- Radiculopathy
- Plexopathy
- Peripheral neuropathy
- Myasthenia Gravis
- Lambert-Eaton
- Myopathy: Dystrophy, inflammatory (e.g.,

Peripheral Neuropathy: Example of Nerve
Temporal Mas V
Oculi VII
Orb oris VII
Pharynx X
Sterno mastoid XI
Trapezius XI
Tongue XII
Neck Flexion C1-6
Neck Extension C1-T1
Deltoid C5-6
Lat Dorsi C6-8
Pectoralis C5-T1
Infraspin C5-6
Supraspin C5-6
Serrat ante C5-7
Rhomboid C5-6
Biceps C5-6
Triceps C6-8
Brachiorad C5-6
Supinator C5-6
Pronator teres C67
Wrist ext C7-T1
Finger ext C78
FDP C7-T1
FDS C7-T1
FPL C7-T1
Pron quad C8-T1
Thenar (med) C8-T1
Hypothenar C8-T1
Interossei C8-T1
Abdominal T8-12
Back ext
Rectal sphincter S234
Iliopsoas L2-4
Hip adduction L2-4
Hip ext L5-51
Knee ext L34
Knee flex L55-1
Ant tibialis L45
Peroneal L5 S1
Soleus/gastro L5 S1
Post tib L5 S1
Ex hall long L5
Toe ext L5 S1
Toe flex L5 S1
EDB/L5 S1
AH & foot muscles S1
A Sensory
Hypoesthesia
Hyperesthesia
Paresthesia
Pain
Burning
Positive vs negative signs
B Motor
Weakness
e.g., toes catching on ground
Objects fall out of hands
Difficulty standing from chair/bank
Difficulty with stairs
Joint injuries
C Autonomic
Incontinence, Urine retention
Constipation, diarrhoea
Erectile dysfunction
Brady-/tachycardia
Blood pressure $\uparrow\downarrow$
Sweating $\uparrow\downarrow$
Hypo/hyperthermia
Dry eyes/mouth
Night blindness

Commonest Causes
(Mayo Clinic: 205 “undiagnosed” $\Rightarrow$
Dx in 76%)
With detailed examination - ± ½ hereditary)
- Leprosy $\pm \times 10^6$ in world
- D.M. ($2\times10^6$ in U.S.A)
- Hereditary (esp HMSN II)
- Inflammatory – Guillain Barre, CIDP
- Toxins – As Pb, hexane, B6
- Medications – tryptophane
- HIV
- Alcohol (? Nutritional)
- Malignancy (≥ 7% $\Rightarrow$ neuropathy)
- Gammopathy e.g., MGUS – IgM
  POEMS – IgG
- Vasculitis e.g., Siögrens, PAN, RA etc.
### Classification

**Etiology**
- Hereditary – HMSN, CMT (Charcot-Marie-Tooth), etc.
- Acquired - Vascular
  - Inflammatory
  - Toxic/traumatic
  - Metabolic
  - Infectious
  - Neoplastic

**Clinical**
- Type of symptoms: Sensory, Motor, Autonomic
- Course: Acute/Subacute/Chronic
- Symmetry: Mono = 1 nerve/focal, Poly = bilateral ± symmetrical, Multifocal, Radiculopathy = roots
- EMG and Biopsy:
  - Demyelinating
  - Axonal
  - Large/small fibre

### Course

**Acute:**
- Trauma (e.g., Saturday night palsy)
- Swelling – e.g., anterior tibial syndrome
- Hemorrhage
- Ischaemia – PAN, RA, DM

**Subacute:**
- Guillain-Barre
- Bells
- Diptheria
- Toxins e.g., TCIDP
- Metabolic e.g., uremia

**Chronic:**
- Toxins e.g., hexanes
- Metabolic e.g., DM
- Malignancy
- CIDP
- Malnutrition

**Very chronic:**
- A. Genetic/HMSN
  - HSN
  - Tangier
  - Fabry
  - Andrade
- B. Acquired: DM
  - Vitamin B1
  - B12
  - CA
  - Uremia
  - Hypothyroidism
  - Amyloidosis
  - Leprosy
  - Vasculitis

### Predominantly Sensory

- Diabetes mellitus
- Leprosy
- B12 ↓
- Amyloidosis
- HSN
- Paraneoplastic
- Medication: Vincristine, INH, furantoin, statins
- Toxins: Arsenic, thallium
- ↑ Vitamin B6
- HIV (late)

### Mainly Motor

1. Guillain Barré – Campylobacter
2. CIDP (chronic inflammatory demyelinating polyneuropathy)
3. Porphyria
4. Lead
5. Infections mononucleosis
6. Diptheria
8. HIV – AIDP/CIDP
9. MMN (multifocal motor neuropathy)
**Mainly Autonomic**

1. Diabetes Mellitus
2. Amyloidosis
3. HSAN – e.g., Riley Day (A=autonomic)
4. Acute idiopathic

**Painful**

1. Diabetes Mellitus
2. Alcohol
3. Porphyria
4. **↓** Vit B1
5. Myeloma
6. Small fibre neuropathies
7. HIV

**Special investigations**

NB: Clinical picture (Tests expensive)
- Blood: FBC; ESR; U&E; Ca++; LFT; TSH; B12/folate; glucose (fasting); Lipids; SPEP; HIV; Porphyrins; U&E; RF; ANF; ENA; RPR
- Urine: Bence Jones
  - Heavy Metals: Pb; As; Au; Tl; Hg
- CSF: Proteins
- EMG
- Nerve biopsy
- Other: CXR; metastatic bone survey (>50 ...); fat aspirate; lip biopsy; bone marrow biopsy; CASE; Q Sart, etc.

**Symmetry**

- **±** Symmetry: metabolic/toxic/inflammatory etc.
- Asymmetric => Ischaemic
  - Vasculitis
  - MMN (Multifocal Motor Neuropathy)

**Demyelinating vs Axonal**

- **↓** NCV’s **↑** DL’s (ie slow)
- **↑** F’s (>120% NL)
- **↓** CMAP’s **↑** SNAP’s (ie low amplitudes)
- e.g., Guillain Barre
  - e.g., AMAN

**Treatment**

- Treat cause e.g., control blood sugar, remove toxin, etc.
- Physiotherapy, occupational therapy, psychological support.....
- Respiratory care
- Surgery
- Immunomodulation
  - Plasma exchange (GBS, CIDP)
  - IVIG (GBS, MMN)
  - Steroids
  - Immunosuppressant’s – Imuran
  (Azathiaprine, etc.)
- Pain treatment:
  - Analgesics
  - Anti-epileptics – Tegretol, Neurontin, Lyrica, etc.
  - Anti depressants – Amytriptilene, Nortriptilene (with orthostatism)
  - Membrane stabilisers – Mexilitene
  - Sympathectomy
- Future:
  - ? Growth factors
  - ? DNA therapy
**CIDP PATTERN RECOGNITION**

- Occasional papilledema
- Usually symmetrical
- Polyradiculopathy
- Proximal and distal limbs
- Atrophy less than weakness
- Hyporeflexia ± 90%
- Mayo (1975)
  - 45:53 – mixed
  - 5:53 – motor
  - 3:53 – sensory

**ABBREVIATIONS**

- AMAN=Acute Motor Axonal Neuropathy
- CA=Carcinoma
- CIDP=Chronic Inflammatory Demyelinating Neuropathy
- CMAP=Compound Muscle Action Potential
- CXR=Chest X Ray
- DM=Diabetes Mellitus
- DTR=Deep Tendon Reflex
- DL=Distal Latency
- HMSN=Hereditary Motor and Sensory Neuropathy
- IVIG=Intravenous Immunoglobulin
- MGUS=Monoclonal Gamopathy of Undetermined Significance
- PAN=Polyarteritis Nodosa
- Pb=Lead
- RA=Rheumatoid Arthritis
- SNAP=Sensory Nerve Action Potential
- TOCP=Tri Ortho Cresyl Phosphate

**LANDRY-GUILLAIN-BARRE-STROHL SYNDROME**

- AIDP

**GBS**

- AIDP=Acute Inflammatory Demyelinating Polyneuropathy
- 1859: Landry: Acute Ascending Paralysis
- 1916: Guillain, Barre, Strohl: 2 Soldiers with Paralysis, Areflexia, Paresthesias (Later raised cerebrospinal protein without cells)
- Characterised by lymphocyte and macrophage infiltrations in nerves-> demyelination-> axonal damage
**CLINICAL PICTURE**

- **INCIDENCE**: 1-2/100000/year
- >60: 3/100000/year
- M slightly > F
- >70% something preceding in previous 1-4 weeks:
  - Upper respiratory tract infection
  - Gastroenteritis (Campylobacter Panner O19+41)
  - Immunisation Jersey/A (1976) H1N1
  - Surgery
  - HIV (seroconversion)

**MAIN FEATURES**

- Usually begins with distal weakness which ascends or spreads proximally (variations e.g. can begin in face)
- Approximately symmetrical
- Deep tendon reflexes decrease, may disappear
- Develops within 4 weeks

**OTHER FEATURES**

- Paresthesias common (sensory decrease usually mild)
- Muscle Pain esp. lower back, esp. at night
- 10-20% Respiratory distress
- Autonomic dysfunction: hyper/hypotension, tachy/bradycardia, incontinence, etc.
- Rare CNS signs: Babinski, papilloedema, etc.

**VARIENTS**

- Fisher Syndrome: Ataxia, areflexia, ophthalmoplegia (AAO)
- Polynuclear cranialis
- Acute pandysautonomia
- AMAN
- AMSAN
DIFFERENTIAL DIAGNOSIS

- Porphyria (acute)
- Poison: organophosphate, hexane, heavy metals
- Botulism
- Metabolic: Low potassium, phosphate
- Tickbite paralysis
- Diphtheria
- Transverse myelitis
- Basilar artery thrombosis
- HIV (esp. with seroconversion)
  CSF leukocytes >50/ul

SPECIAL INVESTIGATIONS

- Cerebrospinal fluid: raised protein (esp. after week 1), normal cells (albumin-cell dissociation), raised tau
- EMG: Most slow NCV’s, prolonged DL’s, F’s. Low amplitude CMAP’s
- Other: Hyponatremia (SIADH), proteinuria (immune complex deposition glomerulonephritis)
  Nerve biopsy rarely needed

PROGNOSIS

- Best in world care-> 2% mortality
- Inadequate care-> 33% mortality
- Most stabilise at week 2-4 then slowly improve
- Relapses 3%

POOR PROGNOSIS

- Require ventilation
- Bed bound within 4 days
- >40
- Low CMAP’s
- Autonomic failure
- Plateau> 3 weeks
- Raised CSF tau
- Without optimal treatment above factors reduce chances of walking at 6/12 to <20%
TREATMENT

- Nursing, Physiotherapy, OT, Psych support
- Ventilation: FVC<12ml/kg, Po2<70mmHg, respiratory distress (dyspnoea, tachycardia, sweating)
- Rx infection (esp. lungs, bladder)
- Prevent deep venous thrombosis: Clexane, etc.
- Rx pain: NSAID’s, quinine, opiates
- Protect eyes (Bell’s)
- Rx Autonomic dysfunction
- Neurorehabilitation

DEFINITIVE TREATMENT

- N.B.: Steroids DO NOT work!!
- Plasma exchange 40-50ml/kg/day X3-10 (Daily or alternate days)
- Intravenous Immunoglobulin (Polygam) 0.4 g/kg/day