UMN & LMN Disorders

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Motor system generates three general TYPES OF MOVEMENTS:
Reflex responses - simplest form of coordinated movement - *rapid, stereotyped involuntary* movements; elicited by sensory stimulus that requires quick reaction at involuntary level.
Rhythmical movements (e.g. walking, running) require *stereotyped* sequence of muscle activation.
Voluntary movements - *most complex* - goal-directed, initially require *conscious direction*.

- **spinal cord** contains circuitry for reflex responses and some rhythmical motor patterns.
- **brain stem** contains circuits for more complex patterns of motor movements including rhythm generators.
- **cortex** is command center that plans and initiates movements and uses reflex and patterned responses of brain stem and spinal cord to generate details of movement.

LOWER MOTONEURON (LMN) = α-motoneuron – neuron directly innervating **striated skeletal muscles**.

UPPER MOTONEURON (UMN) – term used in two senses:
a) ***senso stricto*** – cortical neurons forming **tractus pyramidalis**.
b) ***senso lato*** – all neurons forming descending tracts that **ultimately play on LMN** (tr. pyramidalis, tr. reticulospinalis, tr. rubrospinalis, tr. vestibulospinalis, etc).

WEAKNESS (LOSS OF VOLUNTARY MOVEMENT)

- muscle cannot exert normal force – most important clinical feature of motoneuron (UMN, LMN) disorders.

PARESIS – ***reduced*** voluntary movement;
PARALYSIS (s. **-PLEGIA**) – ***complete*** loss of voluntary movement.

- **PALSY** is older term (has been used interchangeably with either paralysis or paresis); currently, its use is confined to historical diagnoses (e.g. Bell's palsy, cerebral palsy).
- distribution of paralysis / paresis is defined by prefixes:
  mono- (one limb);
  para- (both legs);
  hemi- (limbs on one side of body);
  quadri- or **tetra-** (all four limbs);
  alternating (s. crossed) hemiplegia - hemiplegia on one side with contralateral cranial nerve palsies.
  bibrachial paresis – both arms.
- if clinical evaluation of weakness is limited by *pain* or *lack of patient effort*, **needle EMG** can provide objective information.

TREATMENT

- occupational therapist and physical therapist:
1. **Strengthening & stretching exercises** - maintain weak muscles in maximum tone, keep joints from developing contractures.
2. Patient is trained to use **adaptive movements** - to facilitate function, to use canes and walkers.
3. **Splints & braces** - to stabilize joints.

MUSCLE TONE ABNORMALITIES

Muscle tone changes usually accompany weakness!

muscle tone = resistance to passive muscle stretch

- tone is evaluated by passive movements of limbs. see p. D1 >>
- main components of muscle tone:
  1) low-level background ***α-γ co-activation***.
  2) ***alteration in stretch reflexes*** (most important determinant of pathological alterations in tone!) – via changes in rate of discharge in γ-*neurons* + changes in general excitability of *motor neuron pool*.
  3) ***viscoelastic properties*** of muscle & tendons (contribute to increased tone in chronic spasticity and rigidity!).

TONUS↓ - A(HYPO)TONIA (S. FLACCIDITY) - *LMN disease*, *cerebellar disease*, *sensory nerve damage*.

TONUS↑:
a) SPASTICITY - *UMN disease*; resistance depends on:
– VELOCITY of passive motion - if limb is rapidly* moved: free interval → gradual increase in tone (*lengthening reaction, s. spastic catch* due to *hyperactive muscle stretch reflex*) → sudden decrease (*inverse muscle stretch reflex*) as limb goes through its range of motion (***"clasp-knife"***).
*it is important to move rapidly because rate of stretch is important in eliciting maximum stretch reflex response.
– DIRECTION of passive motion - tone is greater in ***antigravity muscles*** (arm flexors, leg extensors & adductors).
spasticity in leg adductors causes "scissoring" over good leg (most easily seen in spastic paraplegia).

Modified Ashworth scale (MAS) measures resistance during passive soft-tissue stretching and is used as a simple measure of spasticity (Bohannon and Smith, 1987):

0: No increase in muscle tone

1: Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension.

1+: Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM.

2: More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved.

3: Considerable increase in muscle tone, passive movement difficult.

4: Affected part(s) rigid in flexion or extension.

b) RIGIDITY - *extrapyramidal UMN disease*.
- *symmetric* - similar resistance at all angles of motion; doesn't depend on passive motion velocity; constant through range of motion - ***"lead-pipe" rigidity*** (plastic type of rigidity – limbs accept positions they are left in) or ***"cogwheel" rigidity*** (superimposed on tremor).
- cogwheeling is enhanced by voluntary movement of contralateral limb (reinforcement).

N.B. cogwheeling can occur in patients with *essential or familial tremor* (may be confused with parkinsonism), but clinician feels alternate activation of flexors and extensors that produce tremor, but does not feel hypertonicity!

c) PARATONIA / GEGENHALTEN (German "hold against") – *diffuse forebrain dysfunction* (*dementia*, *frontal lobe* or *thalamic disorders*).
- pseudovoluntary* ***resistance by patient*** against any passive movement of limb (i.e. not true increase in muscle tone!) - each attempt at moving limb by examiner is met with equal and opposing force.
- felt as increase in tone that fluctuates with repetitive passive movements.
- often accompanied by **tonic grasp reflex**.

*it is involuntary to extent that patient has great difficulty in voluntarily suppressing urge to resist.

TREATMENT OF SPASTICITY

Spasticity may be helpful in compensating for weakness, especially in gait - overzealous treatment of spasticity (esp. with systemic drugs) may in fact cause decrement in function!

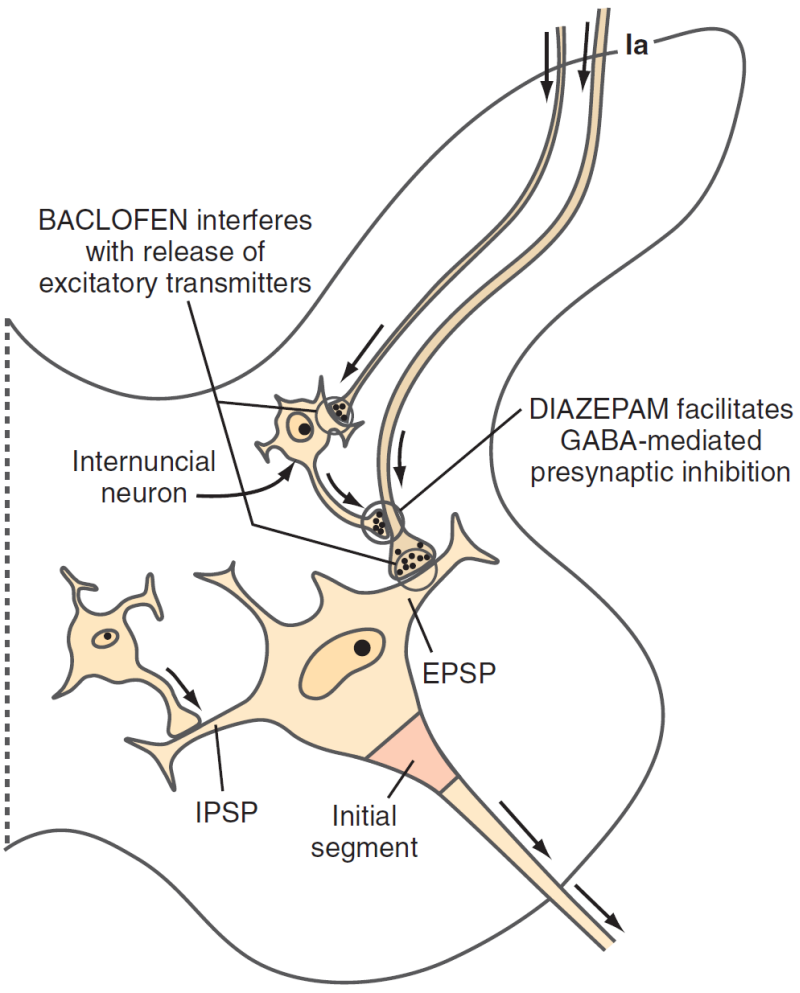
1. **Stretching exercises** (to maintain joint mobility).

   at least passive range of motion (ROM) activities (to prevent contractures) are started in immediate setting if patient cannot participate actively

- full range motion exercises; avoid over-stretching of soft tissues (deformity may result!).
- avoid knee hyperextension.
- keep feet flexed at 90° (use pillow between soles and bed foot).
- *electrical stimulation of antagonist muscles* and *splinting* may help.

2. **Drugs with systemic effects** (sedation is usually limiting barrier, esp. for school-age children!) - primarily used in patients who are ***confined to wheelchair or bed*** (drugs allow easier transfers from bed to chair, facilitate hygiene, alleviate painful flexor spasms):

1) **$GABA_B$ agonist** - **BACLOFEN** (20-240 mg/d in divided doses q8hrs*) - most effective drug available! *i.e. single oral max dose is 70-80 mg
   - originally synthesized as an anticonvulsant but it was found to have no significant anticonvulsant activity.
   - in severe cases - *intrathecal* via implanted pump; see p. Op240 >>
   - intrathecal baclofen given to normal patients does not interfere with movement or decrease strength, but the same dose given to a spastic patient markedly decreases spasticity and muscle tone.
   - activation of the $GABA_B$ receptors reduces the influx of calcium into the presynaptic terminals, the result being a reduction in the release of excitatory transmitters:



Baclofen withdrawal – "itchy, twitchy, bitchy" (severe itching without a rash, excessive sweating, priapism, mood fluctuation, rebound spasticity↑ can progress to severe rigidity, fever from increased muscle activity, irritability/insomnia/confusion/agitation/hallucinations, labile blood pressure, seizures); potentially lethal - can lead to rhabdomyolysis, DIC, organ failure, and can look like autonomic dysreflexia, malignant hyperthermia (vs. opioid withdrawal), septic shock.

Treatment: oral baclofen, IV benzodiazepines (DIAZEPAM, 2-5 mg q 6 hours) or CYPROHEPTADINE (6 mg q 6 hours for 24 hours), if due to IT system failure and unable to replace full dose orally (try oral baclofen 20 mg po q6-8hrs) → insert temporary IT catheter and post for surgery.

Baclofen overdose may result in somnolence, respiratory depression, hypothermia, seizures, rostral progression of hypotonia, coma.

Treatment: no antidote (if no heart conduction defects, PHYSOSTIGMINE 0.5-2 mg often reverses the somnolence and respiratory effects), aspirate drug from pump reservoir, aspirate 30-40 mL of CSF. The central effects of an overdose should clear in 24 to 48 hours.

2) **$GABA_A$ agonist** - DIAZEPAM (2-4 mg at bedtime) - for leg spasms that interrupt sleep; CNS depressant!
   - unlike baclofen, which directly activates GABA receptor, diazepam works only when GABA is released, and it enhances response to the transmitter.

3) **α2-agonists** (central muscle relaxants):
   a) TIZANIDINE (Zanaflex®) (4-8 mg q8h)
   b) CLONIDINE.

4) **direct muscle inhibitor** - DANTROLENE (25 → increase up to 100 mg qid) - for nonambulatory patients; no cognitive / sedative adverse effects!

5) **CYCLOBENZAPRINE** (Flexeril®, Amrix®)
   - dosage: 10 mg q 6 h (5 and 10 mg tablets).
   - chemical structure related to first-generation tricyclic antidepressants.
   - mechanism of action is unclear; studies from 1980s in rats indicate that drug activates locus ceruleus → ↑ release of norepinephrine in ventral horn of spinal cord → inhibitory action on alpha motor neurons.
   - decreases pain in first two weeks, peaking in first few days, but has no proven benefit after two weeks (therapy should not be continued long-term).
   - not useful for spasticity due to neurologic conditions such as cerebral palsy.
   - adverse effects: drowsiness (38% of patients), dry mouth (24%), urinary retention (in males with large prostates).

6) **METHOCARBAMOL** (Robaxin®) - central muscle relaxant.
   - dosage: 1500 mg q 6 h for 2-3 days then decrease to maintenance 1000 mg q 6 h.
   - adverse effects: CNS depressant, may cause urine to turn black, blue, or green.

7) **CARISOPRODOL** (Soma®) – not recommended! (converted into benzodiazepines – addictive potential!)

8) **CHLORZOXAZONE** (Lorzone®, Parafon®)

9) **METAXALONE** (Skelaxin®)

10) **ORPHENADRINE**

3. **Local injections** of BOTULINUM TOXIN (effect for 3-6 months) - no deleterious effects on helpful spasticity; target muscles:
   1) *leg adductors* - to facilitate nursing care.
   2) *arm muscles* - to relieve painful spasms;
      article about arm spasticity and botulinum toxin injections:
      http://www.medscape.org/viewarticle/865168
   3) *gastrocnemius-soleus muscle* - to convert toe walking to plantigrade foot placement.

4. **SURGICAL MEASURES – ORTHOPEDIC**
   - if fixed contracture has developed → **surgical tendon release** (most commonly - Achilles, thigh adductor, hamstring tendons).
   - for CP kids, ortho procedures are delayed after spasticity is addressed.

5. **SURGICAL MEASURES – NEUROSURGICAL**
   N.B. ablative procedures (convert spastic into flaccid paralysis) - reserved for extensive or complete loss of cord function!
   – patients sometimes use some spasticity for support during ambulation

   1) **intrathecal baclofen delivery system**. see Op220 >>
   2) **selective posterior rhizotomy** (procedure of choice for *spasticity due to cerebral palsy*).
      - exposure of cauda equina (through L_{2-5} laminectomy).
      - after anatomic identification of L_2 root at its exit foramen, S_1 anterior root is identified by low-frequency stimulation.
      - fascicles of each of **L_2-S_1 posterior roots** are isolated and stimulated - those fascicles, stimulation of which causes ipsilateral tetanic or multisegmental motor responses or any contralateral motor responses*, are sectioned.
        *intraoperative clinical responses are correlated with intraoperative EMG.
      - usually, ***60-80% fascicles are sectioned*** (diminished sensation lasting no longer than several weeks) - if patients are young, have adequate cognitive function and aggressive physical therapy is carried out postoperatively, results are excellent.
      - spare fascicles innervating sphincters!
      - can be done **percutaneously** - may be performed at any segment (e.g. RF, local or general anesthesia, fluoroscopy and low-frequency stimulation to verify electrode positioning, therapeutic response may last several years)
   3) limited ablative procedures (for spasticity *confined to bladder or to single limb*):
      a) **posterior root ganglionectomy** of sacral segments (for spastic bladder).
      b) **selective peripheral neurotomy** (sectioning nerve fascicles - identified by intraoperative stimulation - which maintain spastic tone; e.g. tibial nerve at popliteal region for spastic foot; obturator neurotomy).
   4) **spinal cord stimulation (SCS)** - better when stimulating **epidural electrode** is implanted caudal to level of injury.
      - also benefits reflex and voluntary *bladder control in MS*.
   5) **Bischof myelotomy (longitudinal myelotomy)** - **dividing cord into anterior and posterior halves** over segments involved in flexor spasms (typically L_2-S_1) - interrupts local reflex arcs; may not prevent spasms triggered by stimuli from segments rostral to L_2 or caudal to S_1.
   6) **stereotactic dentatotomy** (limited usefulness in management of spasticity)
      N.B. selective posterior rhizotomy provides much higher success rate.
      - indication - *congenital spasticity with congenital choreoathetosis*: thalamotomy controls choreoathetosis; if subsequently worse spasticity develops → ipsilateral dentatotomy.

FATIGABILITY

FATIGUE - feeling of being tired and not being able to put out full effort:

NORMAL FATIGUE - results from ***intense*** muscular contraction.
- accompanied by firing *frequency*↓ in motor-unit - result of reduced excitatory drive to motoneurons (central mechanism!).

FATIGABILITY (dysfunction at *neuromuscular junction*) - muscles become weaker and weaker with repetitive but ***normal*** use (inability to sustain performance of activity).

- accompanied by *amplitude*↓ of muscle action potentials.
  N.B. with exception of neuromuscular junction disorders, fatigue is rarely complaint of diseases of motor unit!!!

"Fatigue," "tiredness", "lack of energy" are common complaints in following disorders:

1) UMN disease (bilateral corticospinal tract or extrapyramidal disease)
2) multifocal CNS disease (e.g. established MS)
3) sleep disorders, psychiatric and behavioral disorders
4) chronic fatigue syndrome
5) fibromyalgia
6) renal, hepatic, cardiac, pulmonary diseases, anemia
7) hyperventilation, hypoglycemia

Pyramidal UMN lesion

ACUTE UMN LESION

CEREBRAL SHOCK - transient depression of reflex activity below level of injury; in addition to **PARALYSIS**:

1. **Hypotonia** of muscles
2. **Absence of reflexes** (muscle stretch, plantar, abdominal & cremasteric)

If lesion transects spinal cord (SPINAL SHOCK → see p. Spin1 >>), it is also accompanied by:

3. **Hypotonic paralysis of bowel & bladder**
4. **Hypotension**, **anhydrosis**

CHRONIC STAGE OF UMN LESION

1. **Paralysis involves large areas** (hemi-, para-, quadriplegia) – at and distal to *capsula interna* small lesion affects large body regions; *rostral to capsula interna*, pyramidal neurons are dispersed (e.g. small stroke in arm area of motor cortex can produce brachial monoplegia).
   - CORTICOSPINAL lesions: ***distal*** muscle groups are affected more severely than ***proximal*** ones, and ***axial*** movements are spared unless lesion is severe and bilateral.
   - CORTICOBULBAR lesions: weakness only in ***lower face*** and ***tongue***; extraocular, upper facial, pharyngeal, and jaw muscles are almost always spared (but with bilateral corticobulbar lesions → **PSEUDOBULBAR PALSY**). *see below >>*

2. **Muscle atrophy** of *disuse only* (late and slight).

3. **Spasticity** (muscle tonus↑)
   - spasticity is more pronounced in ANTIGRAVITY MUSCLES – ***arm*** flexors, ***leg*** extensors (**WERNICKE-MAN posture**).
     N.B. when intact, tr. pyramidalis constantly inhibits muscle tone!
   - resistance depends on velocity and direction of passive motion → **"clasp knife" phenomenon**. *see above >>*
   - if patient can walk, spasticity causes SCISSORS GAIT (in bilateral lesions), leg circumduction (in unilateral lesions). see p. Mov7 >>
   - *pure pyramidal tract lesions cause mild paralysis without spasticity* – because control of tone is mediated by other tracts (particularly ***corticorubrospinal*** and ***corticoreticulospinal***) - this may explain why degrees of weakness and spasticity often do not correspond.

4. **Hyperreflexia** (lost UMN inhibition on various reflexes):
   1) **muscle stretch reflexes**↑↑
   2) **CLONUS** (rhythmic, rapid alternation of muscle contraction and relaxation caused by sudden, passive tendon stretching) about mechanism → see p. A18 >>
      N.B. only ***sustained clonus*** suggests UMN damage!
   3) **BABINSKI sign** and other pathologic withdrawal reflexes (normally, they are inhibited by intact pyramidal system).
      - *normally* only painful stimulus elicits withdrawal reflex.
      - when *UMN is damaged* (but also in normal infants – immature CNS), lighter nonpainful stimulus may elicit withdrawal reflex - *strength of response parallels extent* to which *UMN lesion* has allowed upregulation of reflex:
        - *small hemispheric lesion* - only ***small fragment*** of reflex may be elicited (i.e. extension of great toe - *Babinski sign*);
        - *complete spinal cord transection* - ***entire*** withdrawal reflex (with flexion at hip, knee, and ankle) may occur.

      Symmetrical hyperactive reflexes in presence of ***down-going toes*** are usually normal!

5. **Absent normal skin reflexes** (abdominal, cremasteric).

6. **Synkinesias**

7. **Movements are slow, coarse** but with normal rhythmicity and coordination (e.g. finger-nose-finger and heel-knee-shin are performed slowly but adequately); "incoordination" is obvious with rapidly repeated movements (e.g. tapping index finger on thumb).

EMG - ***normal number*** of motor units are activated at given frequency but in which maximum discharge ***frequency*** is decreased (vs. LMN lesions - number↓, frequency normal).

PSEUDOBULBAR PARALYSIS

- bilateral *corticobulbar tract* lesion (i.e. central-supranuclear palsy of CN 7, 9, 10, 12):
  1) *bifacial* paresis
  2) *spastic* 3D (dysarthria, dysphonia, dysphagia)
  3) *hyperactive* gag reflex, hyperactive facial and jaw jerks (CN 5 → CN 7);
     uvula movements are more vigorous on reflex than on volition (i.e. uvula does not move well (or at all) on phonation, but vigorous response is seen in pharyngeal or gag reflex).
  4) *oral automatisms* (snout, suck, etc)
  5) *emotional incontinence* (reflexive *crying** and spasmodic, mirthless *laughing* with minimal provocation) - release of limbic functions; patient is aware of lack of control!
     *can be erroneously regarded as reactive depression because of diagnosis.
     H: SSRI!!! (FLUOXETINE, SERTRALINE), NORTRIPTYLINE, LEVODOPA.
     NUEDEXTA® (DEXTROMETHORPHAN HYDROBROMIDE + QUINIDINE SULFATE) capsules - FDA approved first treatment for *pseudobulbar affect*!
- most common causes: bilateral hemisphere lesions, bilateral lacunar infarctions in internal capsule.
- patients may have *dementia* (due to pathology involving bilateral frontal areas).

"LOCKED IN" SYNDROME (s. PSEUDOCOMA)

- bilateral *basis pontis* lesion, i.e. damage to corticospinal-corticopontine-corticobulbar tracts *below reticular formation* (therefore sparing consciousness) but *above ventilatory nuclei of medulla* (therefore, precluding death).

- most commonly due to ***basilar artery infarction***; other causes - *central pontine myelinolysis*.
- almost complete de-efferentation:
    1) **quadriplegia** – due to corticospinal tracts damage.
    2) paralysis of **horizontal eye movements** (horizontal ophthalmoplegia) – due to PPRF and CN6 nuclei, corticopontine tracts damage.
    3) paralysis of **jaw-face-bulbar muscles** (facial & bulbar diplegia; no volitional vocalization!) – due to CN7 nuclei, corticobulbar tracts damage.
- very resembles coma, but:
    1) fully ***conscious*** and ***mentally intact***
    2) ***can feel, see, hear***
    3) preserved ***vertical eye movements*** – the only way to communicate!; when patient is not actively moving eyes, spontaneous ***ocular bobbing*** may occur.
    4) eyes are open and partially ***blink*** (via inhibition of levator palpebrae) – another way to communicate!
- if lesion also affects *dorsal pontine tegmentum* → sudden coma, pinpoint pupils, ophthalmoplegia, hyperthermia, progression to death.
- patients must be identified rapidly for intravenous rt-PA treatment.
- mortality rate is high (40-70%); survival in locked-in state has lasted as long as 18 years.
- recovery to independence can occur over weeks to 3-4 months (magnetic stimulation of motor cortex producing motor evoked potentials is positive prognostic feature).

Similar state may occur in severe Guillain-Barré syndrome, but *vertical eye movements are not selectively spared*.

LMN lesion

"Three **A**":

1. **A(hypo)reflexia** (all reflexes ↓↓↓ or absent – grade 1 or 0) – lost efferent portion of reflex arc!

   N.B. reflexes present only with reinforcement (grade 1) imply intact reflex pathway and may or may not be abnormal!
   – loss of **γ-motoneurons** does not cause weakness but decreases tension on muscle spindles → tendon reflexes↓
2. **A(hypo)tonia**
3. **Atrophy** of *denervation* (early & severe – in 2-3 months muscle loses 50% of its mass!), abnormal electrical activity.
   – maximum degree of denervation atrophy after acute injury to axons occurs in 90-120 days and reduces muscle volume by 75-80% (vs. disuse atrophy does not reduce muscle volume by more than 25-30%); in 3-4 years, most of denervated fibers will have degenerated
4. **Paralysis of individual muscles** (or groups of muscles)
5. **Fasciculations**, **Fibrillations** *see below >>*

EMG - ***recruitment*** of motor units is delayed / reduced (fewer than normal are activated at given discharge frequency).

BULBAR PARALYSIS

– peripheral (LMN) palsy of CN 9, 10, 12:
1. **3D**: **d**ysphagia, **d**ysphonia, **d**ysarthria
2. **Absent swallowing & gag reflexes** (vs. in pseudobulbar paralysis!)
3. Tongue atrophy and fasciculations
4. Velum palati does not elevate during "aaaa"; uvula deviates to intact side.

Primary SENSORY neuron lesion

1. **Hypotonia**
2. **Areflexia** (absent all reflexes) – lost afferent portion of reflex arc!
3. Volitional movements and their strength remain normal!
4. Patient's appearance looks normal!
5. Coordination normal only with eyes open.

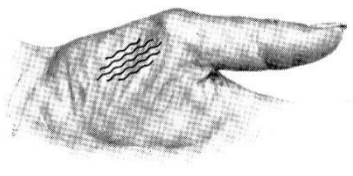
SPONTANEOUS MOVEMENTS

Cause of spontaneous movements can reside at any level of nervous system:
– movements that occur in **entire limb** or in **more than one muscle group concurrently** are caused by ***UMN disease***:
    a) *extrapyramidal* see p. Mov1 >>
    b) *seizure disorders*
– movements confined to **single muscle** are likely to be reflection of disease of ***motor unit*** (***LMN*** of brain stem and spinal cord ÷ ***muscle***).

FASCICULATIONS, FIBRILLATIONS

FASCICULATIONS - visible **fine, rapid, flickering / twitching** movements in ***small group of muscle fibers*** (fascicles or bundles).
FIBRILLATIONS - invisible contractions of ***individual muscle fibers*** - can be detected by EMG
→ see p. D20 >>

- vary irregularly in frequency and extent.
- do not move joint!
- etiology – ***LMN disease***:
    1) diseased anterior horn cell may spontaneously discharge → FASCICULATIONS.
    2) Acch receptors in denervated muscle fibers fail to cluster at motor end plate and become spread across muscle membrane → muscle fibers may then discharge spontaneously → FIBRILLATIONS.



Source of picture: Barbara Bates "A Guide to Physical Examination", 3rd ed. (1983); J.B. Lippincott Company; ISBN-13: 978-0397543991 >>

- FASCICULATIONS are seldom seen with peripheral nerve lesions (atrophy without fasciculations is more compatible with peripheral nerve lesion).
- in long-standing muscle denervation and reinnervation, motor unit size enlarges and fasciculations may be so large as to produce movement of limbs, particularly of fingers (**MINIPOLYMYOCLONUS**).

N.B. fasciculations are commonly experienced as **benign phenomenon** in absence of any disorder! (e.g. in incompletely relaxed muscles)

FEATURES	**Benign** fasciculations (*Denny-Brown, Foley syndrome*)	**Malignant** (neuropathologic) fasciculations
Gender predilection	males*	–
Predilection for certain muscle groups	calves and thighs	–
Nature	repetitive twitch in same muscle fascicle; may be accompanied by frequent cramps	random nonstereotyped twitches of many parts of muscle
Associated weakness or atrophy	–	+
Electrophysiology	appears like normal motor unit; no features of muscle denervation	complex, longer duration, higher amplitude

*medical students, physicians, and other medical workers - they are only people in society who know malignant implications of fasciculating muscles

MYOKYMIA

- continuous involuntary quivering or rippling (numerous, repetitive fasciculations) of muscles at rest.

- caused by spontaneous, repetitive firing of groups of motor units – specific EMG pattern.

see p. D20 >>

- etiology:
  a) **lesions of pons** (e.g. neoplasm or multiple sclerosis) - **FACIAL MYOKYMIA** - nearly continuous twitching of facial muscles (palpebral fissure narrowing, continuous undulation of facial skin surface = "bag of worms" appearance).
  b) defects of **nerve K^+ channels** (e.g. neuromyotonia).
  c) **amyotrophic lateral sclerosis**.

CRAMP (S. SPASM)

- sudden ***transient*** (up to few minutes) intense tonic contraction of ***single / multiple muscles***.

- associated with severe pain.
- prolonged severe cramps can produce ***muscle injury*** (e.g. creatine kinase↑ in blood, myoglobinuria).
- etiology:
  1) ORDINARY MUSCLE CRAMPS.
  2) **neurogenic disease** of LMN (esp. ALS), nerve roots, peripheral nerve.
  3) **myogenic disease** - muscle ischemia, myopathy (e.g. phosphorylase deficiency, phosphofructokinase deficiency).
  4) dehydration, hyponatremia, pregnancy, hypothyroidism, uremia
- EMG - brief, periodic bursts of motor unit potentials at 200-300 Hz (much higher than with voluntary contraction), intermingling with similar discharges from adjacent motor units.
  – several foci within same muscle may discharge independently.
  – electrical activity clearly arises within LMN (whether it occurs in soma, in peripheral nerve, or in intramuscular nerve terminals is still debated); chemical mechanisms are not understood.

ORDINARY MUSCLE CRAMPS - cramps in **normal** persons.

- can affect almost ***any voluntary muscle***; most frequently in *lower extremities* (e.g. nocturnal calf cramps).
- often *starts with fasciculations* → muscle becomes intermittently hard and knot-like as involuntary contraction waxes and wanes, passing from one part of muscle to another.
- particularly common in *older patients*.
- provoked by trivial movement or by contracting shortened muscle; may occur during vigorous exercise, but are more likely to occur *after exercise ceases*.
- treatment - stretching affected muscle.
- prophylaxis:
  a) avoid caffeine and other stimulants.
  b) bedtime QUININE SULFATE 300 mg!!! - FDA warns against use of this drug for this unapproved indication "*Qualaquin should not be used for night time leg cramps - may result in thrombocytopenia, HUS/ TTP*"
  c) **calcium supplements** (CALCIUM GLUCONATE 1-2 g bid) - effectiveness is doubtful.
  d) MAGNESIUM OXIDE 100-200 mg bid.
  e) low doses of **benzodiazepines**.
  f) PHENYTOIN, CARBAMAZEPINE
  g) MEXILETINE 150 mg tid - effective when increased LMN irritability is suspected.

TETANY

- intense tonic painful muscle cramps (e.g. carpopedal spasms, laryngospasm, opisthotonus).

- pathophysiology – hyperexcitability* of LMN or peripheral nerves → spontaneous firing of peripheral nerves.

  *demonstrated by reactions to ischemia [Trousseau sign] and percussion [Chvostek sign]

- etiology:
  1) hypocalcemia, hypomagnesemia
  2) tetanus toxin (GABA receptor blocker) – causes **TETANUS**.
  3) strychnine (glycine antagonist)
  4) black widow spider toxin.
  5) latent tetany (s. normocalcemic tetany, spasmophilia)
- EMG - individual motor units discharge independently at 5-25 Hz; each discharge consists of group of ≥ 2 identical potentials.

MUSCLE STIFFNESS

- state of ***continuous*** muscle contraction at rest.

- etiology:
  1) malignant hyperthermia. see p. 3910 >>
  2) neuroleptic malignant syndrome
  3) stiff-man syndrome see p. Spin27 >>
  4) myotonic disorders – myotonic dystrophy, channelopathies. see p. Mus5 >>, p. Mus7 >>

> **MYOTONY** - impaired muscle relaxation after forceful voluntary contraction (painless muscle stiffness).

CONTRACTURE

- prolonged severe, exercise-provoked tonic muscle shortening* (unassociated with muscle membrane depolarization).

  *do not confuse with limitation of joint range of motion (also termed contracture).

- etiology – ***glycolytic enzyme deficiencies*** that interfere with substrate utilization as fuel (e.g. McArdle disease).
- *intensely painful*, and result in muscle damage (→ myoglobinuria → renal failure).
- contractures are *electrically silent* by EMG (vs. cramps - intense motor unit activity).

  N.B. disorders of **muscle contractile system** cause *electrically inactive* contractions!

LESION LOCALIZATION GUIDE

Lesion of pyramidal UMN:

A) **above DECUSSATIO PYRAMIDUM** (*pyramidal tract*) → **CONTRALATERAL hemiplegia** (including lower face; lesions below pons spare face).
- ***bilateral*** lesions can cause PSEUDOBULBAR PARALYSIS. *see above >>*

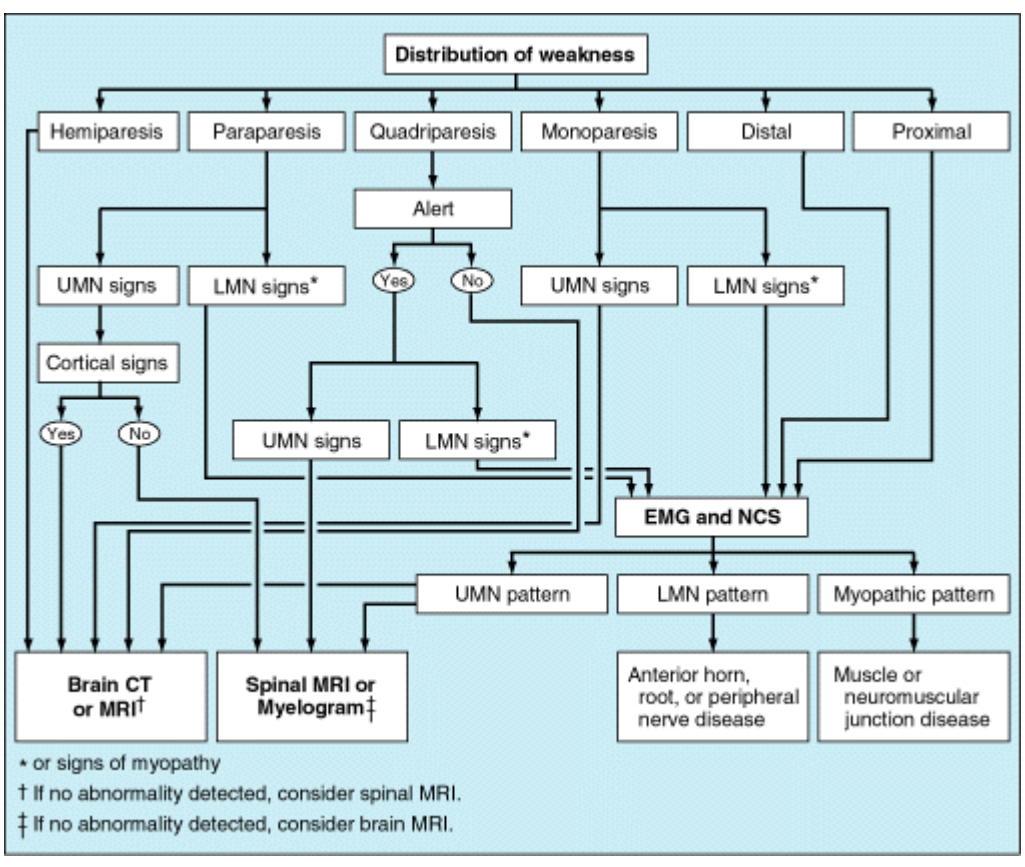
B) **below DECUSSATIO PYRAMIDUM** (*anterior and lateral corticospinal tracts*) → **IPSILATERAL plegia**;
- in some cases only **paresis** (esp. in trunk muscles) – due to contralateral *tr. corticospinalis ant.* (if well-developed – may account for some degree of recovery).

In general, only ***BILATERAL lesions*** cause UMN-type weakness in *trunk* and *cranial* muscles!

PATTERNS OF WEAKNESS

Sign	UMN weakness	LMN weakness	Myopathic weakness
Atrophy	–	+++	+
Fasciculations	–	+	–
Tone	↑ (spastic)	↓	normal / ↓
Distribution of weakness	pyramidal/regional	distal/segmental	proximal
Tendon reflexes	↑↑↑	↓ / absent	normal / ↓
Babinski sign	+	–	–

Weakness distribution, UMN or LMN signs	Lesion location
Hemiparesis (with lower face on same side) (UMN)	Contralateral cerebral hemisphere
Tetraparesis (UMN) + pseudobulbar palsy (UMN)	Bilateral cerebral hemispheres
Hemiparesis (UMN) + cranial nerve signs (LMN)	Brain stem
Tetraparesis (UMN) + cranial nerve signs (LMN)	Bilateral brain stem
Tetraparesis (UMN)	Mid or upper cervical cord
Paraparesis (UMN) + hands (LMN)	Low cervical cord
Paraparesis (UMN)	Thoracic spinal cord
	Bilateral medial motor cortex
All limbs, proximal > distal (LMN)	Muscle (myopathy or dystrophy)
Legs, distal > proximal (LMN)	Nerve (polyneuropathy)
Ocular muscles, eyelids, jaw, face, pharynx, tongue (LMN)	Neuromuscular junction (NMJ)
Jaw, face, pharynx, tongue; sparing ocular muscles, eyelids (UMN and LMN)	Motor neuron disease (ALS)
Specific muscle groups in one limb (LMN)	Nerve root, plexus or peripheral nerve



PARAPARESIS

- lesion location is BILATERAL (!):

Lesion Location	Pattern of Signs
Medial hemispheres (leg area)	Spastic leg paraparesis with no sensory level
Thoracic spinal cord	Spastic leg paraparesis, thoracic sensory level
Lumbar spinal cord	Flaccid paraparesis, double incontinence (flaccid bladder and sphincters)

Paraparesis implies lesion ***below cervical cord***; exceptions:

1) **leg areas** (on medial side of each hemisphere, at apex of motor strip) face each other in interhemispheric fissure - *parasagittal lesion* in interhemispheric fissure (most commonly *parasagittal meningioma*; other - *ACA ischemia*, *superior sagittal sinus thrombosis*) could affect both legs - PARAPARESIS simulating spinal cord lesion.
   N.B. this possibility seems more theoretical than real, however, because no well-documented cases have been reported!
2) *hydrocephalus* may be another supraspinal cause (parasagittal **leg fibers** are stretched most by dilated lateral ventricles).

ETIOLOGY

In adults, most common cause of paraparesis is *multiple sclerosis* ("*spastic paraparesis of middle life*").

Other causes:
- cervical spondylotic myelopathy;
- hereditary spastic paraparesis;
- primary lateral sclerosis;
- HTLV-I infection, HIV myelopathy.

DIAGNOSTIC APPROACH begins with **spinal MRI** or **myelography**.

HEMIPARESIS

- lesions are UNILATERAL (!):

Lesion Location	Pattern of Signs
Cerebral cortex	Contralateral weakness (arm, leg, face; sometimes tongue)*. LEFT HEMISPHERE: aphasia, apraxia. RIGHT HEMISPHERE: left hemi-inattention, extinction of sensory stimuli, constructional apraxia, spatial disorientation. Homonymous hemianopia on weak side. Cortical sensory loss (decreased graphesthesia, stereognosis, point localization). Horizontal eye deviation (toward lesion side).
Internal capsule (posterior limb)**	Contralateral weakness (face = arm = leg); face may be spared! No sensory loss or aphasia
Brain stem: see p. A59 >>	Contralateral weakness (arm = leg) + ipsilateral peripheral cranial nerve palsy:
Midbrain (crus cerebri)	Lesion of CN3 (Weber syndrome), red nucleus, superior cerebellar peduncle (limb ataxia contralateral to hemiparesis side)
Pons (basis pontis)	Lesion of CN6 (Foville syndrome), CN7 (Millard-Gubler syndrome); internuclear ophthalmoplegia
Medulla (pyramid)	Lesion of CN12; face spared
Cervical spinal hemicord (Brown-Séquard syndrome)	Ipsilateral weakness sparing face. Ipsilateral loss of proprioception and vibration. Contralateral loss of pain and temperature.

*face & arm > leg (MCA territory); face & arm < leg (ACA territory).

lesion in **internal capsule may be very small and still cause complete hemiparesis;
- "***pure motor hemiplegia***" - weakness that affects entire side of body equally without associated sensory signs;
- small strokes (lacunar infarcts in posterior limb near genu) can produce more focal weakness (e.g. weakness in face and arm - ***dysarthria-clumsy hand syndrome***).

Another possible cause of ***dysarthria-clumsy hand syndrome*** - lacunar infarction in **basis pontis** (esp. at junction of upper third and lower two-thirds) – lesion of corticobulbar & corticopontocerebellar fibers.

In general, hemiparesis usually signifies **cerebral** lesion and etiology* is likely to be denoted by clinical course + brain-imaging.

* in adults - most commonly cerebral infarction / hemorrhage

DIAGNOSTIC APPROACH - brain CT; if CT normal and ischemic stroke is unlikely → MRI of brain → MRI of cervical spine.

Acute hemiparesis

a) usually **vascular** pathogenesis
b) **traumatic** rupture of normal vessels
c) hemorrhage into primary / metastatic brain **tumors**
d) focal **inflammatory lesion** (multiple sclerosis, sarcoidosis)
e) acute bacterial **abscess**

Subacute hemiparesis

a) subacute **subdural hematoma**
b) **infection** - cerebral bacterial abscess, fungal granuloma or meningitis, parasitic infection.
c) malignant primary / metastatic **neoplasms**
   N.B. AIDS may present with subacute hemiparesis due to toxoplasmosis or primary CNS lymphoma!
d) focal **inflammatory lesion** (multiple sclerosis, sarcoidosis).

Chronic hemiparesis (slowly develops over months)

a) histologically **benign neoplasm**
b) unruptured **AVM**
c) chronic **subdural hematoma**
d) **degenerative disease**.

TETRAPARESIS

- lesion locations are BILATERAL (!):

Lesion Location	Pattern of Signs
Cerebral hemispheres	Pseudobulbar palsy, decorticate posturing (large acute lesions)
Midbrain	Coma, mid-size poorly reactive pupils, decerebrate posturing
Basis pontis	"Locked-in" syndrome
Cervicomedullary junction	Legs > arms, ± weakness of pharynx & tongue, facial hypalgesia (descending tract of CN 5)
High cervical	No cerebral signs (cranial nerve palsies, etc)
Mid cervical	Preservation of shoulder movements
Peripheral nerves (e.g. acute demyelinating polyneuropathy)	Distal weakness
Muscles (myopathy)	Proximal weakness

MONOPARESIS

A. With pain:
   1. Compressive lesion of **spinal cord**.
   2. Acute **brachial plexus** neuritis (neuralgic amyotrophy).
   3. **Peripheral nerve** entrapment syndromes
B. Painless:
   1. **Thoracic spinal** lesions (e.g. ALS, tumor, demyelinative plaque).
   2. **Cerebral** lesions (theoretically; because abnormal signs are almost always present in leg, i.e. syndrome is really hemiparesis) - weakness predominantly in *distal* and *nonantigravity* muscles.

BIBRACHIAL PARESIS

- arms hang limply at side while patient walks with normal movements of legs.

1. **Cervical LMN** lesion in some cases of ALS (with or without UMN signs in legs).
2. **Myopathy** of unusual distribution.
3. **Cerebral** lesion (bilateral prerolandic) – "***man-in-the-barrel syndrome***" seen in comatose patients who survive bout of severe hypotension.

NECK WEAKNESS ("FLOPPY HEAD" SYNDROME)

Never in UMN disorders!

1. **ALS**
2. **Myasthenia gravis**
3. **Polymyositis**

4. **Tick-borne encephalitis**

HYPOREFLEXIA

1. **Normally** hypoactive reflexes.
2. **Hypothyroidism** (delayed relaxation phase of reflex) - this unique "hypoactive" reflex is classic for this metabolic abnormality (best seen in ankle jerk).
3. **Spinal shock**
4. **Acute stroke** (initially, there is hyporeflexia on hemiparesis side; later, hyperreflexia develops).
5. **Holmes-Adie syndrome** (asymptomatic areflexia with large pupil that reacts to accommodation but not to direct light) see p. Eye64 >>
6. **Myopathy**
7. **Neuropathy** (incl. radiculopathy)
   N.B. patient with no reflexes usually has neuropathy!

BILATERAL HYPERREFLEXIA

1. Normal anxious patients
2. Metabolic causes (e.g. hepatic and uremic encephalopathy)
3. Spinal cord compression
4. Multiple sclerosis
5. Amyotrophic lateral sclerosis
6. Multiple small strokes (état lacunaire)
7. Familial spastic paraplegia
8. Cerebral palsy
9. Parasagittal intracranial mass (may affect cortical leg fibers)
10. Hydrocephalus (may stretch leg fibers)

VOICE

LMN impairment → soft, weak, low-pitched, monotonous voice.
UMN impairment → harsh and strained voice.

ACUTE GENERALIZED WEAKNESS

- pace of disease is so rapid that by time patient is seen in hospital weakness has become generalized.

Lesion Location (cause)	**Differentiating Features**
Midbrain (stroke, trauma, tentorial herniation)	**Coma**, mid-size poorly reactive pupils, decorticate/decerebrate posturing, hyperreflexia, bilateral Babinski signs
Basis pontis (stroke)	**"Locked-in" syndrome**
Spinal cord (trauma, infarction, metastatic tumor, transverse myelitis)	**Spinal shock**
Polyradicular neuropathy (acute inflammatory demyelinating polyneuropathy, tick paralysis, poliomyelitis)	Limb weakness (legs before arms), areflexia, absent or flexor toe response, minimal distal sensory loss without sensory level
Neuromuscular junction (botulism, organophosphates)	Ocular (incl. loss of pupillary light reflex) and pharyngeal weakness → **absolutely generalized weakness** with no sensory loss, no decorticate / decerebrate posturing; preserved consciousness

EPISODIC WEAKNESS

- attacks of severe weakness occurring in patient with baseline normal strength.

Disorders	**Key Features**	**Diagnostic Tests**
COMMON		
Transient ischemic attack	All symptoms ***begin at once*** (abrupt and simultaneous onset of weakness in all muscles that will be affected during attack)	Carotid ultrasound
LESS COMMON		
Partial motor seizure, Todd's paresis (postictal weakness)	***Gradual*** "march" of symptoms in ***several seconds to few minutes***	EEG
Hemiplegic migraine	***Gradual*** development over ***several minutes***; family history	
Myasthenia gravis	Fatigability, recovery with rest; predilection for ocular and cranial muscles	Tensilon test, repetitive stimulation test
Hysteria	***Normal reflexes***, nonanatomic distribution of sensory loss	
Cataplexy	***Triggered by emotion***; association with other features of narcolepsy; episodes very brief	Sleep study
Sleep paralysis	Narcolepsy; ***terminated by touch***	Sleep study
Drop attacks *see below >>*	***Sudden loss of postural tone*** without loss of consciousness	MRI, MRA, X-ray of cervical spine with flexion-extension, EEG
Negative myoclonus see p. Mov1 >>	***Sudden, brief, rapid, unpredictable (shocklike)*** inhibition of muscle tone (single muscle ÷ entire body).	
RARE		
Periodic paralyses	***Familial*** channelopathies	Serum K^+

DROP ATTACK

- sudden falling spell (loss of postural tone);
  - no warning, no loss of consciousness!!!
  - attack is very brief; no postictal symptoms; person is immediately able to get to his feet after hitting ground.
- pathophysiology - dysfunction of **pyramidal tracts** in ***medulla*** / ***high cervical cord***.
- etiology
  1) brief **ISCHEMIA** (e.g. vertebrobasilar **ischemic attack**)
  2) transient **MECHANICAL COMPRESSION**:

a) ligament holding odontoid in place destroyed by **RA** or **trauma**: head movement (esp. extension) → excessive odontoid movement → compression of cervicomedullary junction.
b) chronic cerebellar tonsillar herniation (characteristic of **Chiari malformation**).
c) severe **congenital cervical spinal stenosis** during Valsalva maneuvers or after falls.
d) **idiopathic drop attacks** in elderly women; benign prognosis.

- differentiate from disorders with very brief ***loss of consciousness*** (unnoticeable by patient):
  1) ***akinetic seizures*** (H: EEG)
  2) ***syncope*** (H: history of brief warning).

BIBLIOGRAPHY for ch. "Movement disorders, Ataxias" → follow this LINK >>