RENAL REGULATION OF ACID BASE BALANCE BY KIDNEYS

The main Buffer Systems in the kidneys are

1. Bicarbonate System
2. Dibasic phosphate System
3. Ammonia System

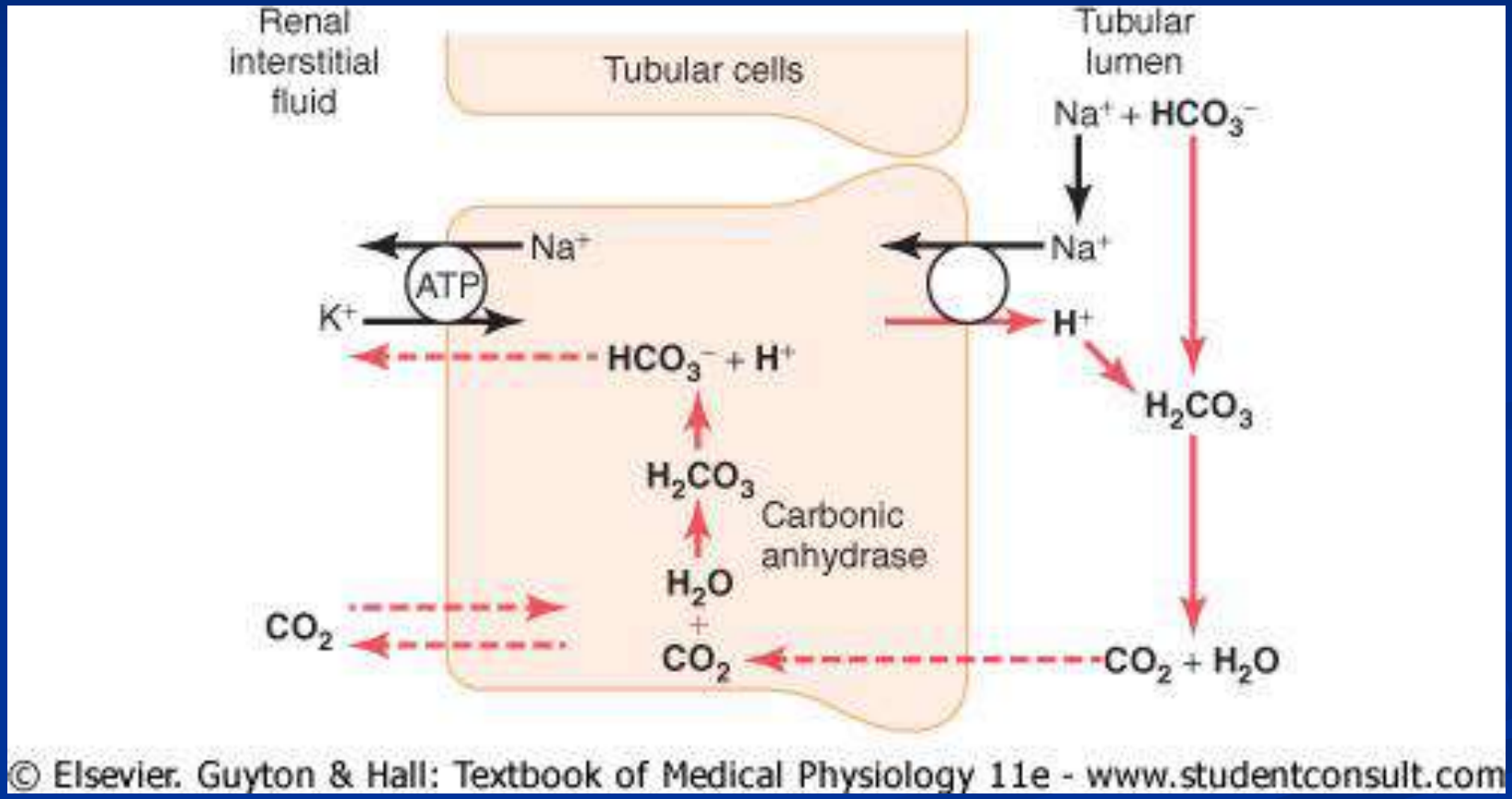
BICARBONATE SYSTEM

- The majority of the bicarbonate ions filtered into the glomerular filtrate are reabsorbed by H^+ ion secretion.

Reabsorption from PCT, Thick ALH and Early DCT

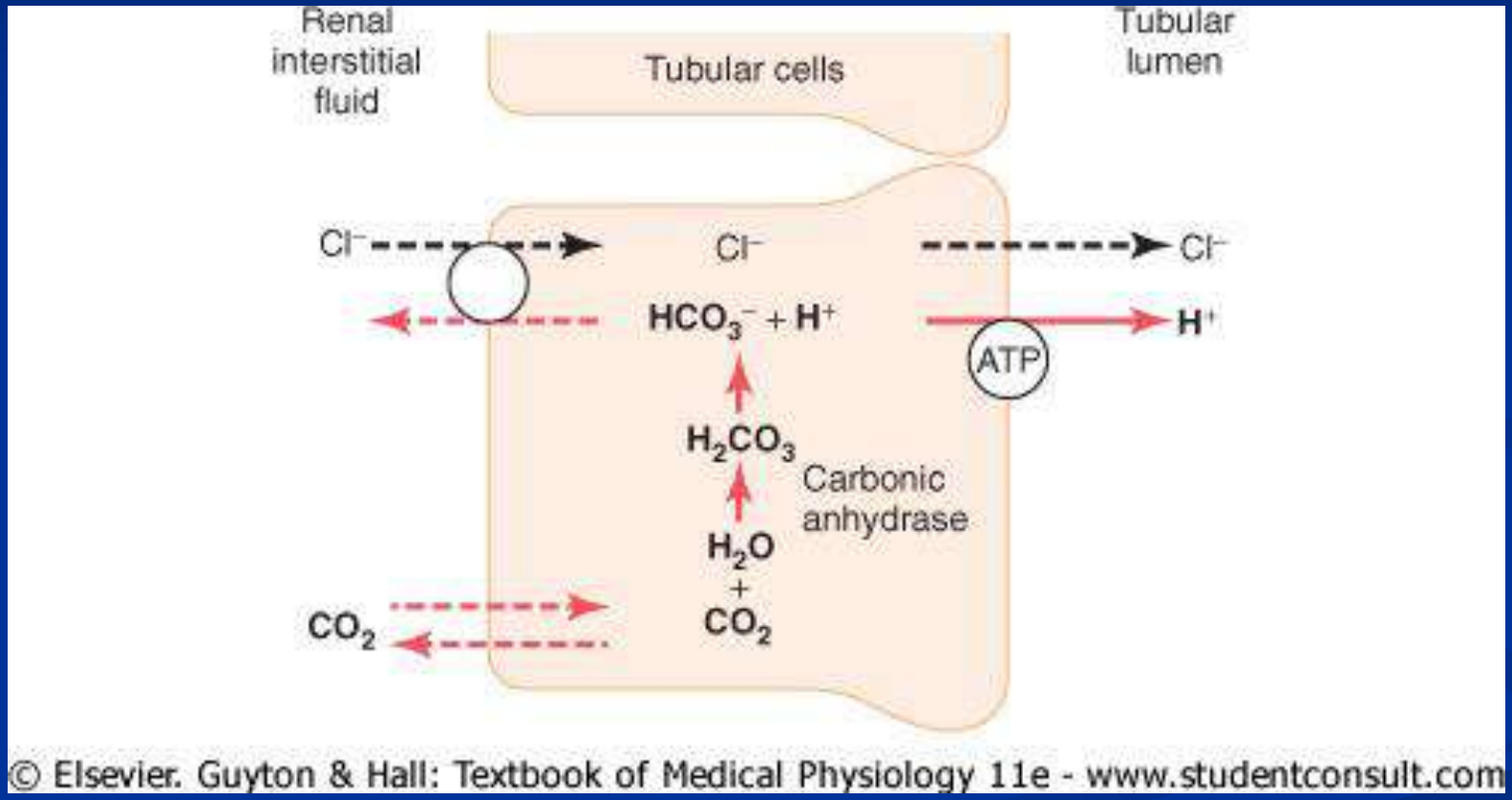
- Approximately 90% of the filtered HCO_3^- is reabsorbed from PCT.
- The secreted H^+ react with filtered HCO_3^- to form carbonic acid.
- H_2CO_3 is converted to H_2O and CO_2 by carbonic anhydrase enzyme present on luminal border of PCT.
- CO_2 and H_2O diffuse back into the PCT cells where they get combined again in the presence of intracellular CA to form H_2CO_3.

- H_2CO_3 dissociates to form H^+ and HCO_3^-.
- This HCO_3^- is newly synthesized and is reabsorbed across the basolateral membrane into the blood.
- The H^+ is secreted again into the tubular lumen by Na^+- H^+ Counter Transport.



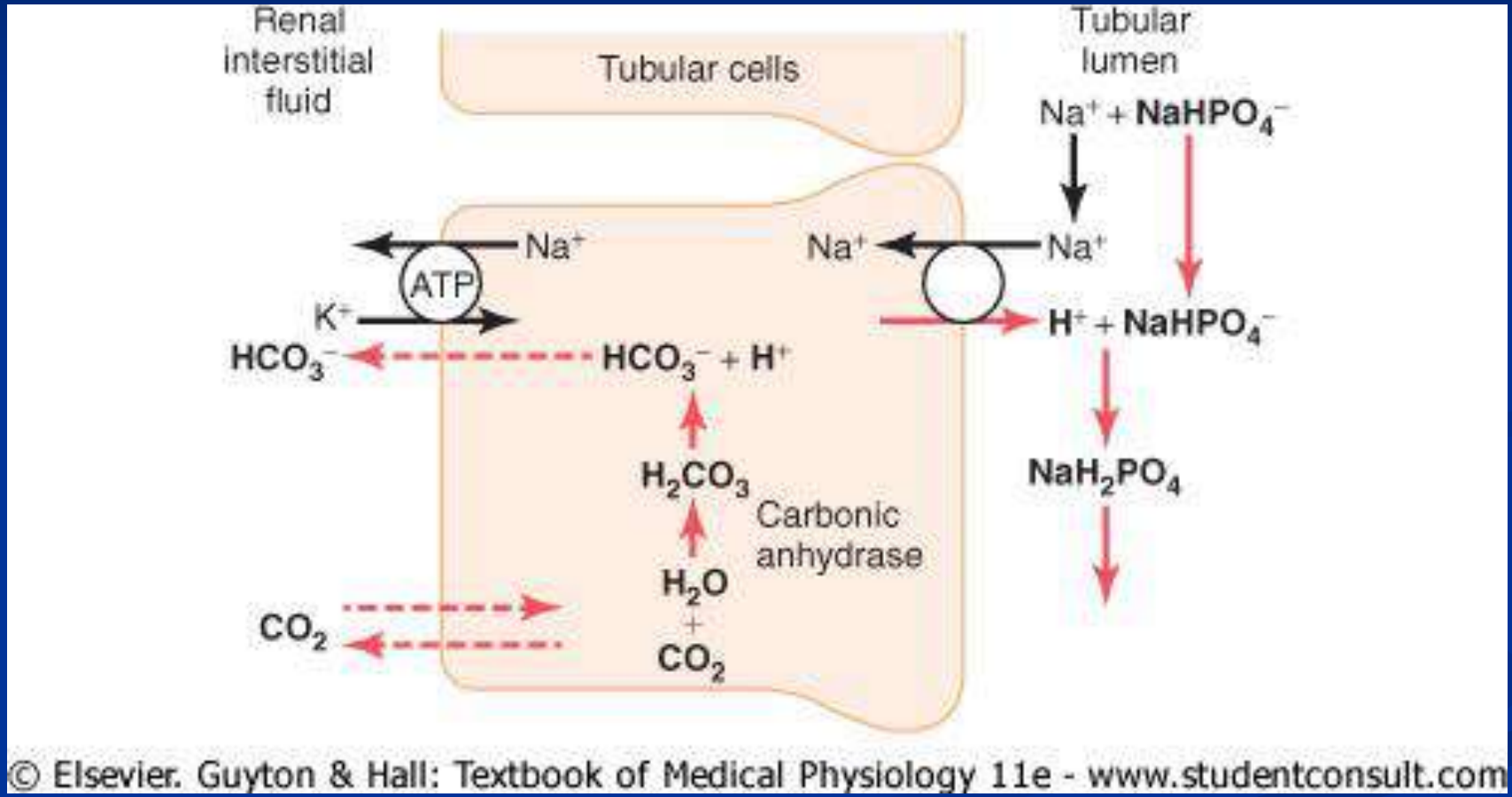
Reabsorption from Late DCT and CT

- The remaining 10% of the filtered HCO_3^- is reabsorbed by the DCT and CT.
- CO_2 inside the cell combines with H_2O to form H_2CO_3 which dissociates into H^+ and HCO_3^-.
- HCO_3^- is absorbed into the blood while H^+ ions are secreted into tubular fluid by Primary Active Transport.



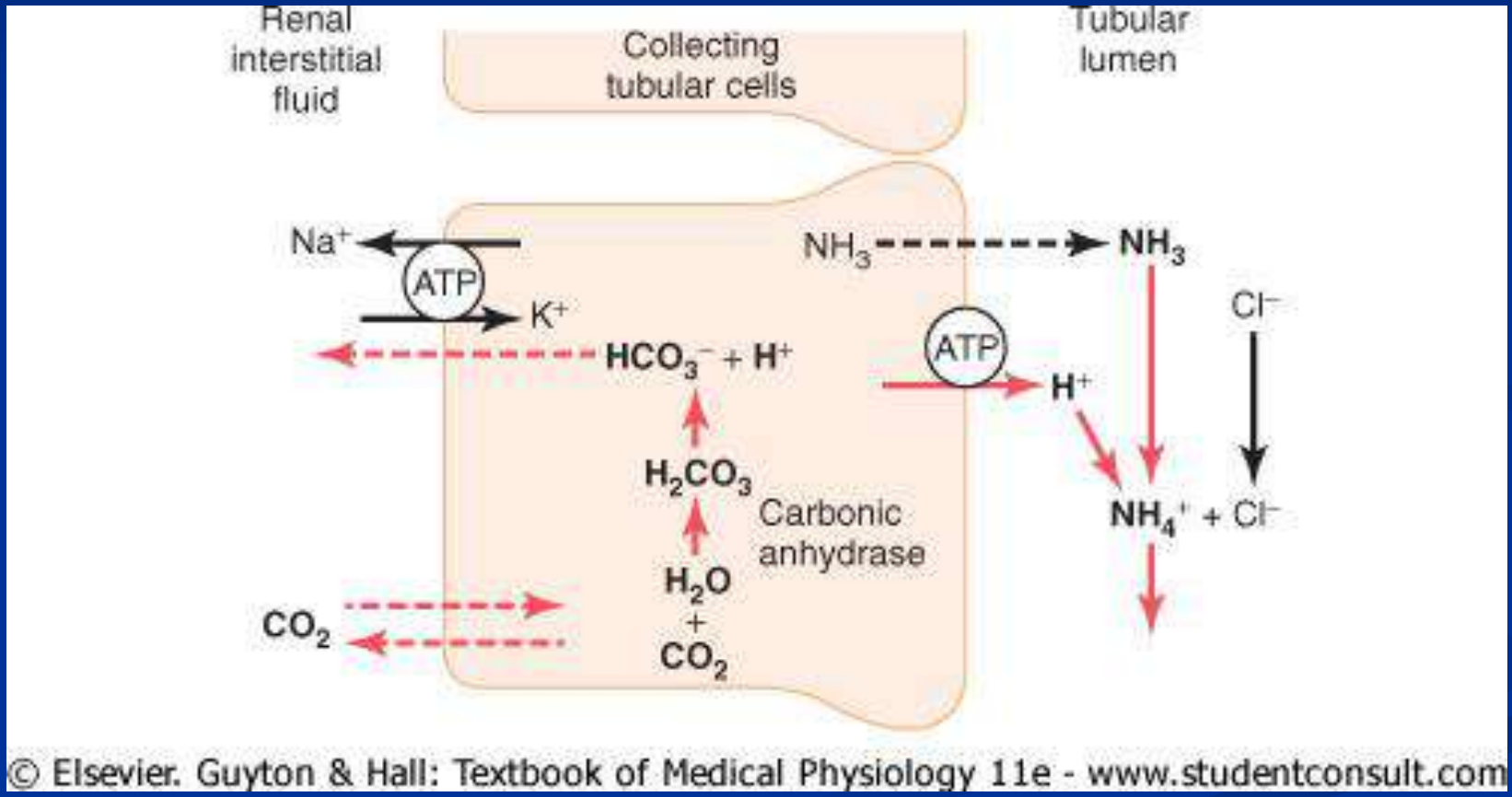
DIBASIC PHOSPHATE SYSTEM

- The phosphate buffer is composed of a mixture of $H_2PO_4^-$ and HPO_4^{--}.
- The H^+ ions secreted into the tubules react with Na_2HPO_4.
- This converts Na_2HPO_4 (Dibasic sodium phosphate) into NaH_2PO_4 (Sodium dihydrogen phosphate) which is excreted in the urine.



AMMONIA SYSTEM

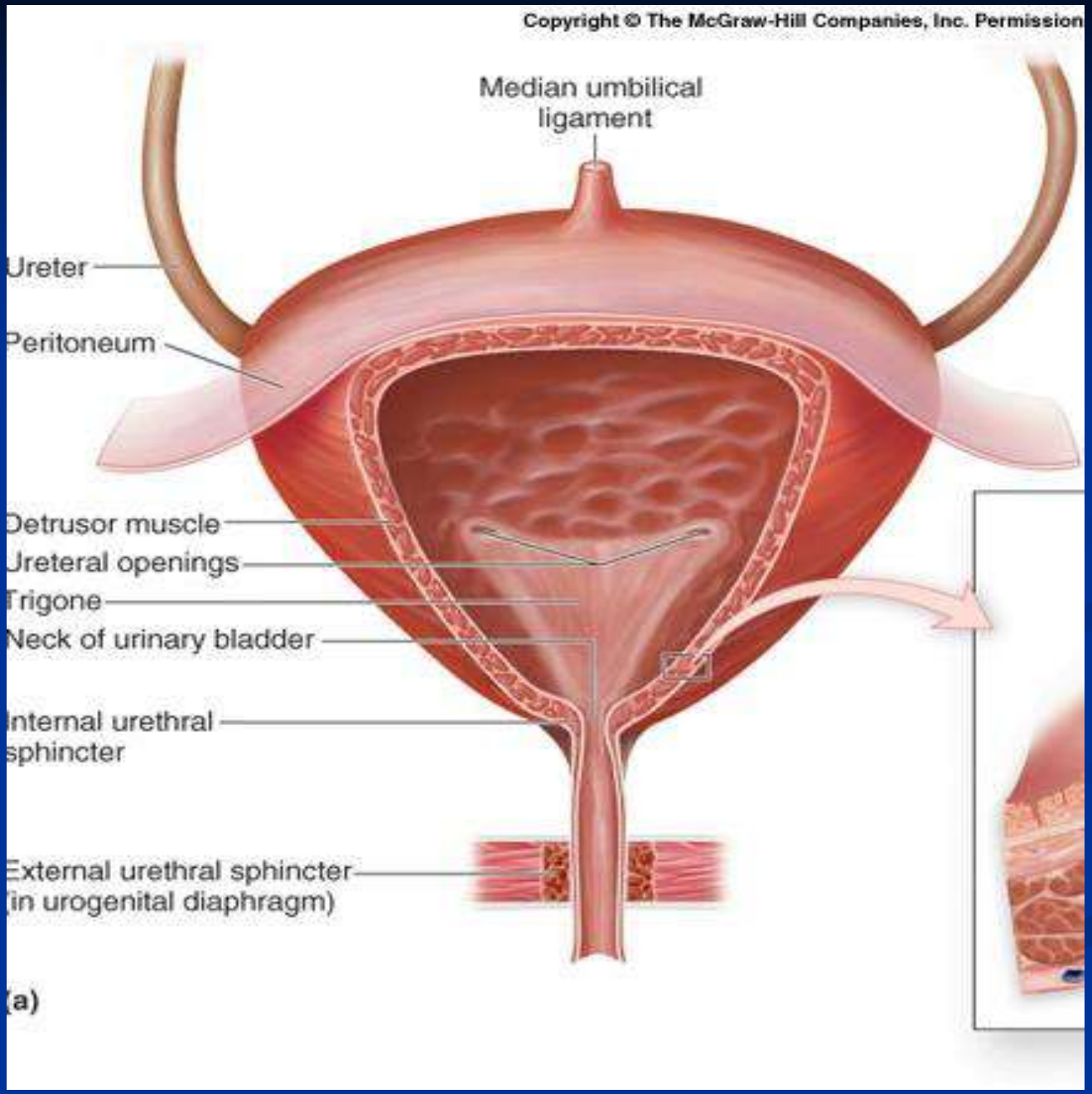
- This system is composed of ammonia (NH_3) and ammonium ion (NH_4^+).
- Ammonia is synthesized by epithelial cells of renal tubules.
- 60% of the ammonia is formed from Glutamine and the remaining 40% from other amino acids or amines.
- This ammonia diffuses into the tubules where it reacts with H^+ ions to form ammonium ions.
- The NH_4^+ ions are then excreted into the urine in combination with chloride ions and other tubular anions.



PHYSIOLOGY OF MICTURITION

MICTURITION

- Emptying of urinary bladder when it becomes filled.
- Physiological Anatomy of Urinary bladder
  - Body: contains Detrusor muscle
  - Trigone: Triangular area near the mouth of urinary bladder
  - Internal Sphincter: Maintain the tonic closure of urethral opening
  - Enternal Sphincter: It is voluntary sphincter and can be relaxed at the time of micturition
- The urine stored in the bladder remains unchanged in chemical composition.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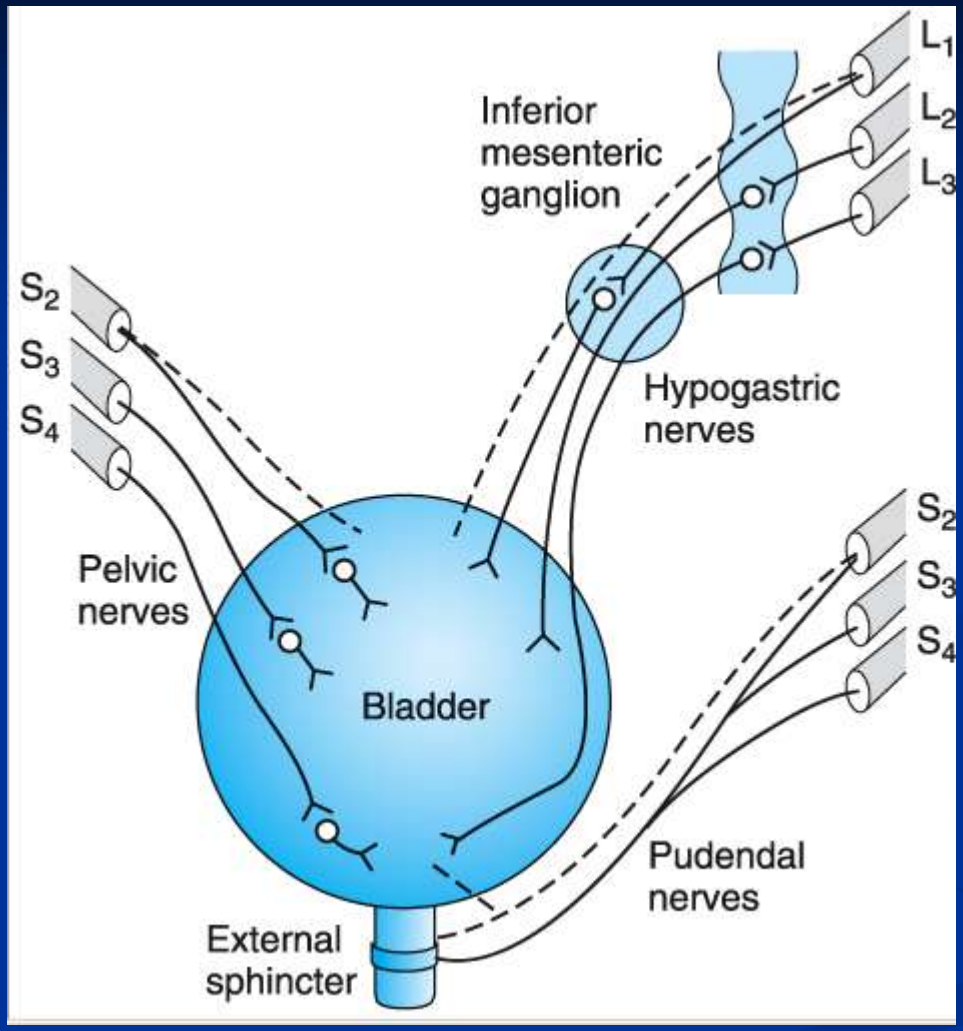
Median umbilical ligament
Ureter
Peritoneum
Detrusor muscle
Ureteral openings
Trigone
Neck of urinary bladder
Internal urethral sphincter
External urethral sphincter (in urogenital diaphragm)
(a)

NERVE SUPPLY OF URINARY BLADDER

- Parasympathetic:
  - From $S_{2,3,4}$ to body, trigone and internal sphincter.
  - It causes contraction of detrusor muscle, relaxation of internal sphincter resulting in emptying of bladder.



Innervation of the bladder. Dashed lines indicate sensory nerves. Parasympathetic innervation is shown at the left, sympathetic at the upper right, and somatic at the lower right.

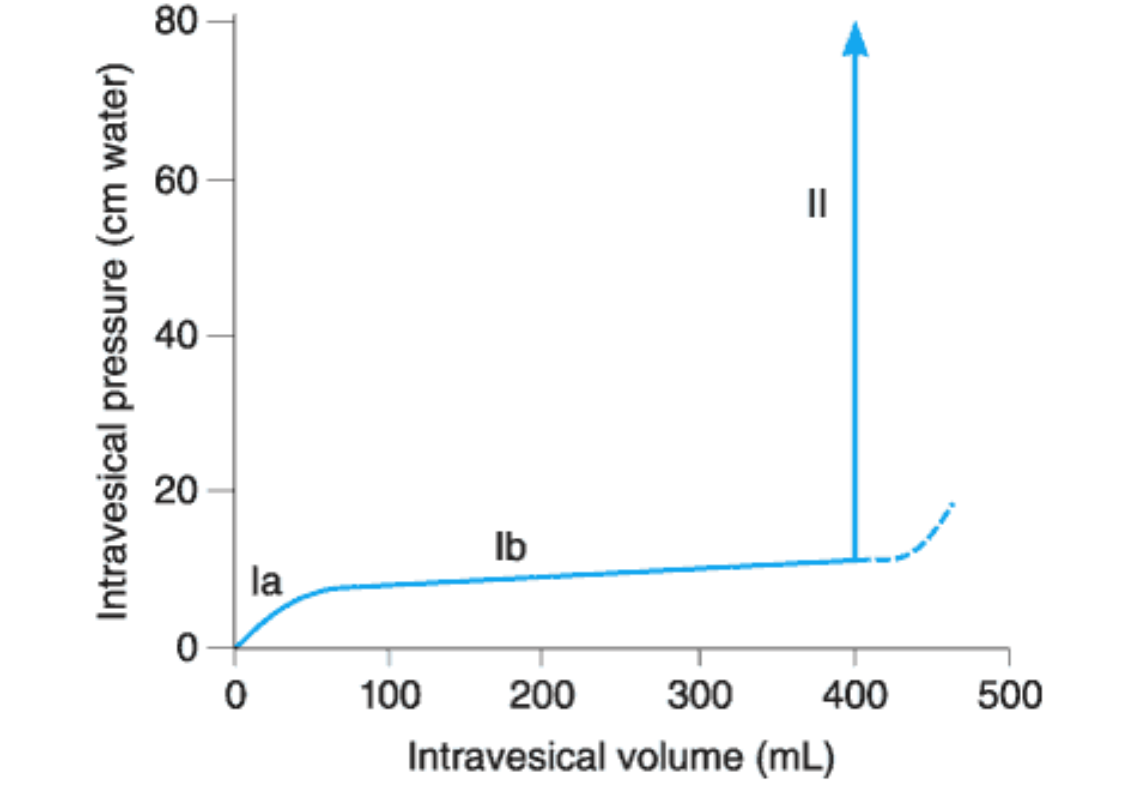
- Sympathetic:
  - From $L_{1,2}$ segments of spinal cord to the body, trigone and internal sphincter.
  - It causes relaxation of detrusor muscle, contraction of internal sphincter resulting in retention of urine.
- Somatic:
  - From $S_{2,3,4}$ via Pudendal Nerve to Posterior urethra and external sphincter.
  - It causes voluntary relaxation or contraction of external sphincter.

PLASTICITY

- The urinary bladder shows property of plasticity i.e. there is no constant relationship between fibre length and tension.

CYSTOMETROGRAM

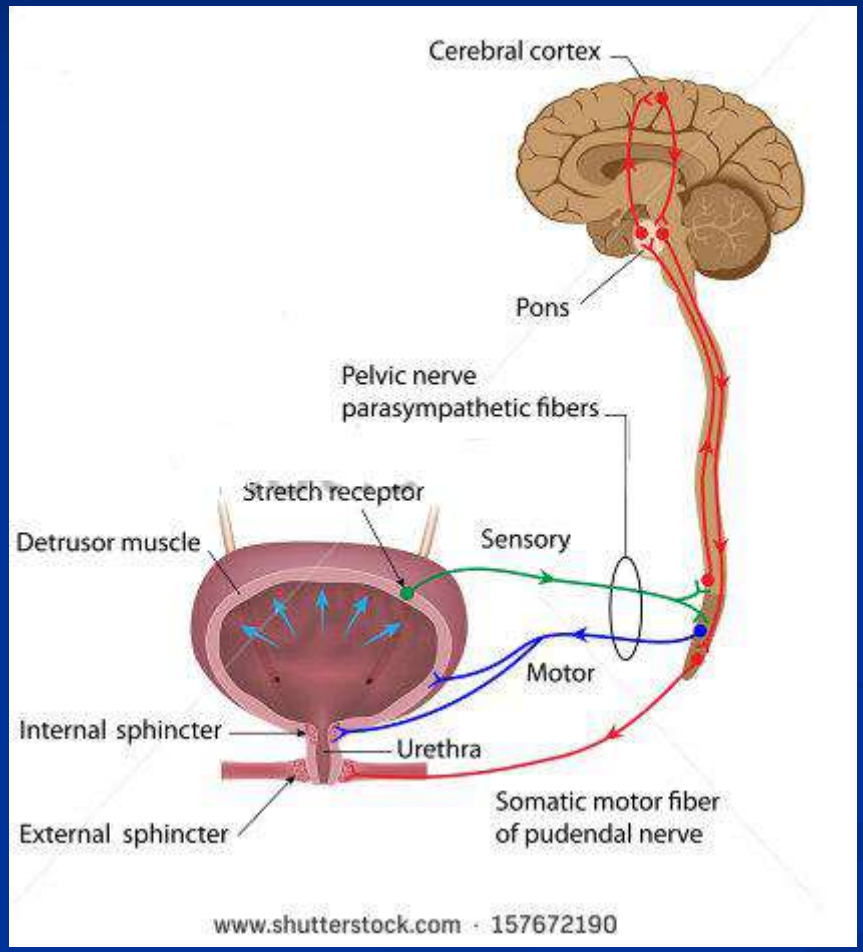
- It is the plot of intra-vesicle pressure against the volume of fluid in the urinary bladder.
- Upto 100ml of volume:
  - Slight rise in pressure.
- From 100-400 ml of volume:
  - The pressure remains constant due to intrinsic tone of urinary bladder.
- Above 400ml:
  - Sharp rise in pressure above 100cm H_2O due to micturition reflex.


80
60
40
20
0
Intravesical pressure (cm water)
0
100
200
300
400
500
Intravesical volume (mL)
Ia
Ib
II

MICTURITION REFLEX

- When the urinary bladder fills with urine, its wall stretches.
- The impulses are initiated by stretch receptors in the bladder wall and pass along sacral parasympathetic nerves to the S2,3,4 segments of spinal cord.
- Then via dorsal column to the brain sensory area, which gives desire to micturate.

MICTURITION REFLEX



- Impulses from motor area in the cerebral cortex pass down to sacral segments and the efferent fibres pass back to the urinary bladder via parasympathetic nerves.
- This causes contraction of detrusor muscle and relaxation of internal and external sphincters causing emptying of bladder.
- This constitutes Micturition Reflex.

Higher control of Micturition Reflex

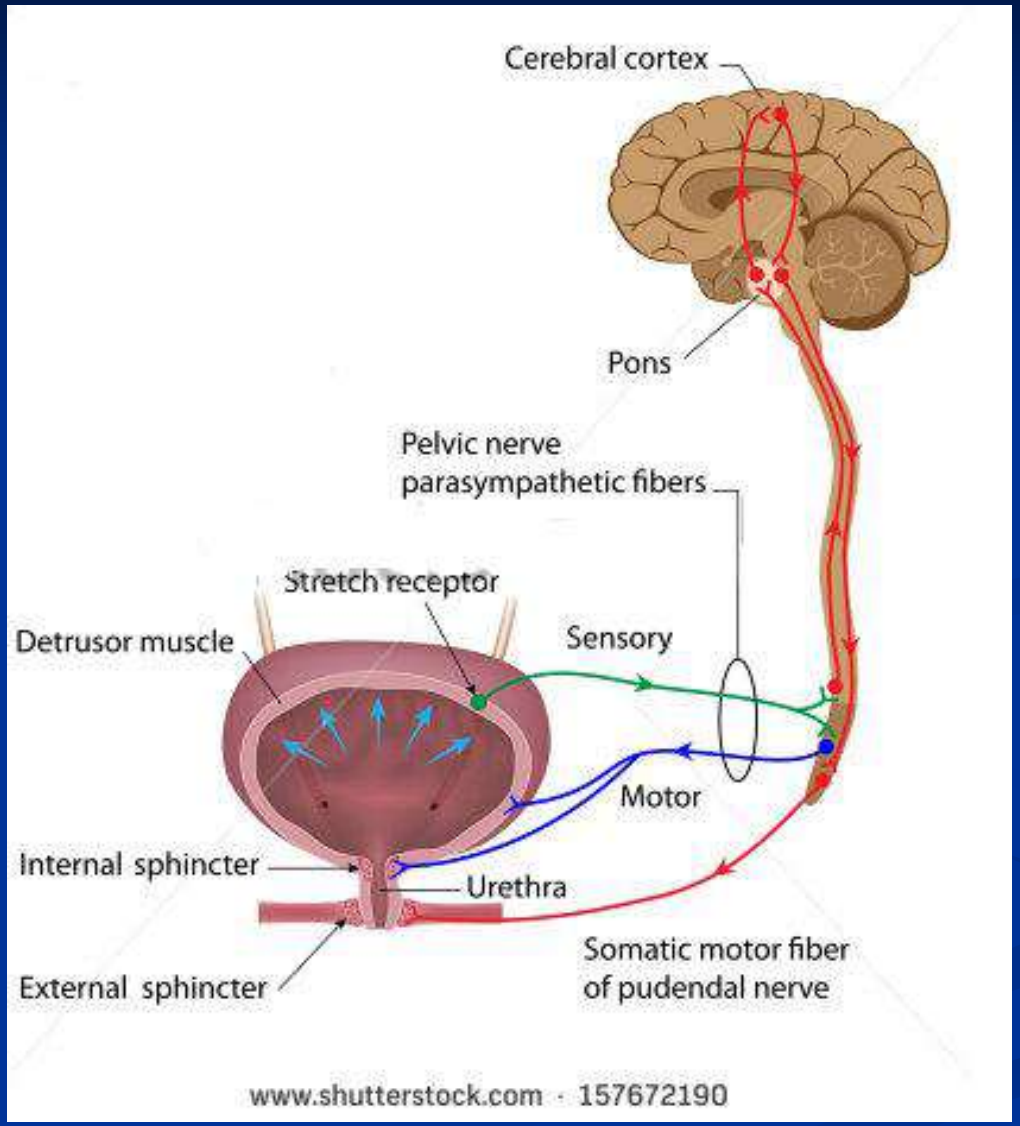
- Micturition reflex is a spinal reflex, facilitated or inhibited by higher brain centres.
- Facilitatory Area:
  - It is located in Pons and Posterior Hypothalamus. It lowers the threshold for micturition reflex.
- Inhibitory Area:
  - It is located in Midbrain.

- Accessory muscles involved in micturition are
  - Perineal muscles are relaxed
  - Abdominal wall muscle contract
  - Diaphragm descends
  - Breathing is held
- The above factors cause increase in intra abdominal pressure causing increase in intra-vesicle pressure.
- First urge to pass urine is felt when urinary bladder is filled with 150ml of urine. Above 400ml there is sense of discomfort.

APPLIED ASPECTS

1. DEAFFERENTATION:

- Caused by injury to afferent nerves.
- Features
  - Patient do not have sense of distension of bladder.
  - Voluntary micturition is possible.
  - If patient does not micturate, there occurs automatic emptying of bladder by contraction of detrusor muscle due to stretch: Automatic Bladder


Cerebral cortex
Pons
Pelvic nerve
parasympathetic fibers
Stretch receptor
Detrusor muscle
Sensory
Motor
Internal sphincter
Urethra
External sphincter
Somatic motor fiber
of pudendal nerve
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2. DENERVATION:

- Caused by injury to both Afferent and Efferent nerves.
- Features:
  - Loss of voluntary micturition
  - Urinary bladder becomes distended: Isolated Bladder/ Decentralized Bladder.

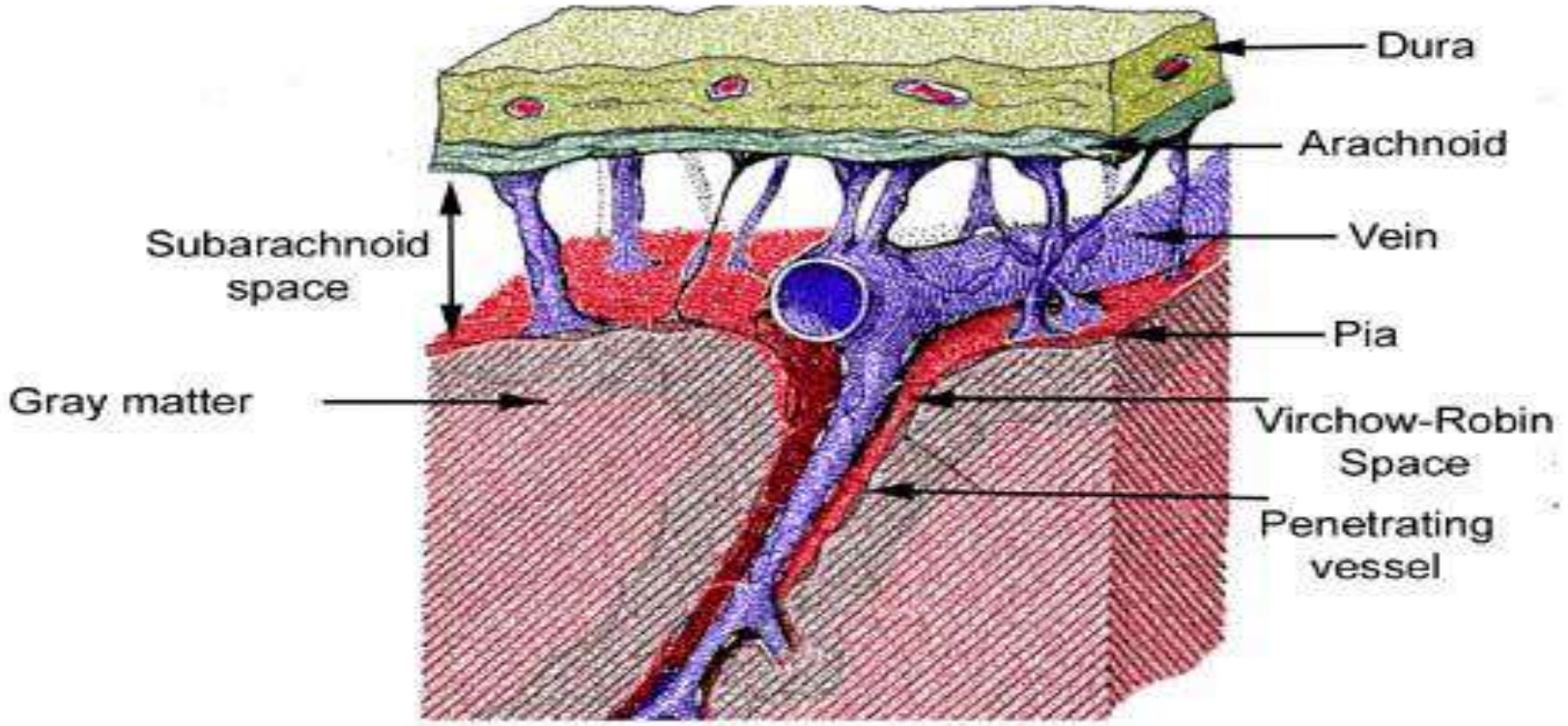
3. EFFECT OF SECTION OF FACILITATORY AND INHIBITORY PATHWAYS:

- Features:
  - Loss of Voluntary micturition
  - Urinary bladder becomes distended causing Retention of Urine.
  - Overstretching of urinary bladder causes Cystitis.
  - Repeated infections of urinary bladder cause hypertrophy of its wall. As a result, bladder shrinks and contracts: Spastic or Neurogenic Bladder.

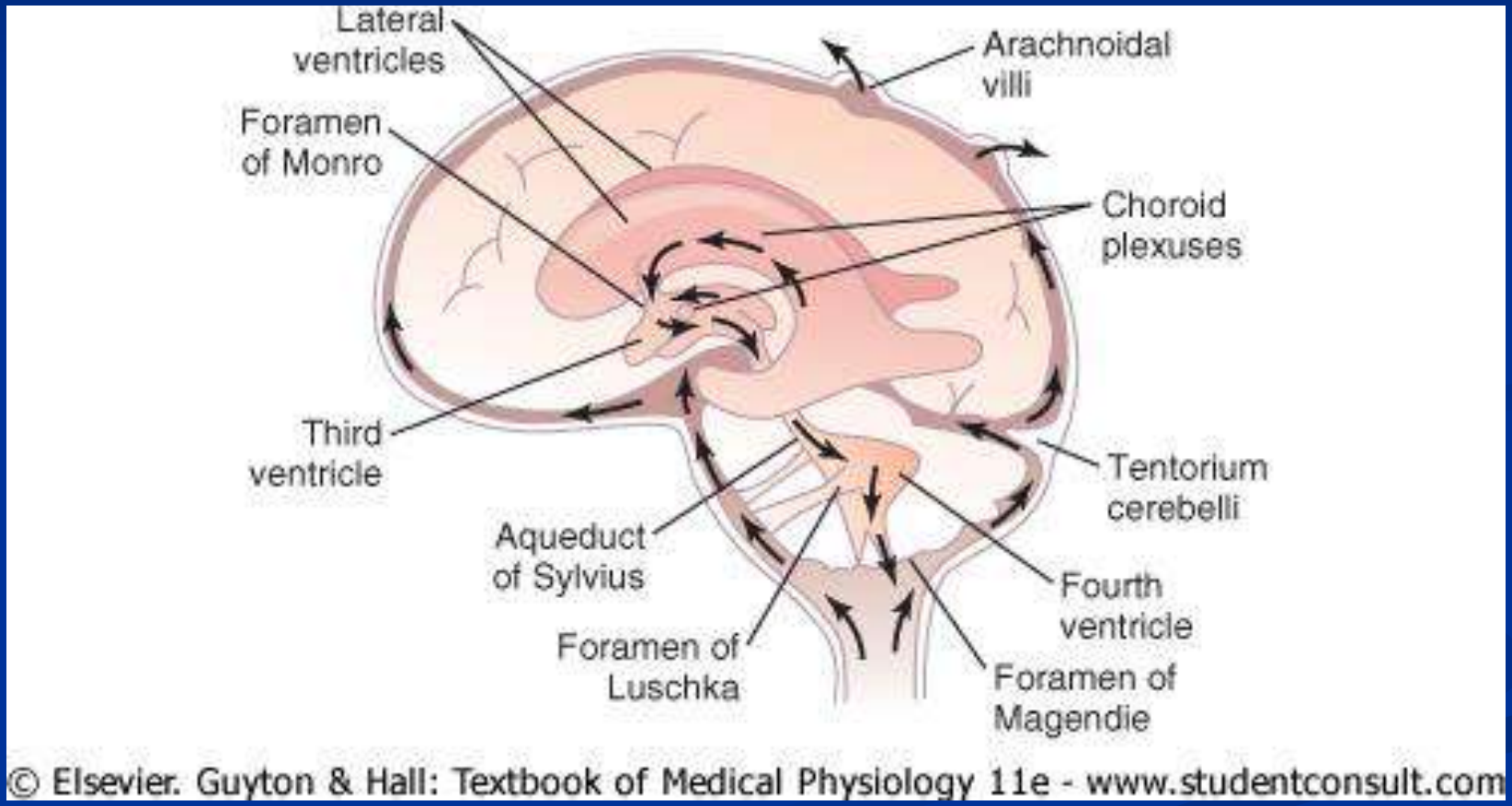
THE CEREBROSPINAL FLUID (CSF)

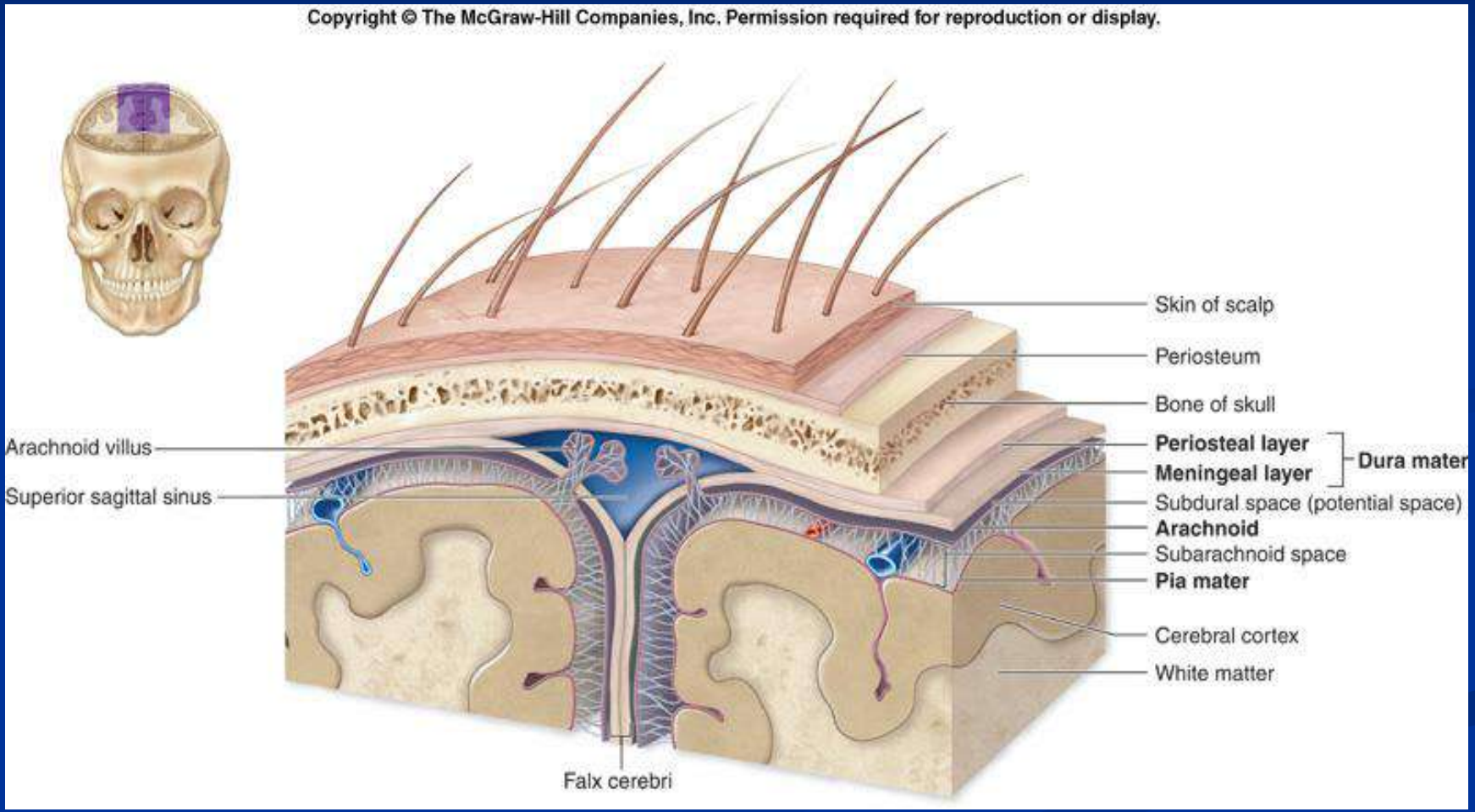
Physiological Anatomy

- Meninges of CNS:
  - Dura
  - Arachnoid
  - Pia
- Subarachnoid space
  - Contains CSF
- Perivascular spaces:
  - Pia is loosely adherent to blood vessels entering the brain
  - Modified lymphatic system for the brain


Dura
Arachnoid
Subarachnoid space
Vein
Pia
Gray matter
Virchow-Robin Space
Penetrating vessel

- Ventricles
  - Lateral ventricle: cerebral hemisphere
  - III ventricle: midbrain
  - IV ventricle: between pons and medulla
- Foramen of Monro
- Aqueduct of Sylvius
- Ependyma: Epithelial lining of ventricles
- Choroid Plexus:
  - Blood vessels that enter the ventricles
  - Lined by pia
  - Forms CSF
- Arachnoid Villi:
  - Projection of Arachnoid Trabeculae into Venous Sinuses
  - Absorbs CSF





Composition of CSF

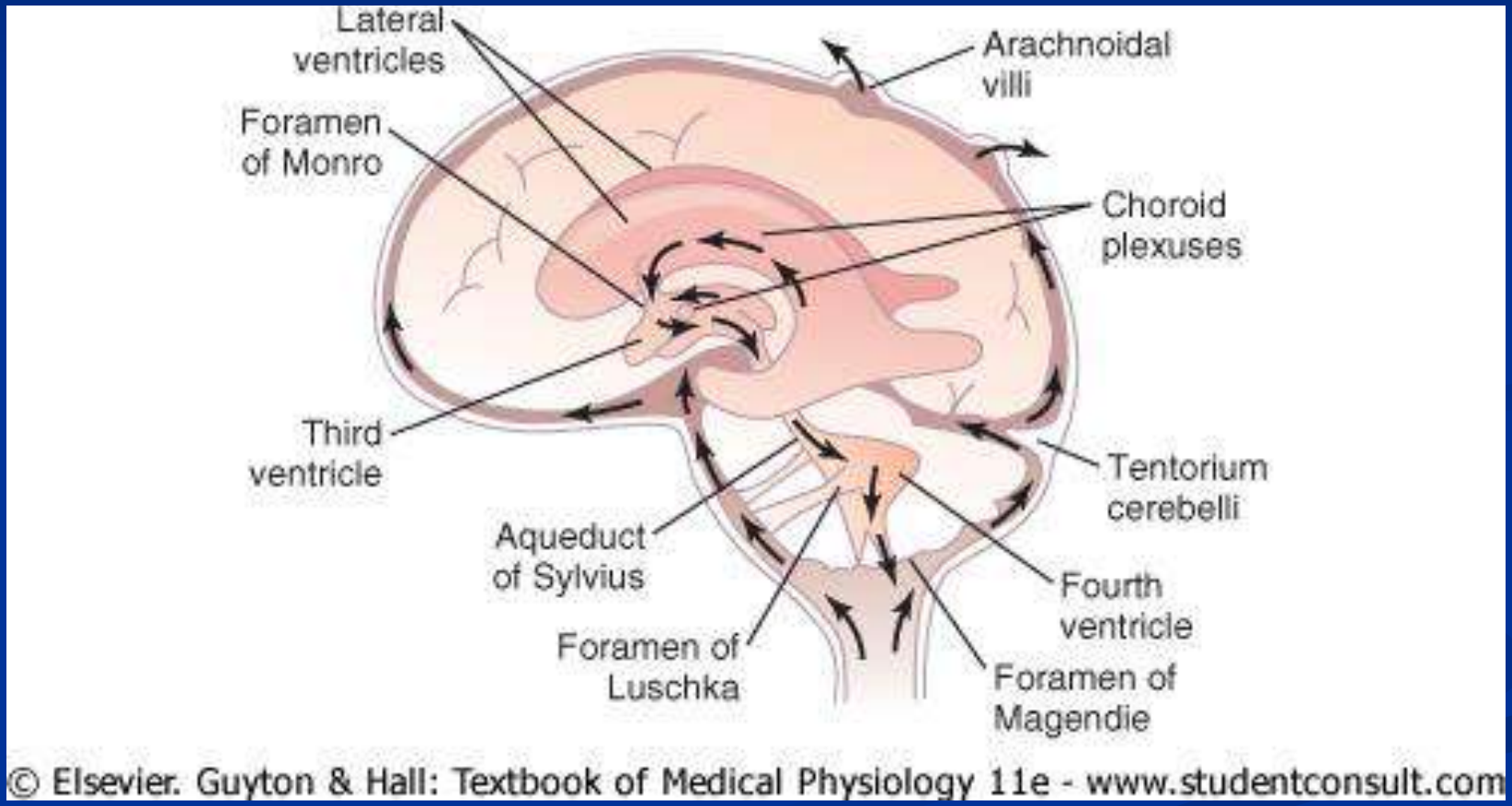
- Colourless, clear, alkaline fluid
- Specific Gravity =1005-1008
- Proteins = 20-30 mg%
- Glucose = 50 mg%
- Lymphocytes = 0-5/cu mm
- Volume = 130-150 ml
- Pressure = 100-200 mm H_2O (130 mm H_2O)

Formation and Absorption

- Formation
  1. Choroid plexuses in the ventricles (50%)
  2. Blood vessels of meninges and ependymal lining of ventricles (40%)
  3. Blood vessels of brain and spinal cord (10%)
- Absorption
  1. 80% by Arachnoid Villi into venous sinuses
  2. 20% by passing through sheaths of cranial nerves and into Perivascular Spaces

Route of Absorption

- Lateral ventricle
- Foramen of Monro
- III ventricle
- Aqueduct of Sylvius
- IV ventricle
- Foramen of Magendie and Luschka
- Subarachnoid Space
- Subarachnoid Villi
- Cerebral Venous Sinuses

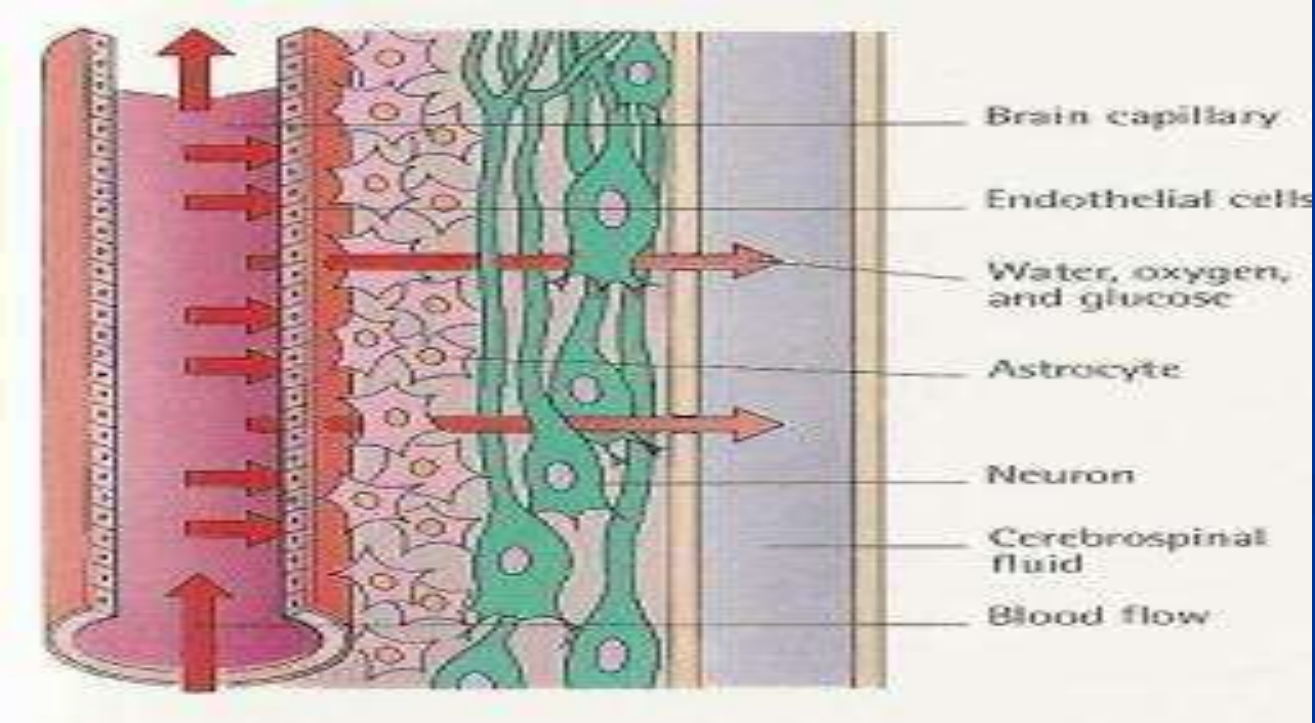


Functions of CSF

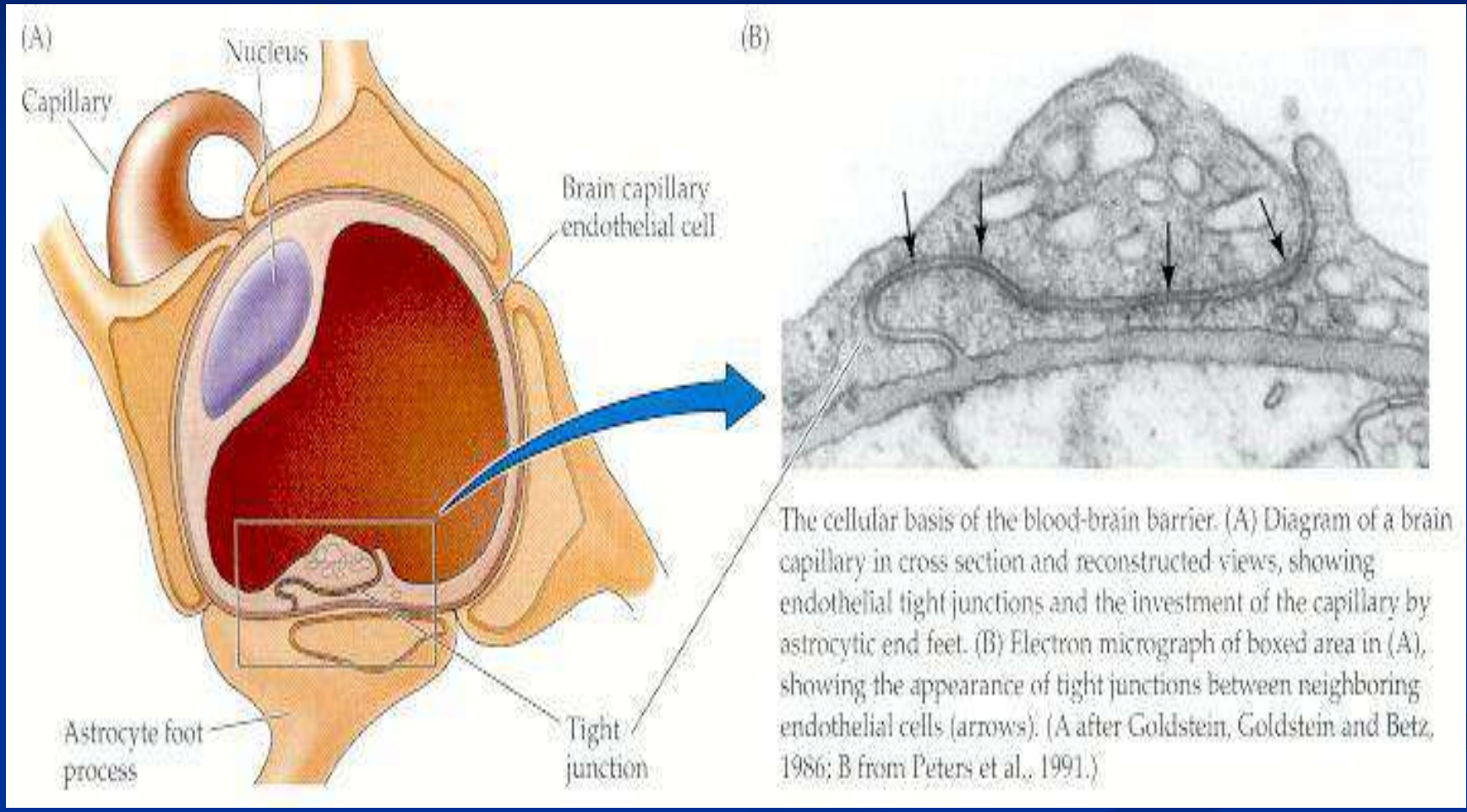
- Acts as fluid buffer: provides optimum environment to neurons
- Protective Function
- Keeps total volume of cranium constant
- Transfers waste products of brain to blood
- Supplies nutrients to the brain

Blood Brain Barrier

- Barrier between blood and the brain tissue
- Exists at 2 places
  - Between CSF and choroid plexus – Blood CSF barrier
  - Between CSF and brain capillaries – True Blood Brain barrier


Brain capillary
Endothelial cells
Water, oxygen, and glucose
Astrocyte
Neuron
Cerebrospinal fluid
Blood flow

- The selective permeability of Blood Brain Barrier is because:
  - The endothelial cells are joined by Tight junctions
  - The endothelial cells are covered by foot processes of Astrocytes
- The Blood Brain Barrier is
  - Highly permeable to water, O_2,CO_2
  - Slightly permeable to electrolytes – Na, K, Cl, HCO_3, glucose
  - Impermeable to Proteins, urea, catecholamines and bile salts
- Blood Brain Barrier is underdeveloped in neonates and infants
  - Kernicterus



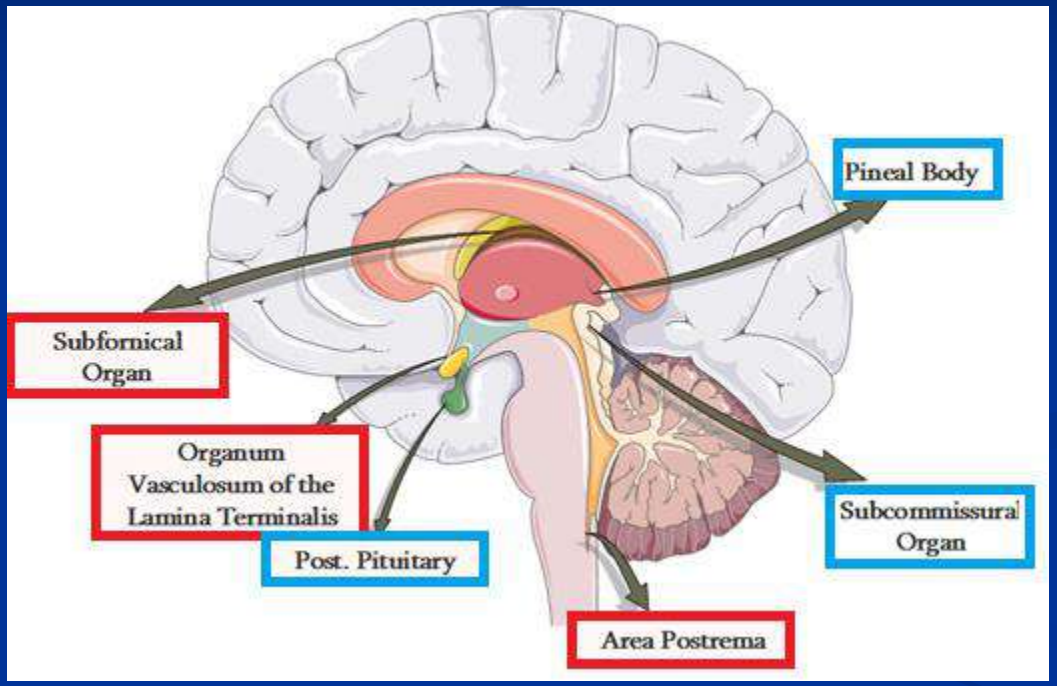
The cellular basis of the blood-brain barrier. (A) Diagram of a brain capillary in cross section and reconstructed views, showing endothelial tight junctions and the investment of the capillary by astrocytic end feet. (B) Electron micrograph of boxed area in (A), showing the appearance of tight junctions between neighboring endothelial cells (arrows). (A after Goldstein, Goldstein and Betz, 1986; B from Peters et al., 1991.)

Functions of Blood Brain Barrier

- Prevents ionic changes in blood to effect cortical neurons
- Protects the brain from endogenous and exogenous toxins
- Prevents the escape of neurotransmitters into the circulation

Circumventricular Organs

- Posterior Pituitary:
  - Releases Oxytocin and ADH
- The Area Postrema:
  - Chemoreceptor Triggor Zone
- Organum Vasculosum of the Lamina Terminalis (OVLT):
  - Site of osmoreceptors controlling ADH secretion
- The Subfornical Organ:
  - Angiotensin II acts on this area to effect water intake


Pineal Body
Subfornical Organ
Organum Vasculosum of the Lamina Terminalis
Post. Pituitary
Subcommissural Organ
Area Postrema

BASAL GANGLIA

PHYSIOLOGICAL ANATOMY

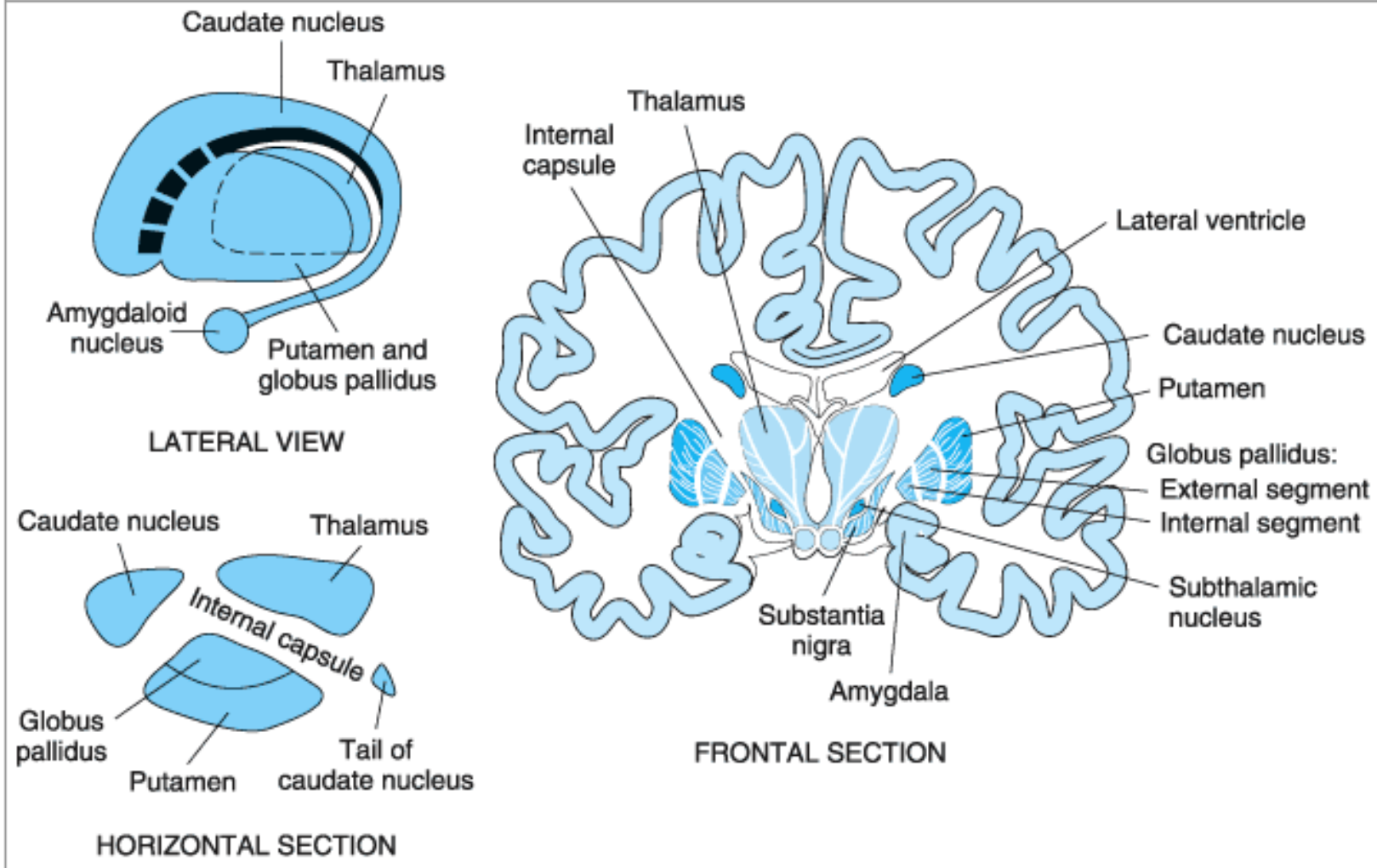
- Group of nuclei in the forebrain and upper part of the brain stem having motor functions

The basal ganglia includes

1. Caudate nucleus
2. Putamen
3. Globus pallidus or Pallidium or Paleostriatum
4. Sub thalamic nucleus
5. Substantia nigra

Caudate nucleus

- It possesses a head and a tail (terminating in the amygdaloid nucleus).
- Corpus Striatum or Neostriatum:
  - The caudate nucleus and putamen



The basal ganglia.

Putamen and Globus pallidus

- Together called as Lenticular Nucleus.
- Globus pallidus is also called Paleostriatum.
- Globus pallidus is subdivided into External and Internal segments by a medial medullary lamina.

Substantia nigra

- Subdivided into two parts:
  - Pars compacta: Dorsomedial
  - Pars reticulata: Ventrolateral

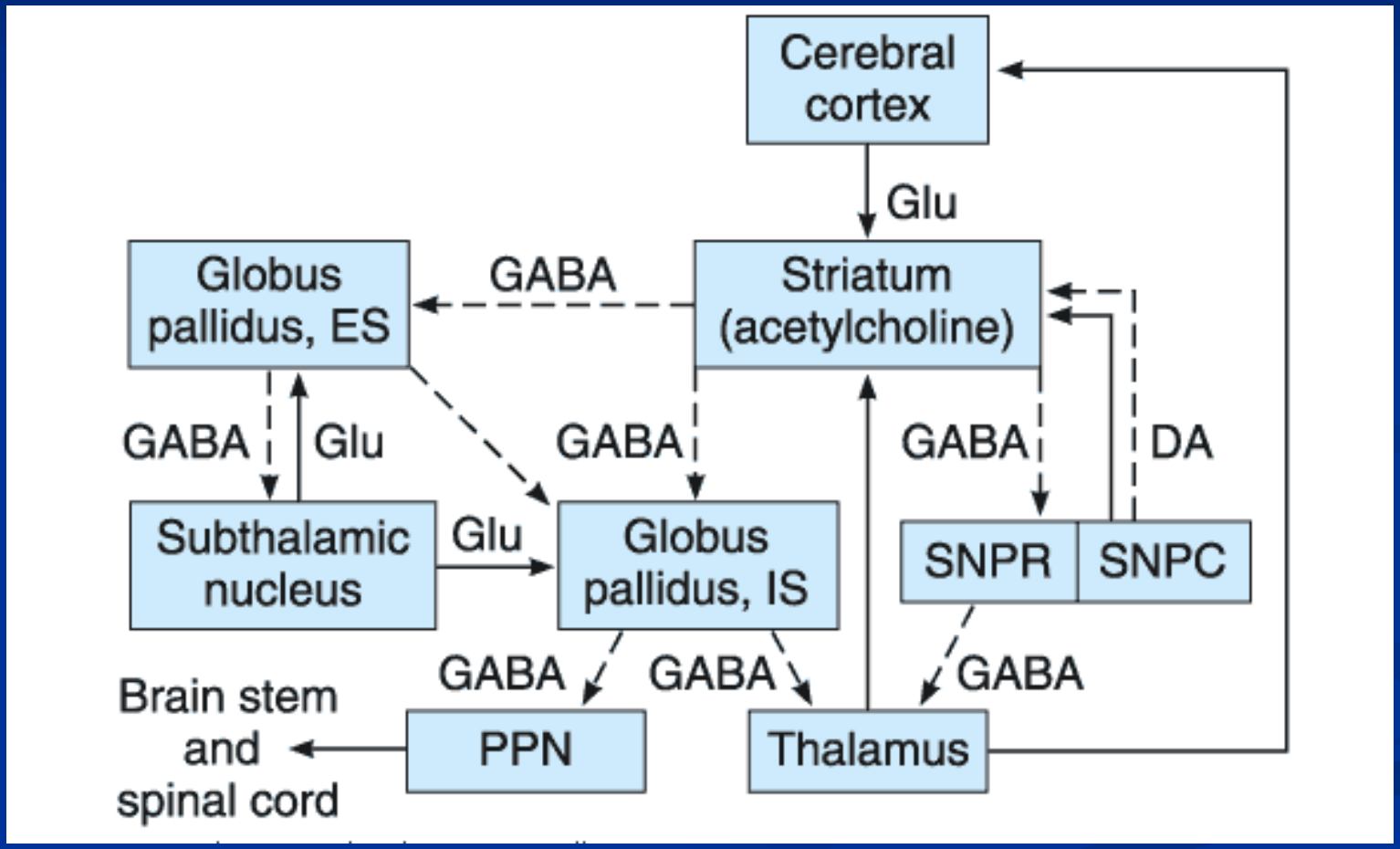
CONNECTIONS OF THE BASAL GANGLIA

- Afferent connections
- Internuclear connections
- Efferent connections

AFFERENT CONNECTIONS

- The main afferent connections to the basal ganglia terminate in the neostriatum and are excitatory (cholinergic neurons).
- They include:

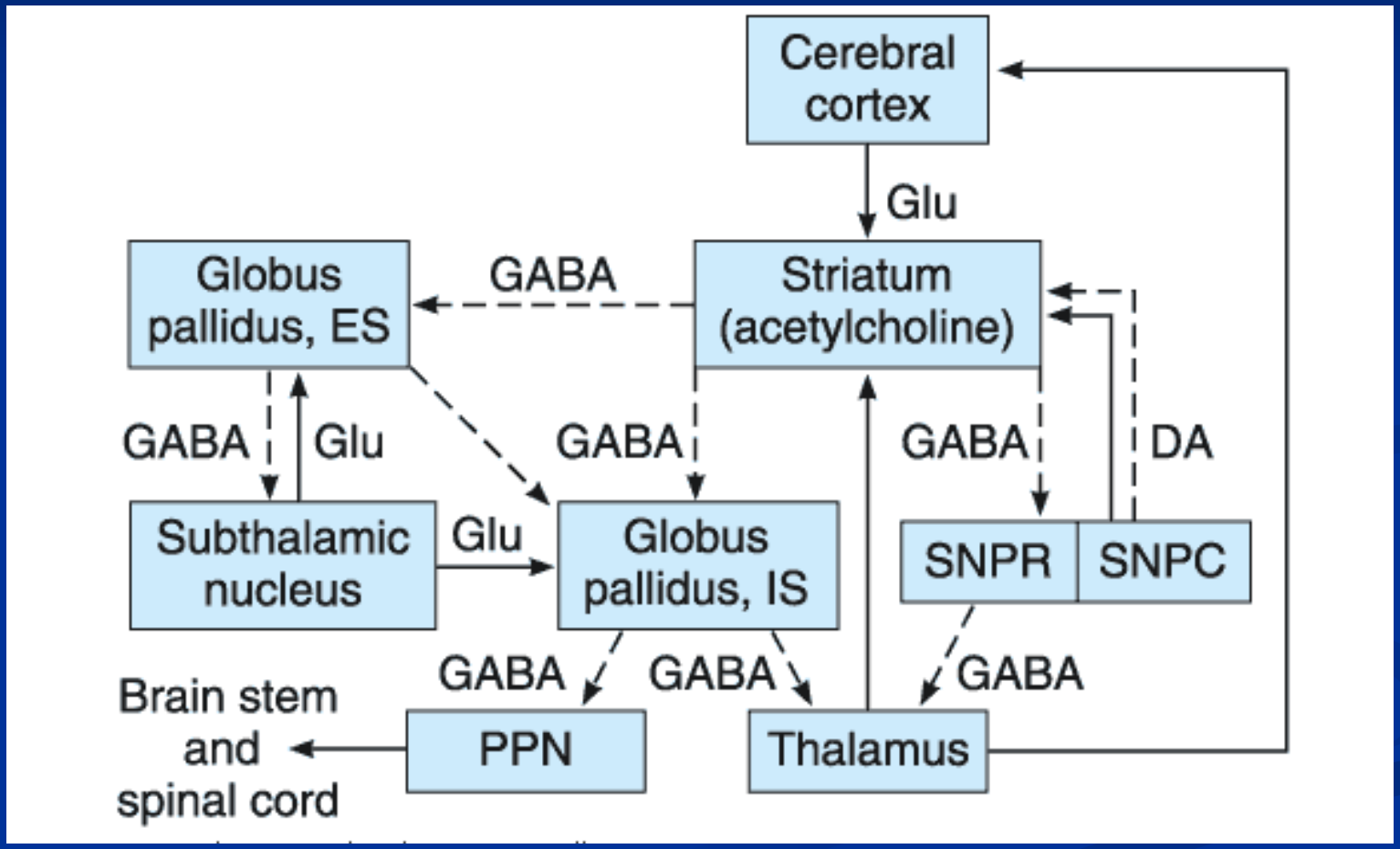
1. Corticostriate projection
   - From all four lobes of the cerebral cortex to the neostriatum.
2. Thalamostriate fibers
   - From the nuclei of the thalamus to the neostriatum.


Cerebral cortex
Glu
Globus pallidus, ES
GABA
Striatum (acetylcholine)
GABA
Glu
GABA
GABA
DA
Subthalamic nucleus
Glu
Globus pallidus, IS
SNPR
SNPC
GABA
GABA
GABA
Brain stem and spinal cord
PPN
Thalamus

INTERNUCLEAR CONNECTIONS

1. Dopaminergic nigrostriatal tract
   - From the Pars compacta of substantia nigra to the neostriatum.
   - Inhibitory dopaminergic fibres
2. GABA-ergic inhibitory projections
   i. The neostriatum projects to
      - pars reticulata of the substantia nigra
      - internal and external segments of the globus pallidus.

   ii. The external segment of the globus pallidus projects to the subthalamic nucleus.
3. Glutamic acid secreting excitatory neurons
   - From the subthalamic nucleus to
     i. both internal and external segments of the globus pallidus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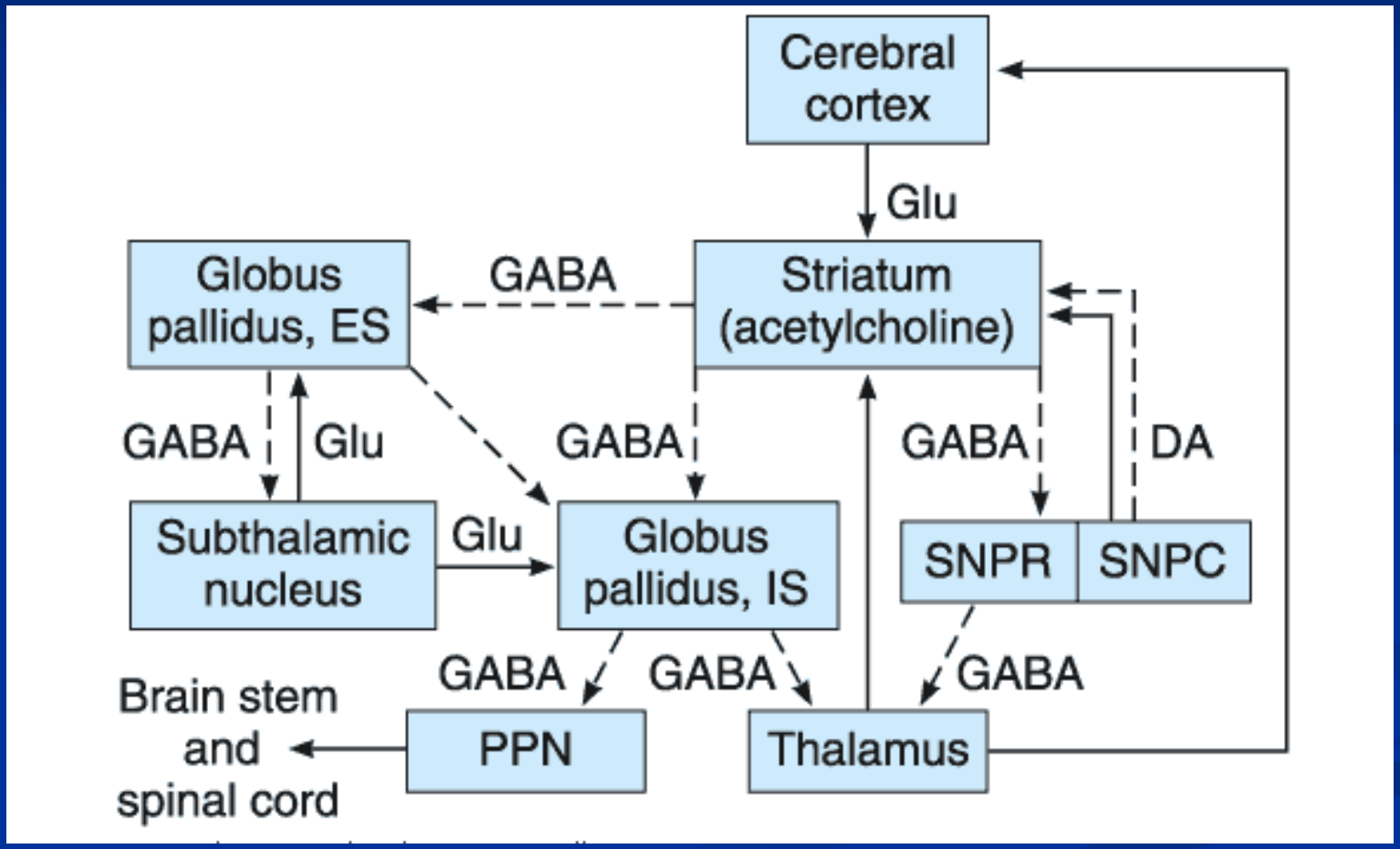
GABA
GABA
GABA
Brain stem and spinal cord
PPN
Thalamus

EFFERENT CONNECTIONS

1. From the internal segment of the globus pallidus
   - To the ventral lateral, ventral anterior and centromedian nuclei of the thalamus.
2. Pars reticulata of the substantia nigra
   - Projects to the ventrolateral and ventroanterior nuclei of the thalamus.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SNPR
SNPC
GABA
GABA
GABA
Brain stem and spinal cord
PPN
Thalamus

FUNCTIONS OF THE BASAL GANGLIA

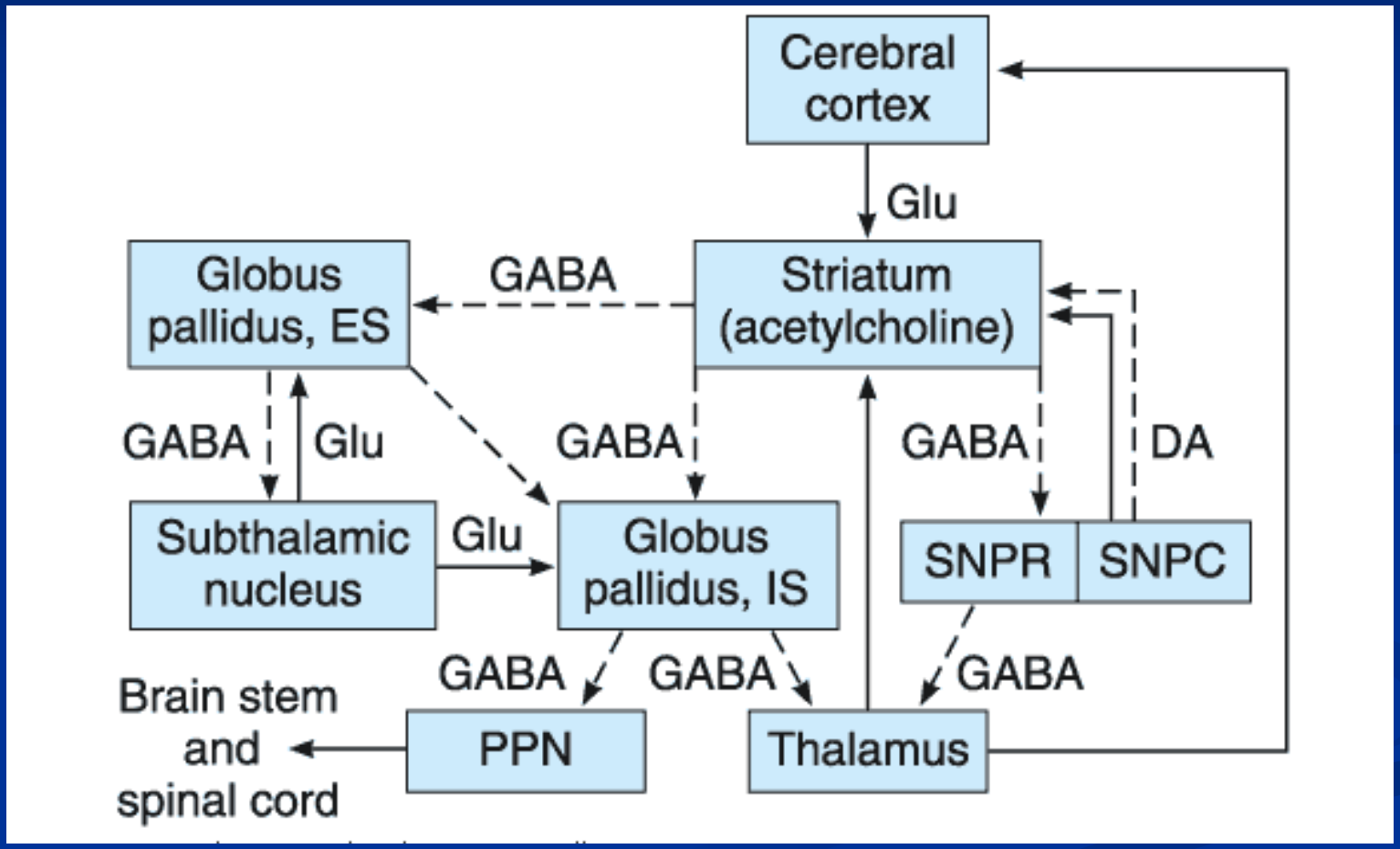
1. Planning and Programming of movements
   - Neurons in the basal ganglia discharge before movements begin.
2. Inhibits the stretch reflex and muscle tone
   - By stimulation of inhibitory motor cortex through thalamocortical feedback pathway

3. Subconscious gross movements
   - Regulated by neostriatum
4. Cognitive processes
   - By the caudate nucleus because of its interconnections with the prefrontal lobe.
5. Coordination of skilled movements
   - Substantia nigra is centre for coordination
6. Control of normal automatic and associated movements
   - Such as swinging of arms during walking.

DISEASES OF THE BASAL GANGLIA

PARKINSON'S DISEASE (PARALYSIS AGITANS)

- Characterized by rigidity, tremors and hypokinesia
- Occurs in late middle age due to degeneration of dopaminergic nigrostriatal tract.
- The concentration of dopamine in the nigrostriatal system is reduced.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SNPR
SNPC
GABA
GABA
GABA
Brain stem and spinal cord
PPN
Thalamus

Characteristic features

Rigidity

- Affects mainly large proximal group of muscles of the limbs
- The commonly affected muscles are the biceps, knee flexors and sternomastoids.
- Posture is that of flexion attitude. The back is flexed, the arms adducted and flexed and the knees are bent.

Parkinson's Posture

Tremor

- Rhythmic and alternate contraction of antagonist and agonist muscles
  - Pill-rolling movements i.e. rhythmic contraction of thumb over first two fingers.
- Common sites: fingers, hands, lips or tongue
- Resting (static) tremor
  - Present at rest but disappears during activity

Akinesia or Hypokinesia

- Weakness of movements which leads to:
  i. Difficulty in initiating voluntary movement
  ii. Slow and monotonous speech
  iii. The face becomes mask-like
  iv. Loss of normal subconscious associated movements
  v. Festinant type gait
    - The patient is bent forward and walks quickly with short steps
  vi. Tendon jerks become sluggish