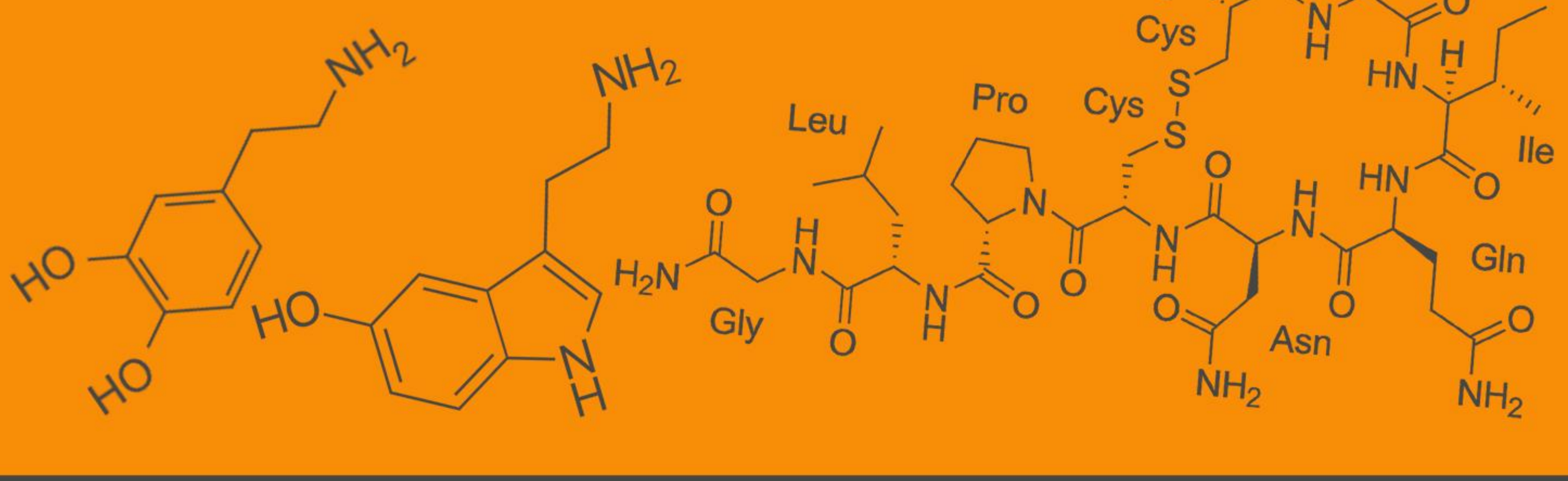


MEDICINE438's CNS PHYSIOLOGY

LECTURE XVIII: Spasticity and Increased Muscle Tone

EDITING FILE GSLIDES

IMPORTANT | MALE SLIDES | EXTRA | FEMALE SLIDES | LECTURER'S NOTES

1 Spasticity and Increased Muscle Tone

Lecture Eighteen

OBJECTIVES

- Define spasticity, rigidity, and hypertonia
- Describe the neurophysiology of spasticity
- Describe causes of spasticity and rigidity

BOX 18-1: Recall from Stretch Reflex Lecture

- **Muscle stretch reflex** (myotatic reflex) is the function of the *muscle spindle.* Whenever a muscle is stretched, the excited spindles cause reflex contraction of the same muscle and also the synergistic muscles. Dynamic response is over within fraction of a second when a weaker static stretch reflex continues for a prolonged period. Muscle tone is generated by muscle spindles by acting through the stretch reflex.
- **Muscle tone** is the constant muscular activity that is necessary as a background to actual movement in order to maintain the basic attitude of the body particularly against the force of gravity. As tone opposes movement and tends to keep muscles at preset lengths, it has to be changed in steps during a movement. Gamma fibers are ideally suited for this and whenever a command is sent to alpha motor fibers, *gamma fibers* are also excited. There occurs *alpha–gamma coactivation* to produce contraction of both **extrafusal** (innervated by **alpha** efferent fibers) and **intrafusal** "spindle" fibers (innervated by **gamma** efferent fibers) according to the position and force commands from the brain to the spinal cord.
- Clinical elicitation of **stretch reflex** is done in two ways:
- **Static:** by *passive stretching* (tone testing).
- **Dynamic:** by *muscle and tendon jerks.*
- The key to the *increased* excitability of the muscle stretch reflex (**muscle tone**) is the **abnormal activity of muscle spindles** which have an intricate relation with the innervations of the extrafusal muscle fibers at the spinal level which are under influence of the supraspinal pathways (inhibitory and facilitatory).

INTRODUCTION

Increased Gamma efferent discharge, by the facilitatory supraspinal centers to gamma motor neurons, is the main cause of increased muscle tone[1].

- Hypertonia refers to increased resistance to passive stretch (passive lengthening) of a muscle. This may mean increased *stiffness* of the muscle.
- Hypertonicity could be due to a neural drive problem such as:
  Spasticity or **Rigidity**

- Resistance of a muscle to stretch is often referred to as its **tone** or **tonus.**
- Muscle tone is static component of stretch reflex .It is a *continuous* mild muscle contraction that acts as background to actual movement.
- A **hypertonic** muscle is one in which the resistance to stretch is high because of hyperactive stretch reflexes.

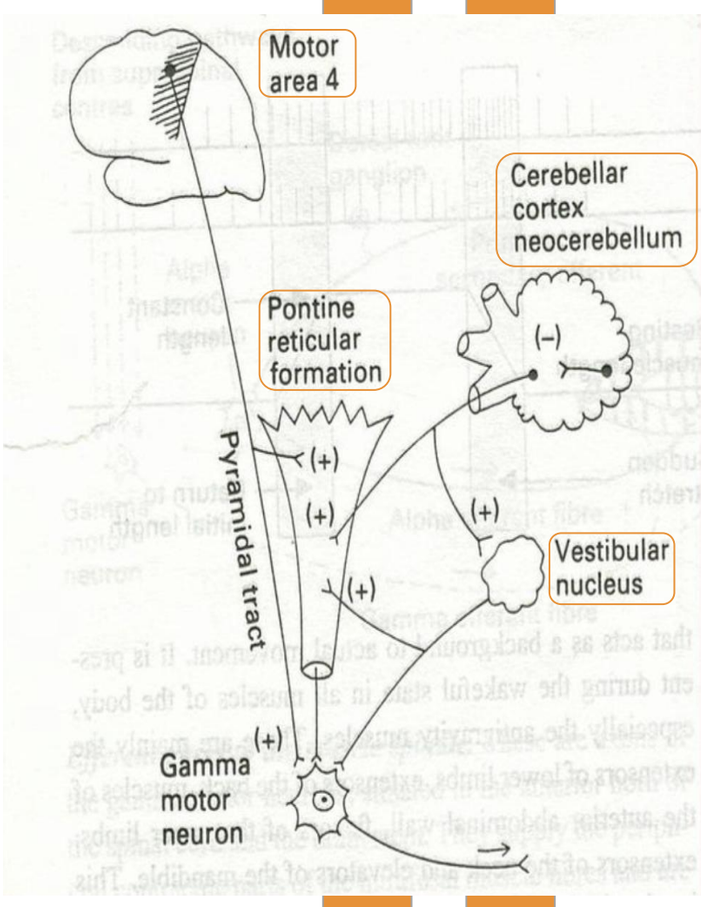


Figure 18–1

FOOTNOTES

1. The activation to gamma motor neurons are mostly from the descending pontine facilitatory reticular formation. This leads to the stretching of muscle spindle, activation of alpha motor neurons and finally a partially contracted muscle. Gamma motor neurons assist in keeping the receptor area of muscle spindle partially stretched, therefore making it more sensitive. As a result, if gamma is hyperactive, the muscle spindle will be hypersensitive to stretch, and will cause a stronger, more abnormal contraction in response to minimal stretch.

SPASTICITY

A. Velocity dependent:

- Increased resistance to passive movement of the muscle due to (hypertonia) which varies with the speed of displacement of a joint.
- The faster you stretch the muscle the greater the resistance.

B. Spasticity is clearly neural in nature and is associated with the UMNL due to Involvement of the corticospinal tract.

C. Spasticity is usually unidirectional (doesn't happen in both flexors & extensors)

- Flexor spasticity in the upper limb & extensor spasticity in the lower limb.

- A simple way to *assess spasticity* is by **fast flexion or extension** of selected joint, typically the *elbow* or *knee*, to elicit a sudden increase in tone and demonstrate the velocity dependent nature of spasticity.
- **Involvement of the corticospinal tract is often associated with UMNL and spasticity.**

Clinical Features That Are Associated With Spasticity

1. Hyperreflexia

2. Clasp-knife spasticity in UMNL[1], describe a sudden release of resistance after an initial hypertonia of selected joint movement.
   If sufficient force was applied, suppose on a spastic flexor muscle by an examiner to cause extension, the tension in the flexor muscle will increase as it tries to resist extension, however eventually the increased tension will trigger the Golgi Tendon reflex, which will cause sudden relaxation of the muscle to relieve tension, thus preventing muscle rupture and tendon tear. The movement of the limb will resemble a clasp-knife. That is, after sufficient force has been applied on the opposite side, the muscle returns to a more resting position.

3. Spasticity with the increased muscle tone together cause a contraction and deformity of a limb.

- Spasticity & hypertonia[1] is a feature of altered muscle performance.
- Usually in **Upper Motor Neuron Syndrome** (UMNS).

➢ Patients complain of *stiffness* and *inability to relax.*
➢ Muscles become *permanently* "**tight**" or **spastic.**
➢ The condition can interfere with walking, movement, or speech.

FOOTNOTES

1. Impaired ability of damaged motor neurons to regulate descending pathways gives rise to disordered spinal reflexes, increased excitability of muscle spindles, and decreased synaptic inhibition. These consequences result in abnormally increased muscle tone of symptomatic muscles.
   - Different patterns of muscle weakness or hyperactivity can occur based on the location of the lesion, causing a multitude of neurological symptoms, including spasticity and rigidity.

3 Spasticity and Increased Muscle Tone

- When there is a *loss* of **descending inhibition from the brain** higher motor-inhibitory centers (**Medullary Reticular Formation, Basal Ganglia and Suppressor Area 4**) resulting in un-antagonized excitatory input from ***brain stem excitatory centers***, As (Pontine Reticular Formation + Vestibular Nucleus) through **Vestibulospinal & Reticulospinal excitatory tracts** to gamma motor neurons causing hypertonia & spasticity of muscles.

- This results in:

1. State of ongoing (unremitting) contraction of muscles (due to hyperactive gamma activity)	2. Decreased ability to control movement	3. Increased resistance felt on passive stretch

Spasticity Is Characterised By Hyper-excitability Of Both Types Of Stretch Reflex

1. Increase in *tonic static stretch reflexes* (**muscle tone**) as one component of the **upper motor neuron (UMN) syndrome**

2. Exaggerated tendon jerks, resulting from hyper-excitability of the *dynamic stretch reflex* as one component of the **upper motor neuron (UMN) syndrome**

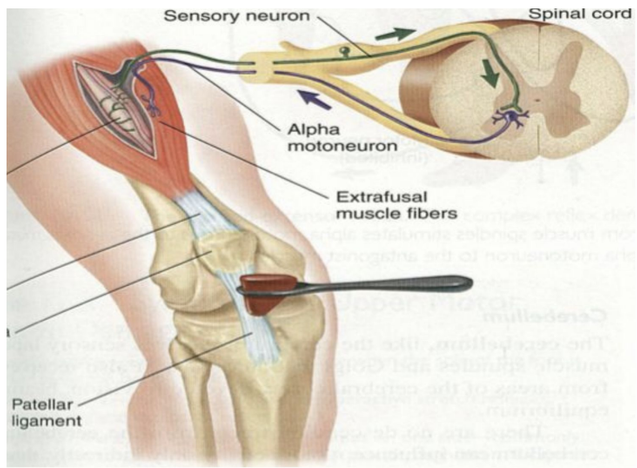


Figure 18-2

FEATURES OF UPPER MOTOR NEURON SYNDROME:

1	Weakness and decreased muscle control.
2	No remarkable muscle wasting, but disuse atrophy.
3	**Spasticity & hypertonia**, frequently called "*Clasp-knife spasticity*": increased resistance at the beginning of muscle stretch due to increased extensor muscle tone then a sudden collapse in resistance due to inhibition of extensor motor neurons by **golgi tendon organs.**
4	Clonus[1] (Repetitive jerky motions), especially when limb moved & stretched suddenly.
5	Exaggerated tendon jerks.
6	Extensor plantar reflex = Babinski sign (dorsiflexion of the big toe and fanning out of the other toes).
7	Absent abdominal reflexes

FOOTNOTES

1. **Clonus** is a series of involuntary, rhythmic, muscular contractions and relaxations. *Clonus* is a sign of certain neurological conditions, particularly associated with **upper motor neuron lesions** involving descending motor pathways, and in many cases is, accompanied by *spasticity* (another form of hyperexcitability). Unlike small, spontaneous twitches known as **fasciculations** (usually caused by *lower motor neuron* lesion), which will be discussed in upcoming lectures.

RIGIDITY

A. Increased resistance to the passive movement of a muscle which is constant throughout the movement and not related to the speed of movement (is not velocity dependent).

B. In rigidity, *resistance* is present in both agonist and antagonist (bidirectional).

C. Rigidity is usually **extrapyramidal in origin** & Rigidity includes other features of increased muscle tone.

- It Is often associated with **basal ganglia disease** such as Parkinson's disease.
- Stiffness is different from rigidity. Stiffness is a principal *symptom* of the patient (complain).

RIGIDITY IN PARKINSONISM

1. Lead-pipe rigidity: Passive movement of an extremity is met with a constant dead feeling resistance like a bending a lead pipe throughout the range of movement.

2. Cogwheel rigidity: resistance varies rhythmically when applying a passive movement. It is because of an underlying resting tremor associated with rigidity.

OTHER TYPES OF RIGIDITY

3. Decerbrate rigidity: extension of head & 4 limbs extensors.

4. Decorticate rigidity: extensor rigidity in legs & moderate flexion of arms if head unturned.[1]

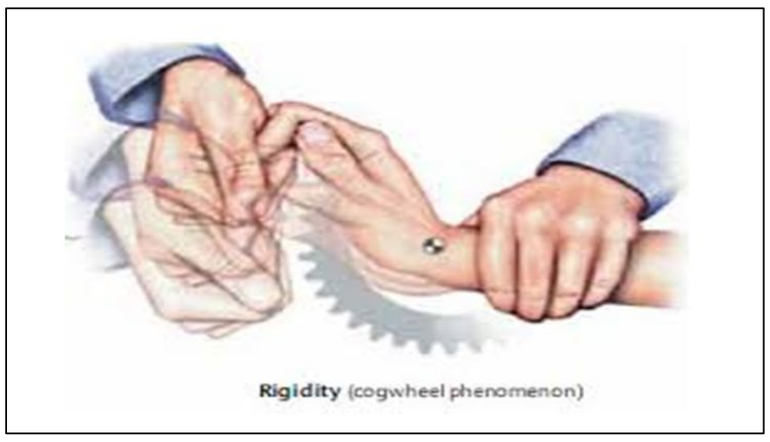


Figure 18-3

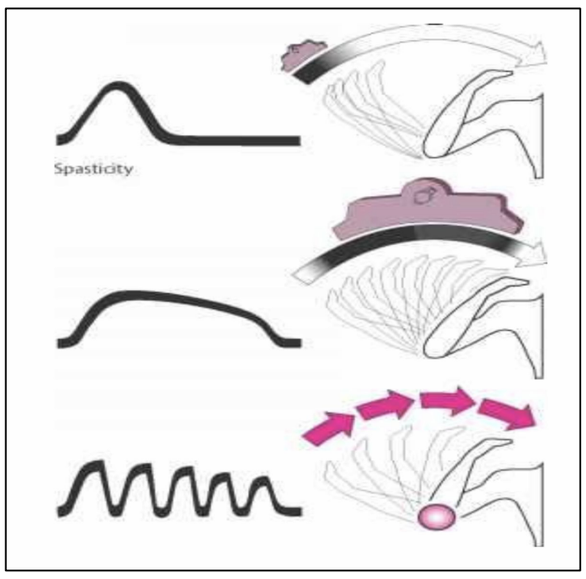


Figure 18-4

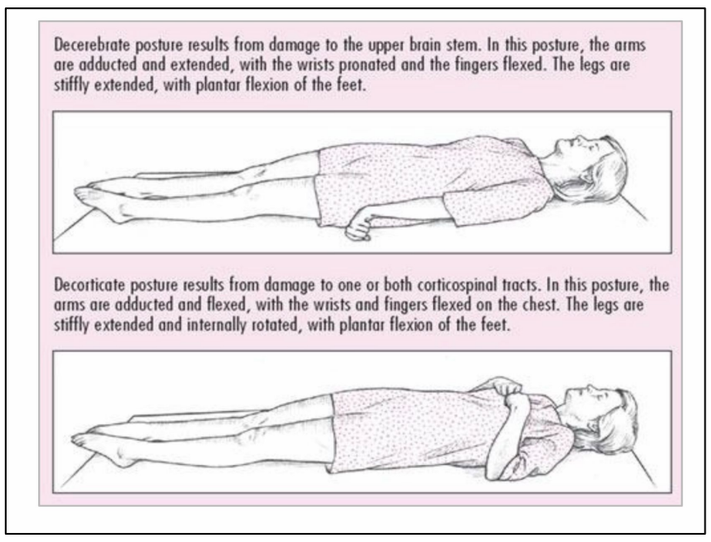


Figure 18-5

FOOTNOTES

1. The emphasis on an unturned head is due to an intact neck static reflex in decorticate rigidity, remember that upon turning the head to one side, the neck static reflex will cause extension of the limb on that side and flexion of limbs on opposite side.

5 Spasticity and Increased Muscle Tone

- To test for rigidity, passively move the joint in *both direction. (To differentiates between rigidity "bidirectional" and spasticity "unidirectional")*
- A relatively uniform rigidity in both agonist and antagonist muscle group is known as **lead-pipe rigidity.**
- When there's *tremor* superimposed with background increase of tone, it's known as **Cogwheel rigidity.** This rigidity is commonly seen in Parkinson's disease.

Spasticity	Rigidity[1]
• Resistance to passive stretch • Involuntary • Velocity-dependent • Unidirectional	• Resistance to passive movement • Involuntary • Not velocity-dependent • Bidirectional

Leads to resistance to movement

Causes of Spasticity				
(UMNS) syndrome				
Cerebral palsy	Multiple sclerosis	Spinal cord injury	Stroke	Acquired brain injury

Causes of Rigidity	
Parkinsonism	Decerebrate & decorticate rigidity

BOX 18-2: EXTRACULLICULAR

There are two categories of movement disorders:

- **Hypokinesia**: characterized by a partial or complete loss of muscle movement due to a disruption in the basal ganglia. Patients with hypokinetic disorders like Parkinson's disease experience muscle rigidity and an inability to produce movement. It is also associated with mental health disorders such as schizophrenia.
  - Hypokinesia describes a variety of more specific disorders: e.g. *Akinesia*, *Bradykinesia*, *dysarthria*, dystonia, and ***rigidity***.
- **Hyperkinesia:** resulting from damage to the basal ganglia, features an exaggeration of unwanted motion, like twitching or writhing in *Huntington's disease* or *Tourette syndrome.*

FOOTNOTES

1. It does not depend on imposed speed and can be elicited at very low speeds of passive movement in both directions. **Cogwheel rigidity** and **lead pipe rigidity** are two types identified with Parkinson's disease:

- ***Lead pipe rigidity*** is sustained resistance to passive movement throughout the whole range of motion, with no fluctuations.
- ***Cogwheel rigidity*** is jerky resistance to passive movement as muscles tense and relax.
- ***Spasticity***, a special form of rigidity, is present only at the start of passive movement. It is rate-dependent and only elicited upon a high-speed movement. These various forms of rigidity can be seen in different forms of movement disorders, such as Parkinson's disease.

CEREBRAL PALSY

- Caused by brain damage due to lack of oxygen, as (near drowning or near suffocation) that cause damage to the motor control centres of the developing brain.
- It can occur during pregnancy, during stressed childbirth (or after birth up to about age *three* by **meningitis**)

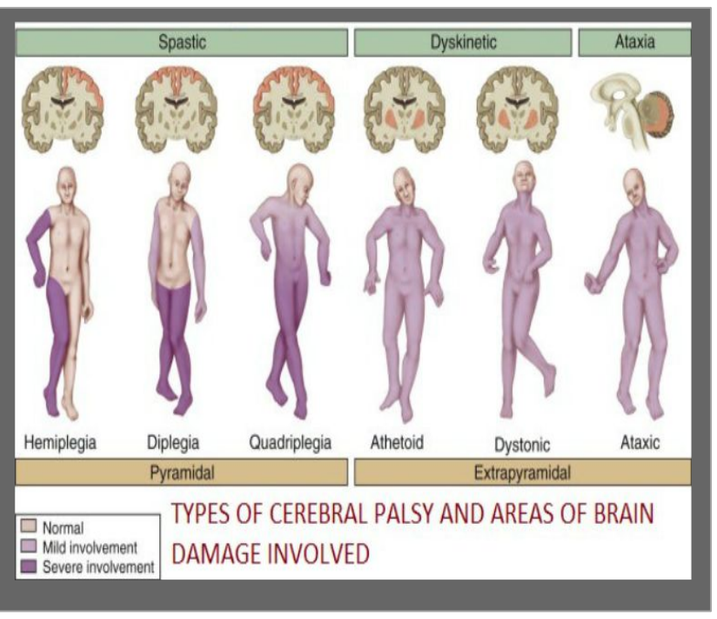
- **Increased muscle tone, tense and contracted muscles**
  - Have stiff and jerky or awkward movements.
  - limbs are usually underdeveloped
  - increased deep tendon reflexes
- **most common form**
- **70-80% of all affected**

BOX 18-3: GANONG'S REVIEW OF MEDICAL PHYSIOLOGY

CEREBRAL PALSY

Cerebral palsy is a term to describe several nonprogressive neurological disorders that occur before or during early childhood. Prenatal factors include exposure of the fetus to hypoxia, infections.

- Symptoms include spasticity, ataxia, loss of vision, hearing. Indicating basically that cerebral palsy is characterized by widespread damage to the cerebrum during prenatal or early life.
- Currently, there is no cure for cerebral palsy. Botulinum toxin, which reduces ACh release, has been injected into muscles to reduce spasticity in some cases. As well as GABA agonists.



MULTIPLE SCLEROSIS

- An autoimmune demyelinating disease, in which the body's own immune system attacks and damages the myelin sheath of myelinated nerves mainly of brain, SC, and optic nerve.
- Loss of myelin sheath (demyelination) prevents axons from saltatory conduction of action potentials causing muscle weakness & wasting.
- Disease onset usually occurs in young adults, and it is more common in females.
- The disease can attack any part of the CNS, and when it causes demyelination of descending motor tracts in the brainstem & spinal cord, the subject develops spasticity and other signs of UMNS.
- The disease frequently remits and relapses because of remyelination & restore of function.
- During acute attacks intravenous corticosteroids can improve symptoms.

STROKE

- Causes:
  - **Haemorrhagic stroke;** as in *cerebral hemorrhage*
  - **Ischaemic stroke;** as in *thrombosis* or *embolism* in brain blood vessels
    - Both cause death of brain tissue and result in paralysis of in the opposite half of the body.
- Gives the picture of upper motor neuron syndrome **UMNL.**
- A lesion in the corona radiata on one side can cause monoplegia in a contralateral limb (UL or LL; depending on the site)
- A lesion in the internal capsule on one side may cause hemiplegia or hemiparesis on the contralateral side

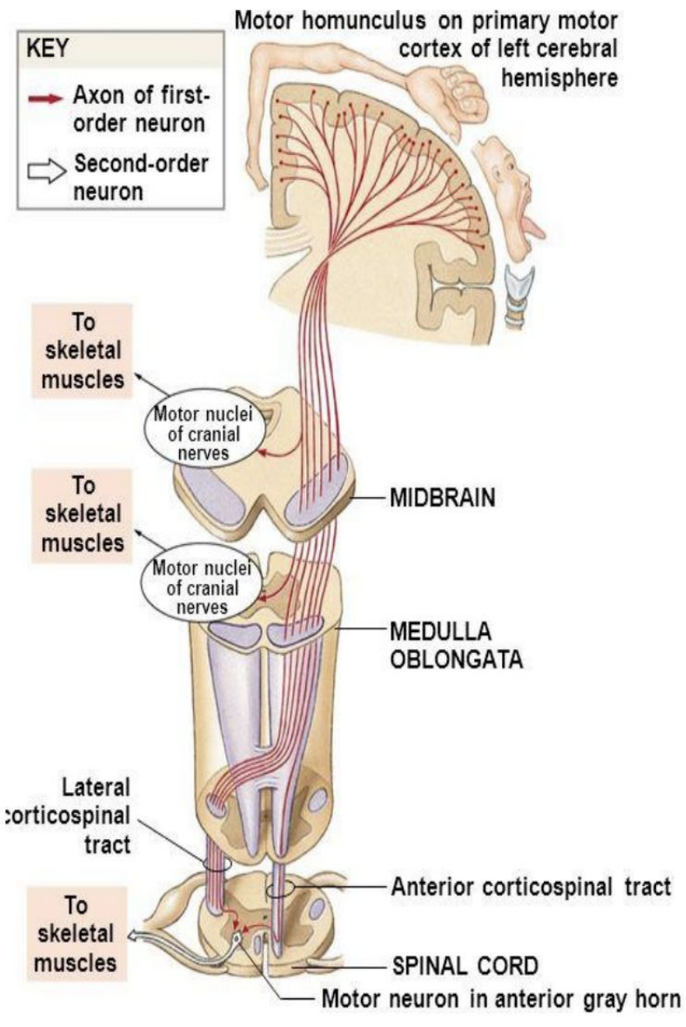


Figure 18-6

COMPLETE SPINAL CORD TRANSECTION (following tumor or trauma)

- Generally, the **higher** the level of the section, the more **serious** are the consequences:

Transection in the **upper cervical** region	Paralysis of all respiratory muscles (due to cut of the phrenic n.)	Immediate death
Transection in the **lower cervical** region below the **5th** cervical segment (they supply UL + LL)	Diaphragmatic respiration is still possible[1]	Complete paralysis of all four limbs (**quadriplegia**)
Transection lower down in the **thoracic** region (UL is saved)	Allows normal respiration	Paralysis of both lower limbs (**paraplegia**)

THE THREE STAGES OF COMPLETE SPINAL CORD TRANSECTION

1) Spinal shock (2-6 weeks)
2) Return of reflex activity
3) Paraplegia in extension

Firstly: spinal shock (Happens in the immediate period following the transection)

- It varies in duration, but usually lasts a maximum of 2-6 weeks, after which some reflex activity recovers.
- Features of this stage:

1. **Loss of vasomotor tone** due to interruption of fibres that connect the vasomotor centres in the medulla oblongata with the lateral horn cells of the spinal cord of sympathetic vasoconstrictor impulses to blood vessels. vasodilatation → a fall in blood pressure (the higher the level of the section, the lower the blood pressure)

2. **Loss of all sensations** (anesthesia) and **voluntary movements** (paralysis) **below** the level of the lesion, due to interruption of all sensory and motor tracts

3. **Loss of tendon reflexes** & **superficial reflexes** (abdominal, plantar & withdrawal reflexes) = complete loss of spinal reflex activity **below** the level of the lesion

4. **Loss of muscle tone** (flaccidity) & **absence of any muscle activity** (muscle pump) → decreased venous return causing the lower limbs to become cold and blue in cold weather

5. **Loss of visceral reflexes (micturition, defecation, and erection reflexes):** The wall of urinary bladder becomes paralysed & urine is retained until the pressure inside the bladder overcomes the resistance offered by the tone of the sphincters → dribbling. This is known as **retention with overflow**

6. Bedsores (also called decubitus ulcers) due to pressure of body-weight against underlining support

FOOTNOTES

1. The diaphragm is supplied by phrenic nerves, which arise from C3-C5, hence why it is affected in upper cervical transections. However, the other important muscle of respiration, the external intercostals, are innervated by intercostal nerves (T1-T11), hence in lower cervical transections, we say diaphragmatic respiration is possible but the intercostals are affected.

Secondly: Return of reflex activity

- As the *spinal shock* ends, spinal reflex activity appears again
- This partial recovery may be caused by **an increase in the degree of excitability of the spinal cord neurons below the level of the section**, due to:
  - i. Sprouting of fibres from remaining neurons
  - ii. Denervation supersensitivity to excitatory neurotransmitters (BOX 18-4)
  - iii. Disinhibition of motoneurons due to absence of inhibitory impulses from higher motor centres

BOX 18-4: EXTRACULLICULAR

LOGIC BEHIND DENERVATION HYPERSENSITIVITY

Neurons of spinal cord receive continuous excitatory signals from higher centers, hence why if the spinal cord is transected, the neurons of the cord below the transection will be depressed for a period of few weeks, however a feature of all neurons of the CNS is that they slowly regain their excitability. A mechanism that causes this is denervation hypersensitivity.

- Now virtually all cells of the body share the same genome, however, some decide to express different genes and therefore make different proteins and become different cells. This also include cell receptors for excitatory neurotransmitters.
- Let us try, as traditionally with our team, to propose a mechanism. Suppose that whenever an excitatory receptor for a neurotransmitter is stimulated, it also initiates an inhibitory biochemical cascade that inhibits transcription of the genes responsible for making receptors for the excitatory neurotransmitters. Thereby inhibiting the neurons from being hyperactive.
- Now let us suppose that the receptors are no longer stimulated due to transection and loss of excitatory signals from facilitatory centers . The inhibitory biochemical cascade for inhibiting transcription of cell surface receptors will not be initiated, therefore there will be increase in cell surface receptors and denervation hypersensitivity. Keep in mind that cells also have sensors for concentrations of certain proteins, and in response to decrease concentration they could initiate gene transcription for those missing proteins.

1 **Gradual rise in arterial blood pressure**; due to the return of spinal vasomotor activity in the lateral horn cells. But, since vasomotor control from the medulla is absent, the blood pressure is **not stable**.

➔ Vasoconstrictor tone in arterioles and venules improve the circulation through the limbs

2 **Return of spinal reflexes**:

➔ **Flexor tendon reflexes** return earlier than extensor ones

➔ **Babiniski sign**[1] (extensor plantar reflex) is one of the earliest signs of this stage +/- flexion reflex

➔ Flexor spastic tone causes the lower limbs to take a position of slight flexion, a state referred to as **paraplegia in flexion**

➔ The return of the stretch reflex (**muscle tone**), & vasoconstrictor tone in arterioles and venules improves the circulation through the limbs

3 **Recovery of visceral reflexes:** return of micturition, defecation & erection reflexes

➔ However, **voluntary control** over micturition and defecation, and the **sensation** of bladder and rectal fullness are **permanently lost** (**automatic micturition**)

4 **Sexual reflexes** consisting of erection or ejaculation on genital manipulation recover

5 **Mass reflex appears:** A minor painful stimulus to the skin of the lower limbs will not only cause withdrawal of that limb but will evoke many other reflexes through spread of excitation (by irradiation) to many autonomic centres. So the bladder and rectum will also empty, the skin will sweat, and the blood pressure will rise.

- Since effective regeneration never occurs in the human central nervous system, patients with complete transaction *never fully recover.*
- Voluntary movements and sensations are permanently lost; however, patients who are rehabilitated and properly managed may enter into a more advanced stage of recovery.

FOOTNOTES

1. Babinski sign refers to an upward flexion of the big toe, and dispersion of other toes from one another when the sole of the foot is scratched. It is a sign of an underdeveloped motor tract hence why it is present in infants and virtually absent in grown ups and replaced by other reflexes. However in this case, the motor tracts have limited regenerative capacity. And the reflex will appear.

Thirdly: Paraplegia in extension

1. **The tone in extensor muscles returns gradually to exceed that in the flexors:**

➔ The lower limbs become spastically extended

➔ Extensor reflexes become exaggerated, as shown by **tendon jerks** and by the appearance of **clonus**

➔ The positive supportive reaction becomes well developed and the patient can stand on his feet with appropriate support.

2. **The flexor withdrawal reflex** which appeared in the earlier stage is **associated** during this stage with the **crossed extensor reflex**

HEMISECTION OF THE SPINAL CORD (BROWN-SEQUARD SYNDROME)[1]

- It occurs as a result of unilateral lesion or hemisection of the spinal cord (due to stab injury, bullet, car accident, or tumor)
- The manifestations of the Brown-Sequard syndrome depend on the **level** of the lesion

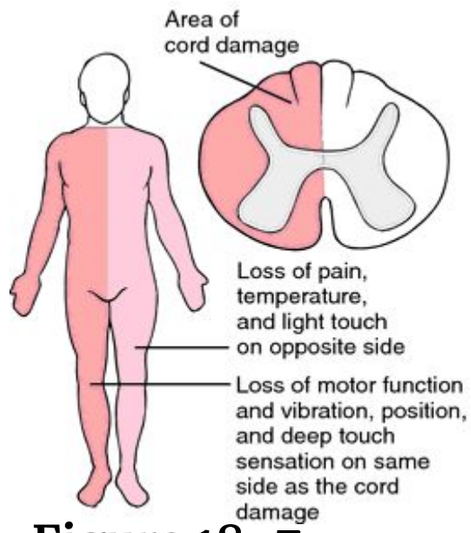


Figure 18-7

➔ an example of such injury involving the *thoracic* spinal cord:

On the same side at the level of lesion All manifestations occur on the same side	1. Paralysis of the lower motor neuron type, involving *only* the muscle supplied by the damaged segments 2. Loss of all sensations in the areas supplied by the afferent fibres that enter the spinal cord in the damaged segments +/- band of *hyperesthesia*[2]. 3. Vasodilatation of the blood vessels that receive vasoconstrictor fibers from the damaged segment
Ipsilaterally below the level of the lesion	1. UMNL/spastic lower limb (spasticity) & clonus. 2. **Fine touch**, **two-point discrimination**, **position** and **vibration** sense are lost. - Why? Cut of the dorsal column 3. Vasodilation 4. Paralysis of UMN type due to interruption of pyramidal and extrapyramidal tracts
Contralaterally below the level of the lesion	**Pain** and **temperature** sensations are lost. - Why? Cut of the spinothalamic tract

FOOTNOTES

1. The hemisection of the cord results in a lesion of each of the three main neural systems:
   - The principal upper motor neuron pathway of the corticospinal tract
   - One or both dorsal columns
   - The spinothalamic tract
2. Hyperesthesia: Unusual sensibility to sensory stimuli, such as pain or touch.

SUMMARY

Clinical features that are associated with spasticity:

- Hyperreflexia
- Clasp-knife spasticity in UMNL, describe a sudden release of resistance after an initial hypertonia of selected joint movement.
- Spasticity with the increased muscle tone together cause a contraction and deformity of a olimb

Spasticity	Rigidity
• Resistance to passive stretch	• Resistance to passive movement
• Involuntary, Velocity-dependent • Unidirectional	• Involuntary, Not velocity-dependent • Bidirectional

➔ Complete spinal cord transection

- ◆ The higher the level of the section, the more serious the consequences:
  - Upper cervical → paralysis of all respiratory muscles → death
  - Lower cervical (below C5) → possible diaphragmatic respiration → quadriplegia
  - Lower region (thoracic) → normal respiration → paraplegia
- ◆ Stages of complete spinal cord transection:

Spinal shock → **Recovery of reflex activity** → **Paraplegia in extension**

➔ Hemisection of the spinal cord (Brown-Sequard syndrome)

- ◆ Manifestations depend on the level of the lesion
- ◆ Example of thoracic spinal cord injury:
  - On the same side at the level of lesion:
    - ***Paralysis*** of the LMN type, only involving the muscle supplied by the damaged segments
    - ***Loss of all sensations*** in the areas supplied by the afferent fibres that enter the spinal cord in the damaged segments +/- band of hyperesthesia
    - ***Vasodilatation*** of the blood vessels that receive vasoconstrictor fibers from the damaged segment
  - Ipsilaterally below the level of the lesion:
    - UMNL, spasticity, clonus
    - Fine touch, two-point discrimination, loss of position and vibration senses
    - Vasodilatation
  - Contralaterally below the level of the lesion:
    - Loss of pain & temperature sensations

QUIZ

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1. Which of the following is a clinical feature associated with spasticity?

A) Parkinson's disease
B) Mask like face
C) Areflexia
D) Clasp- knife

2. Cerebral palsy is caused by brain damage due to lack of:

A) Carbon Dioxide
B) Nitrogen
C) Oxygen
D) Carbon Monoxide

3. A complete spinal cord transection in the lower cervical region below the 5th cervical segment results in:

A) Immediate death
B) Paraplegia
C) Quadriplegia
D) None of them

4. In a complete spinal cord transection, in which stage does automatic micturition occur?

A) Spinal shock
B) Return of reflex activity
C) Paraplegia in extension
D) It is permanently lost

5. What would happen ipsilaterally below the level of the lesion in someone who suffered a hemisection of the spinal cord?

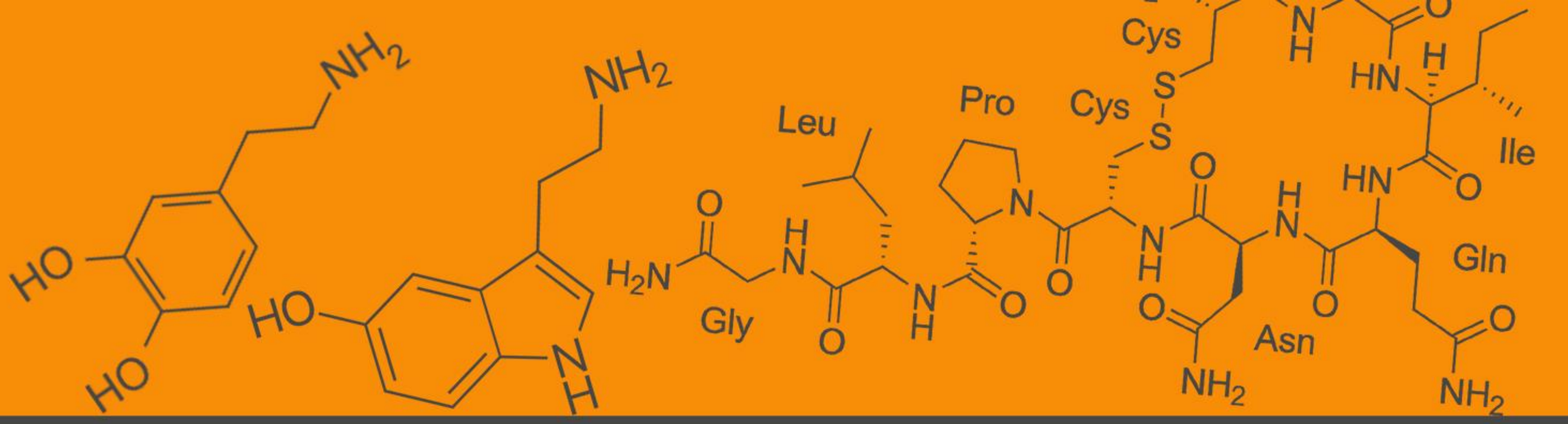
A) Loss of position and vibration senses
B) Loss of pain sensation
C) Loss of temperature sensation
D) Loss of all sensations

SHORT ANSWER QUESTIONS

1) Mention 3 features of UMN syndrome
2) Mention 2 features of the spinal shock stage:

1) Stroke, cerebral palsy, and multiple sclerosis
2) A. complete loss of voluntary movement & all sensations below the level of lesion
   B. Loss of muscle tone & absence of muscle of any muscle activity

ANSWER KEY: D, C, C, B, A



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REFERENCES

- Guyton and Hall Textbook of Medical Physiology
- Ganong's Review of Medical Physiology