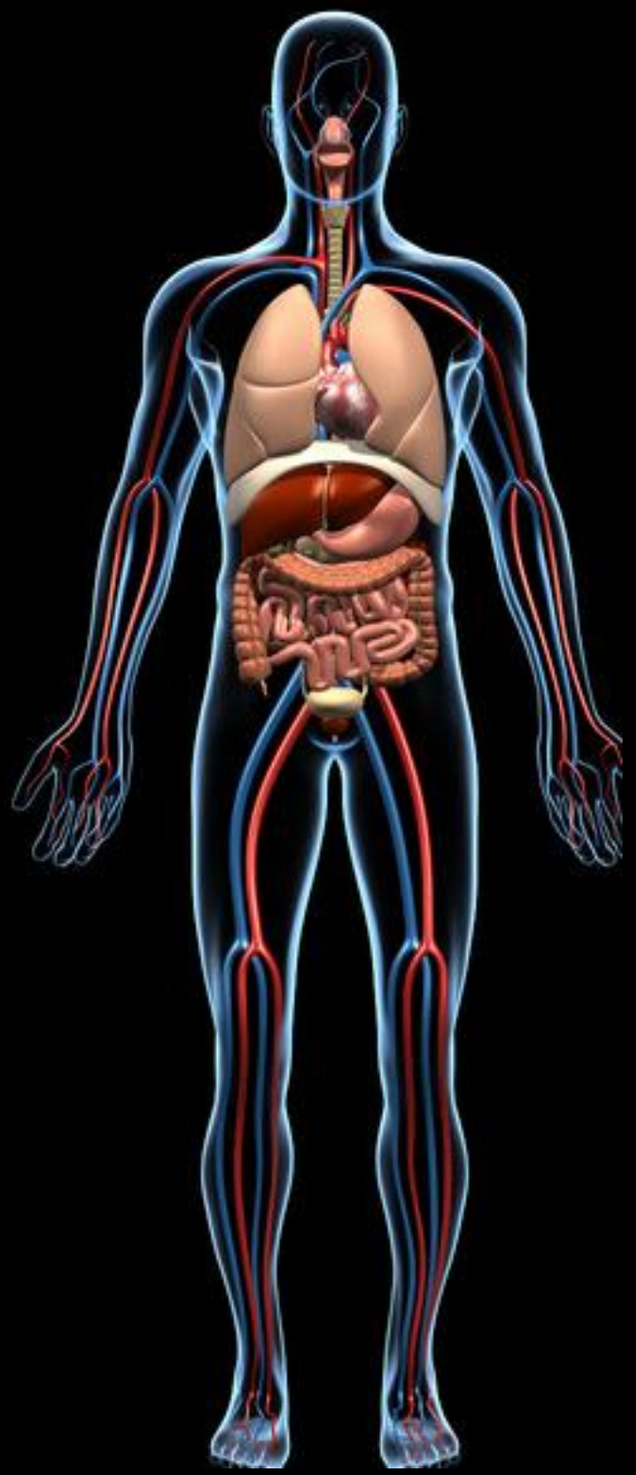
Αναισθησιολογία
Ακαδ. έτος 2018-19

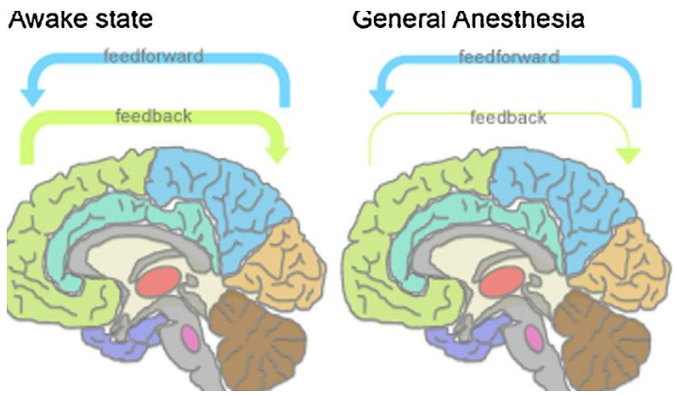


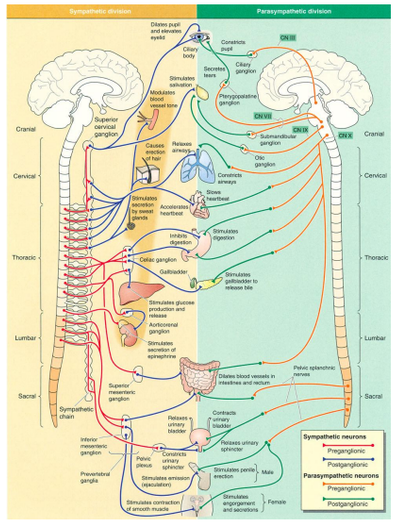
ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

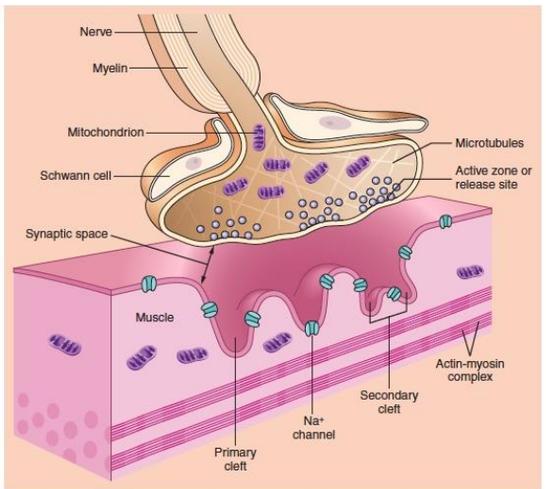
Κων/νος Γ Σταμούλης
Αναισθησιολόγος Επιμ. Α
Αναισθησιολογική κλινική
Π.Γ.Ν.Λάρισας

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Structure and contents

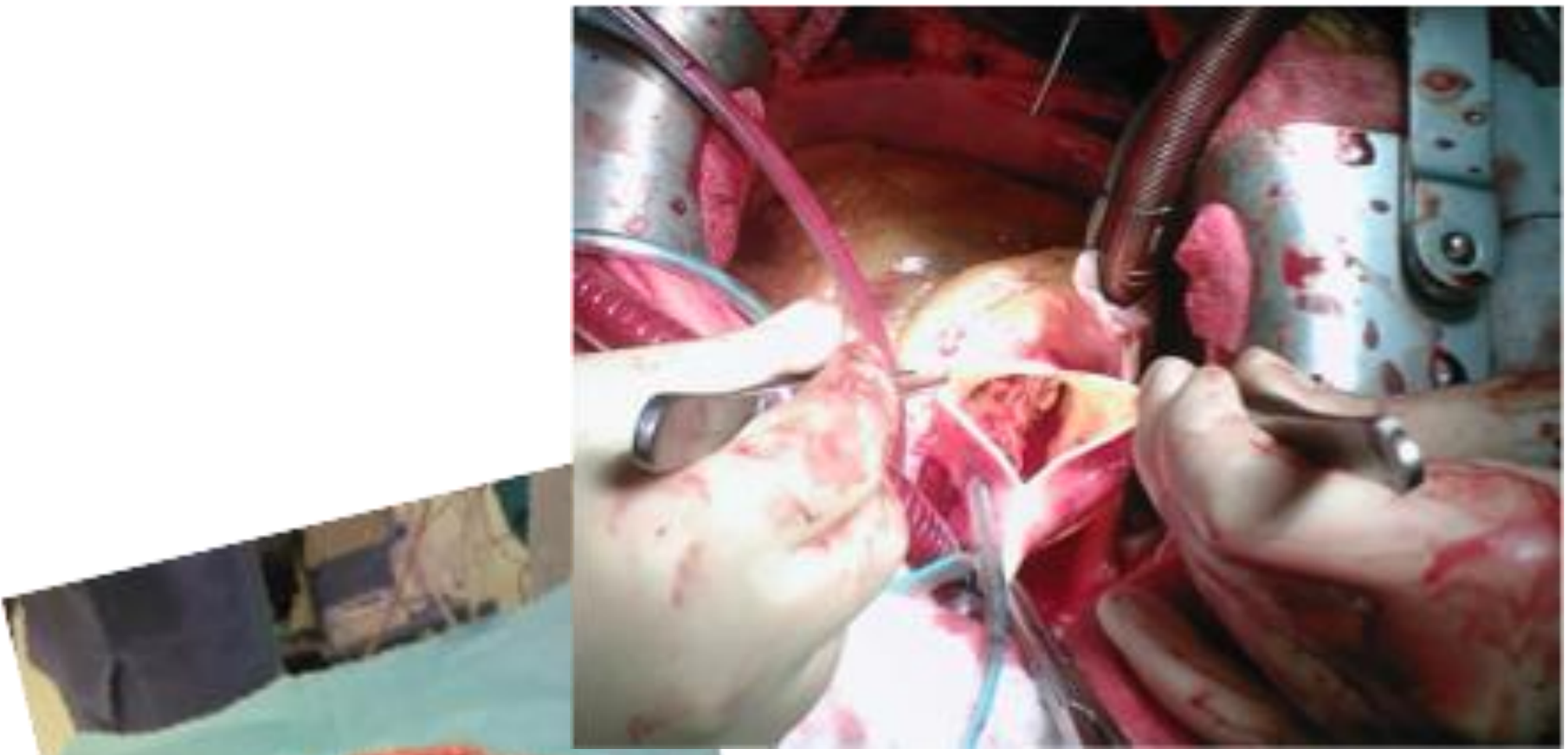






ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory



ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory

- **General anesthesia was absent until the mid-1800's**

- **William Morton** administered ether to a patient having a neck tumor removed at the Massachusetts General Hospital, Boston, in October 1846.

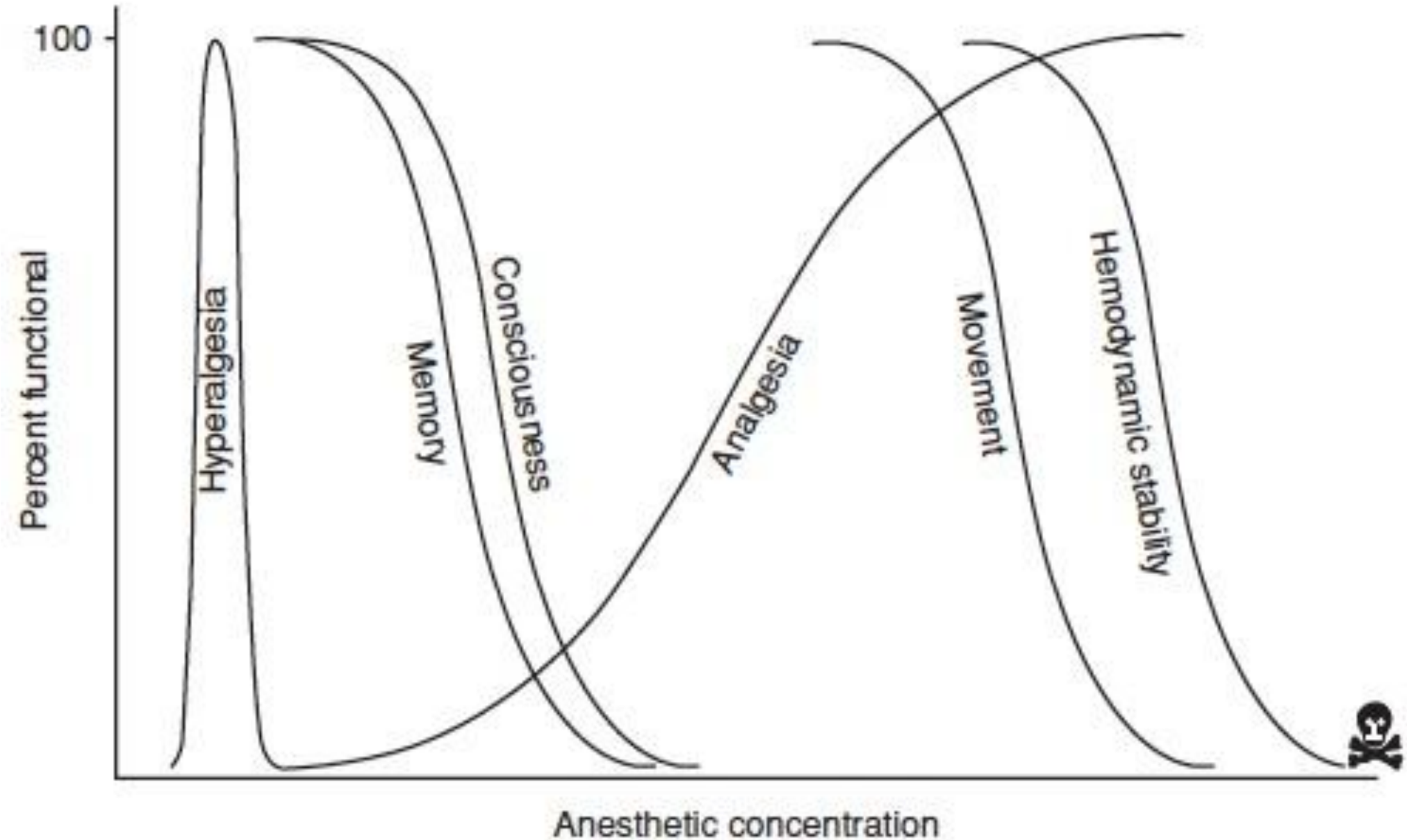
- The discovery of the **diethyl ether** as general anesthesia was the result of a search for means of eliminating a patient's pain perception and responses to painful stimuli.

16th October

WORLD ANAESTHESIOLOGY DAY

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory



ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory

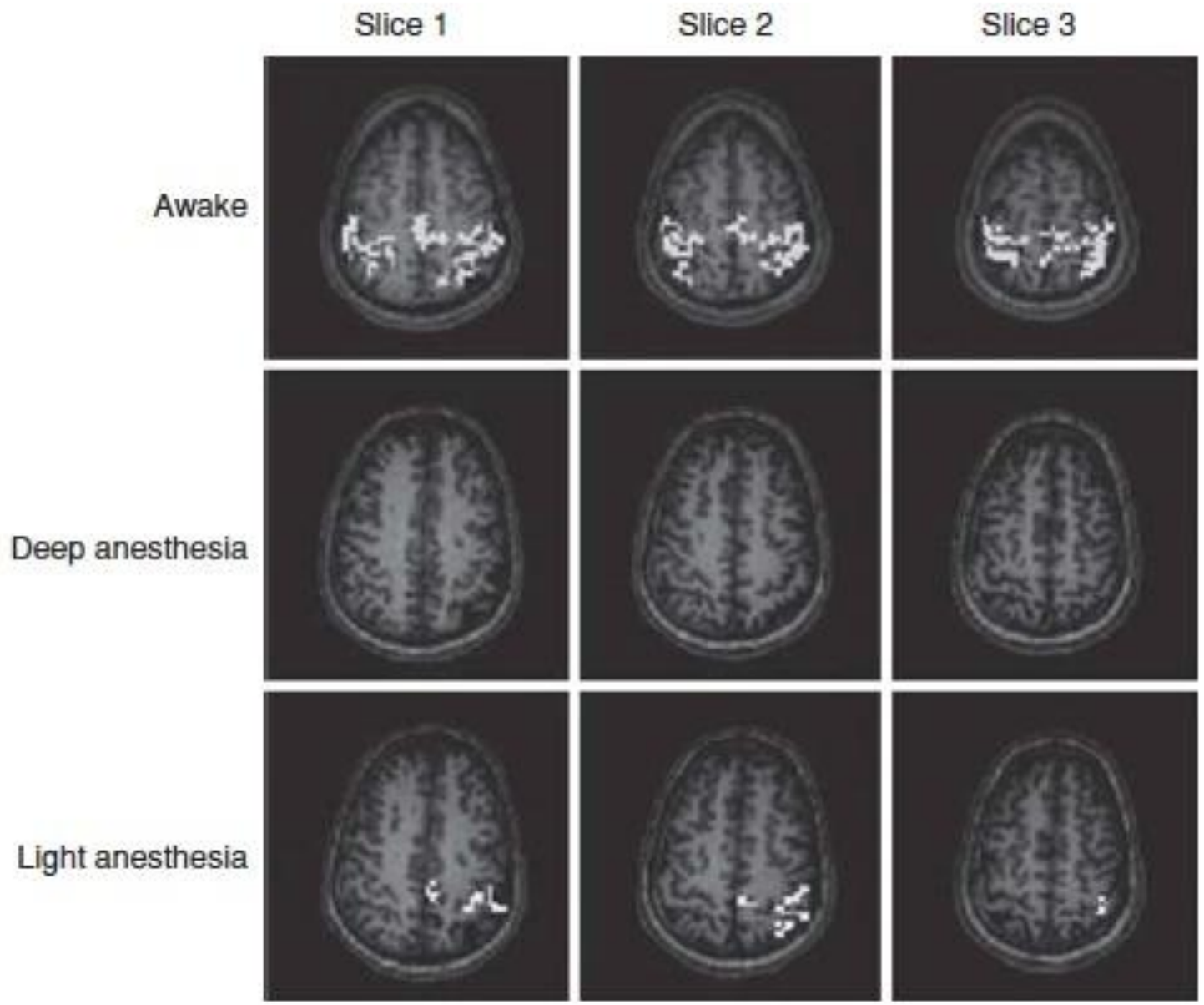
CELLULAR AND MOLECULAR EFFECTS OF GENERAL ANESTHETICS IN THE BRAIN

Table 2.1 THE NEURONAL, PHYSIOLOGICAL AND PHARMACOLOGICAL ROLES OF PUTATIVE ANESTHETIC TARGETS IN THE CENTRAL NERVOUS SYSTEM

MOLECULAR TARGET	CELLULAR FUNCTION	BEHAVIOR AND PHARMACOLOGY
	Ligand–Gated Ion Channels	
$GABA_A$ receptors	Increase Cl^- permeability	Enhanced activity associated with anxiolysis, sedation, and amnesia
	Hyperpolarize membrane	
	Inhibit neuronal excitability	Important role in epilepsy
Glycine receptors	Increase Cl^- permeability	Inhibitory receptor in the spinal cord
	Hyperpolarize membrane	Modulates spinal reflexes and startle response
	Inhibit neuronal excitability	
Glutamate receptors (NMDA subtype)	Fast excitatory neurotransmission	Important receptor in perception, learning and memory.
	Increase permeability to Na^+, K^+, and Ca^{2+}	
	Synaptic plasticity	
Neuronal nicotinic acetylcholine receptors	Increase permeability to sodium, potassium, and calcium	Regulates arousal, memory, nociception, and autonomic function
	Modulates neurotransmitter release	
Serotonin receptors	Increase cation conductance ($5\text{-}HTR_3$)	Regulates neuronal excitation and emesis
	Increase K^+ conductance ($5\text{-}HTR_2$)	
	Other Ion Channels	
Two-pore-domain K^+ channels	Increase K^+ permeability	Regulates neuronal excitability
	Can be activated by pH, chemical, or mechanical stimulation	Chemosensation
ATP-activated K^+ channels	Activated by metabolic activity	Neuroprotection, insulin secretion
Hyperpolarization-activated cyclic-nucleotide gated channels	Activates nonspecific cation current during membrane hyperpolarization	Regulates resting membrane potential
		Modulates dendritic function, neuronal oscillation, and action potential bursting
Voltage activated K^+ channels	Regulation of resting membrane potential and recovery from action potential	Essential for nerve transmission
Voltage activated Na^+ channels	Initiate action potentials	Essential for nerve transmission and neurotransmitter release
Voltage-gated Ca^{2+} channels	Increase permeability to Ca^{2+} during depolarization	Essential for neurotransmitter release Regulates nociception
	Neurotransmitter release	

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory



- shared circuit hypothesis
- disrupting effective connectivity

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Brain: consciousness - sleep - memory

Phases of memory

Encode or establishment

▼

Consolidation

▼

Retrievemcent

▼

Reconsolidation

Key points

➡ Main parts of brain relevant to memory are parietal lobe, amygdala, thalamus

➡ Amnesia caused by subanesthetic doses

➡ Anaesthetics may cause amnesia acting on arousal or attention

➡ No common mechanism

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous system

- Responsible for the body's involuntary activities (including cardiovascular, gastrointestinal, and thermoregulatory homeostasis).

- Divided into two major branches:

Sympathetic Nervous System (SNS) fight or flight" responses

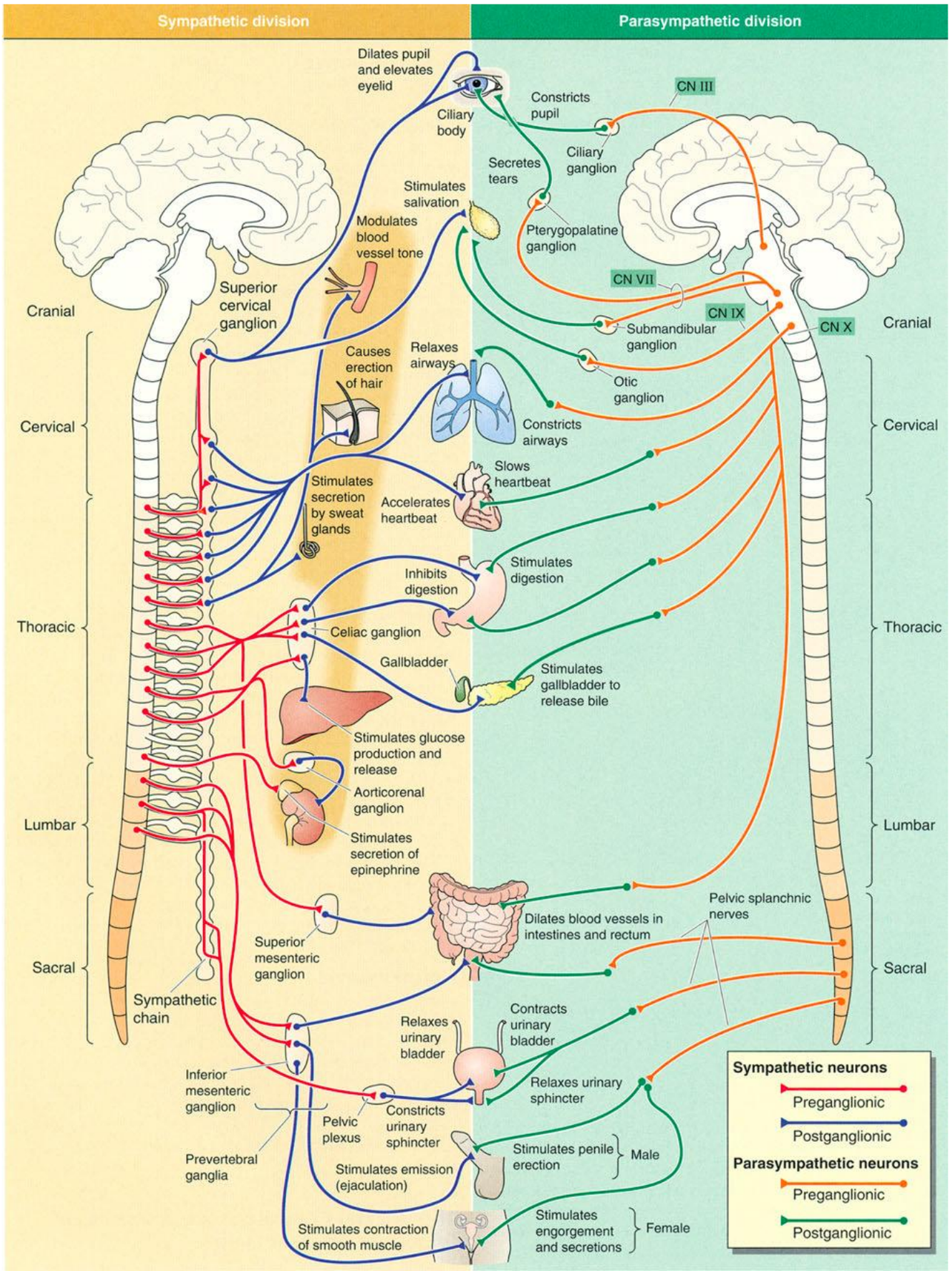
- Preganglionic fibers originate from the thoracolumbar region of the spinal cord
- The postganglionic neurons of the SNS then travel to the target organ
- A sympathetic response, is not confined to the segment from which the stimulus originates

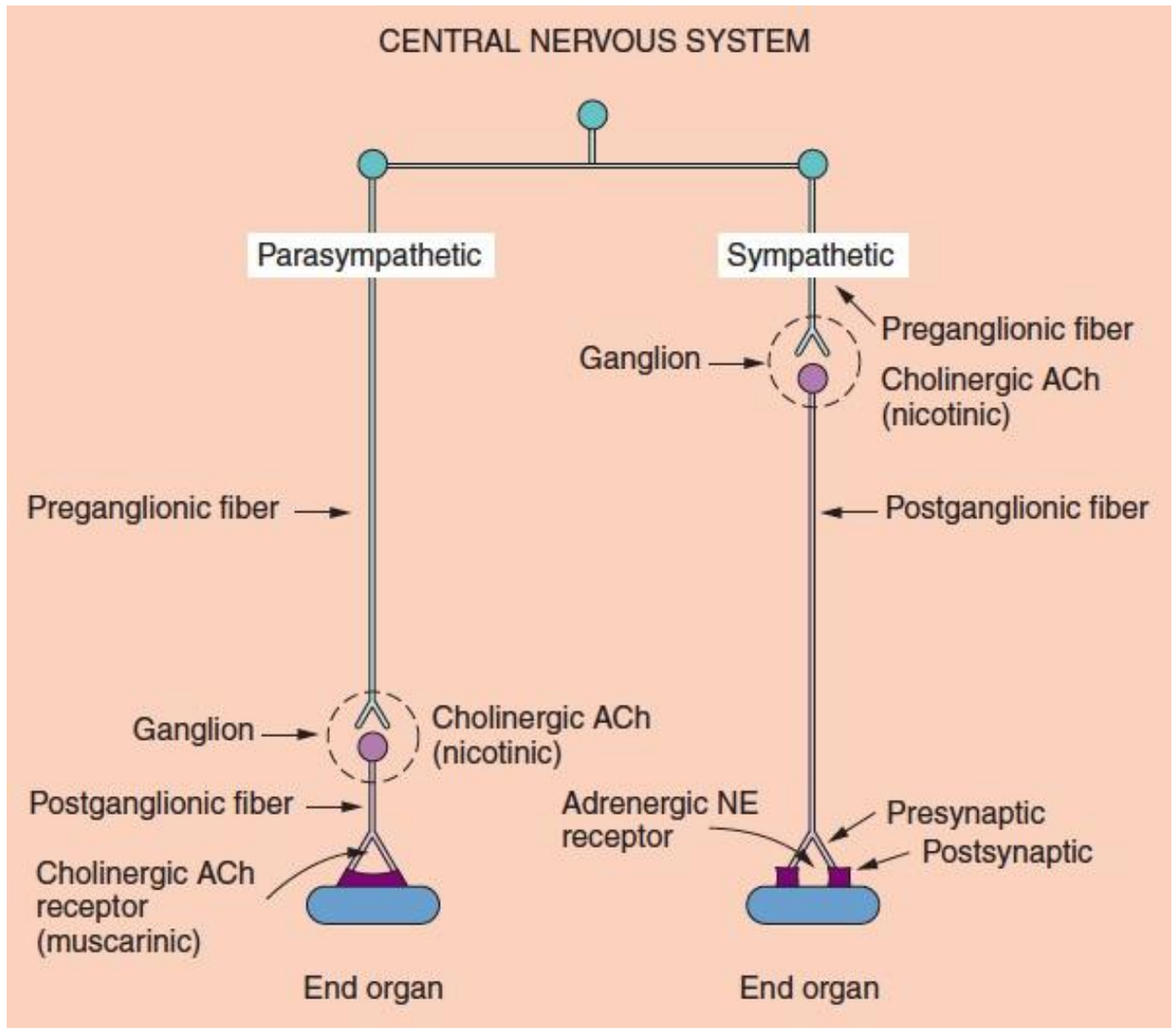
Parasympathetic Nervous System (PNS)" oversees the body's

- The PNS arises from cranial nerves III, VII, IX, X & from sacral segments
- The ganglia of the PNS are in close proximity to (or even within) their target organs

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous system





ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ
ΑΥΤΟΝΟΜΟ ΝΕΥΡΙΚΟ ΣΥΣΤΗΜΑ

Heart			
SA node	Decreases heart rate	β_1	Increases heart rate
Atria and ventricle	Decreases contractility	β_1, β_2	Increases contractility
AV node and Purkinje	Decreases conduction velocity	β_1, β_2	Increases conduction velocity
Arterioles			
Coronary	—	α_1, α_2	Constriction
		β_2	Dilation
Skin	—	α_1, α_2	Constriction
Skeletal muscle	—	α_1	Constriction
		β_2, Muscarinic	Dilation
Abdominal viscera	—	α_1	Constriction
Salivary glands	Dilation	α_1, α_2	Constriction
Renal	—	α_1	Constriction
Systemic veins	—	α_1, α_2	Constriction
		β_2	Dilation

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous sytem - Pharmacology

Sympathetic nervous system

Non selective agonists

- **Endogenous catecholamines**
  - Norepinephrine
  - Epinephrine
  - Dopamine
- **Synthetic catecholamines**
  - Isoproterenol
  - Doputamine
  - Fenoldopam
- **Noncatecholamine Sympathomimetic Amines**
  - Ephedrine

Selective agonists

- **a1-Adrenergic Agonists**
  - Phenylephrine
- **a2-Adrenergic Agonists**
  - Clonidine
  - Dexmedetomedine
- **b2 adrenergic agonists**

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous sytem - Pharmacology

Sympathetic nervous system

Table 7-2 Pharmacologic Effects and Therapeutic Doses of Catecholamines

Catecholamine	Mean Arterial Pressure	Heart Rate	Cardiac Output	Systemic Vascular Resistance	Renal Blood Flow	Cardiac Dysrhythmias	Preparation (mg/250 mL)	Intravenous Dose (µg/kg/min)
Dopamine	+	+	+ + +	+	+ + +	+	200 (800 µg/mL)	2-20
Norepinephrine	+ + +	–	–	+ + +	– – –	+	4 (16 µg/mL)	0.01-0.1
Epinephrine	+	+ +	+ +	+ +	– –	+ + +	1 (4 µg/mL)	0.03-0.15
Isoproterenol	–	+ + +	+ + +	– –	–	+ + +	1 (4 µg/mL)	0.03-0.15
Dobutamine	+	+	+ + +	–	+ +	–	250 (1000 µg/mL)	2-20

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous sytem - Pharmacology

Sympathetic nervous system

a-ADRENERGIC RECEPTOR ANTAGONISTS

- Phenoxybenzamine
- Prazocin

b-ADRENERGIC RECEPTOR ANTAGONISTS

- selective
  - Esmolol
  - Metoprolol
- non selective
  - Propranolol
  - Labetalol

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Autonomic nervous sytem - Pharmacology

Parasympathetic nervous system

Cholinesterase Inhibitors

- physostigmine
- neostigmine
- pyridostigmine
- edrophonium

Anticholinergic agents (muscarinic antagonists)

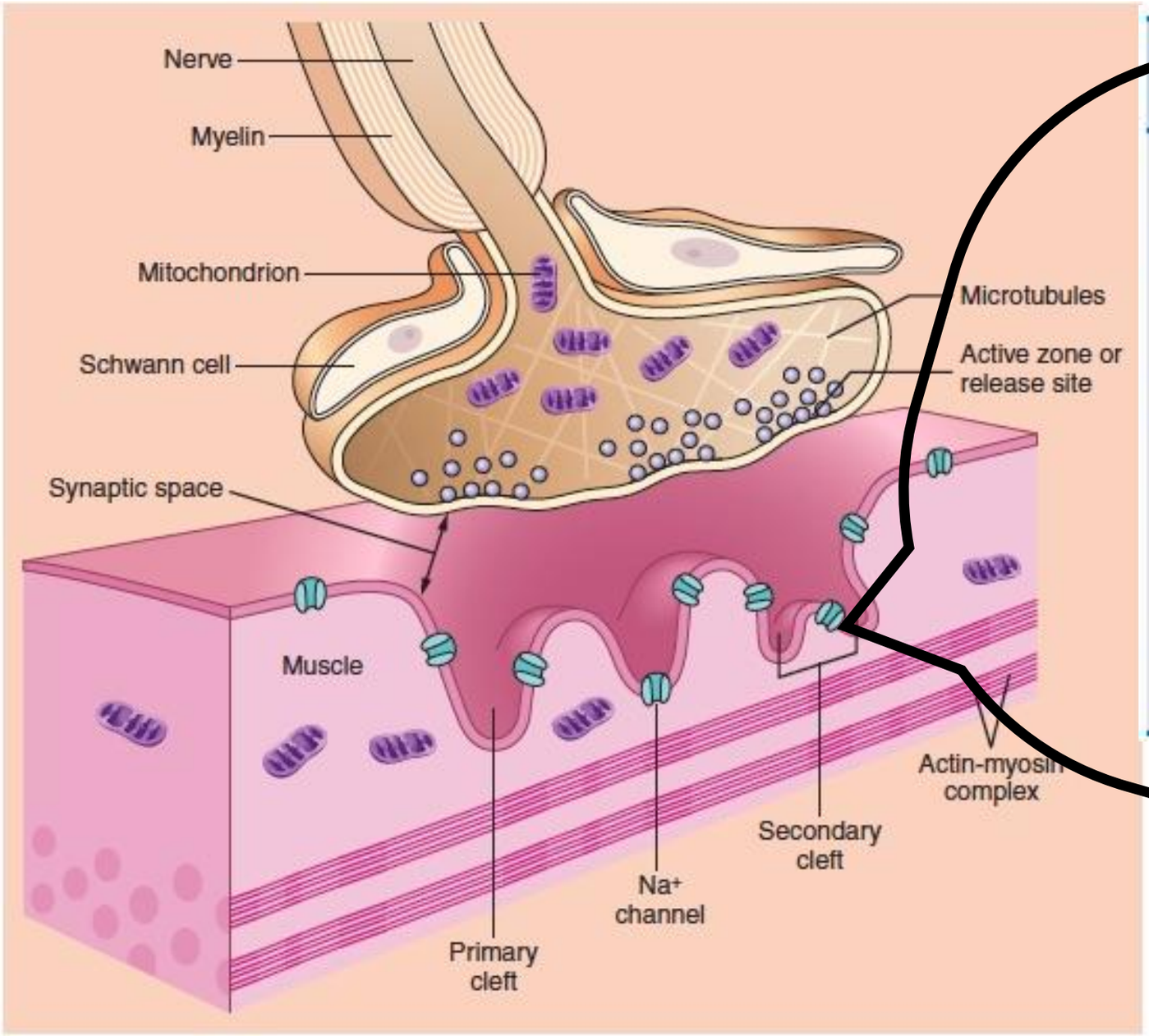
- Atropine
- Scopolamine
- Glycopyrrolate

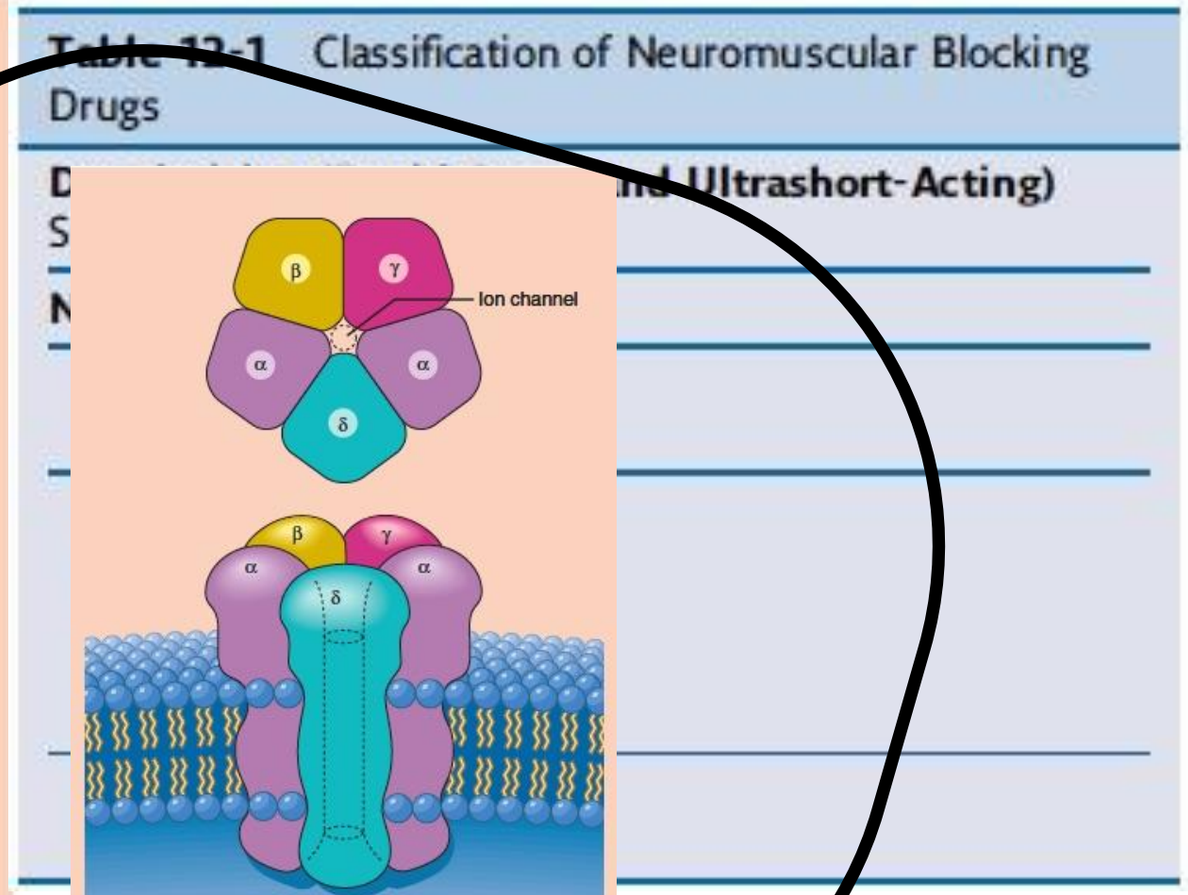
Table 7-3 Comparative Effects of Anticholinergics Administered Intramuscularly as Pharmacologic Premedication

Effect	Atropine	Scopolamine	Glycopyrrolate
Antisialogogue effect	+	+++	++
Sedative and amnesic effects	+	+++	0
Increased gastric fluid pH	0	0	0/+
Central nervous system toxicity	+	++	0
Relaxation of lower esophageal sphincter	++	++	++
Mydriasis and cycloplegia	+	+++	0
Heart rate	++	0/+	+

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Neuromuscular transmission





Neuromuscular transmission

Interactions with other drugs & factors which influence the duration of NMB

- Systematic diseases
- Other drugs: (volatile aesthetics, antibiotics, Mg.
- Hypothermia
- Acid base & electrolyte abnorma
- Age & others comorbitities
- Hepatic/renal failure

Disease
Amyotrophic lateral sclerosis
Autoimmune disorders Systemic lupus erythematosu Polymyositis Dermatomyositis
Burn injury

Drug	Effect on Depolarizing Blockade	Effect or Nondep Blockad	
Antibiotics	+		
Anticonvulsants	?		
Antiarrhythmics	+		
Cholinesterase inhibitors	+		
Dantrolene	?		
Inhalational anesthetics	+		
Ketamine	?		
Local anesthetics	+		
Lithium carbonate	+	?	Prolongs onset and duration of succinylcholine
Magnesium sulfate	+	+	Doses used to treat preeclampsia and eclampsia of pregnancy

Pediatric	Succinylcholine – should not be used routinely Nondepolarizing agents – faster onset Vecuronium – long-acting in neonates
Elderly	Decreased clearance – prolonged duration, except with cisatracurium
Obese	Dosage 20% more than lean body weight; onset unchanged Prolonged duration, except with cisatracurium
Hepatic disease	Increased volume of distribution Pancuronium and vecuronium – prolonged elimination due to hepatic metabolism and biliary excretion Cisatracurium – unchanged Pseudocholinesterase decreased; prolonged action may be seen with succinylcholine in severe disease
Renal failure	Vecuronium – prolonged Rocuronium – relatively unchanged Cisatracurium – safest alternative
Critically ill	Myopathy, polyneuropathy, nicotinic acetylcholine receptor up-regulation

Systematic effects

Depolarizing

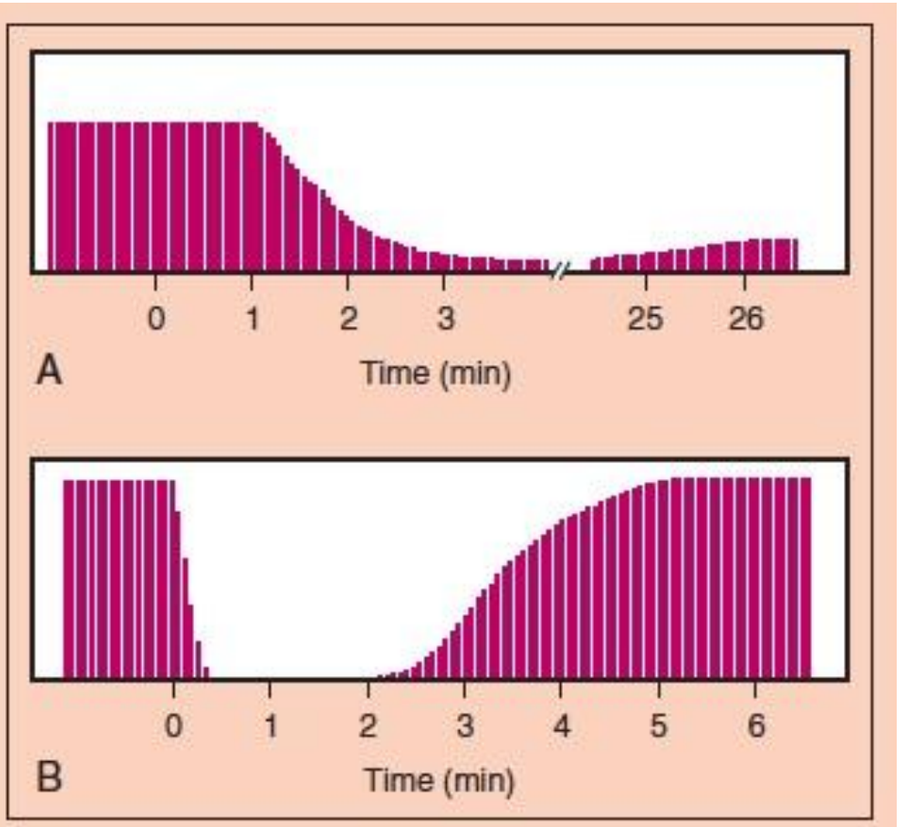
* Bradycardia, hyperkalemia, respiratory problems, increase of intraocular and intragastric pressure, malignant hyperthermia

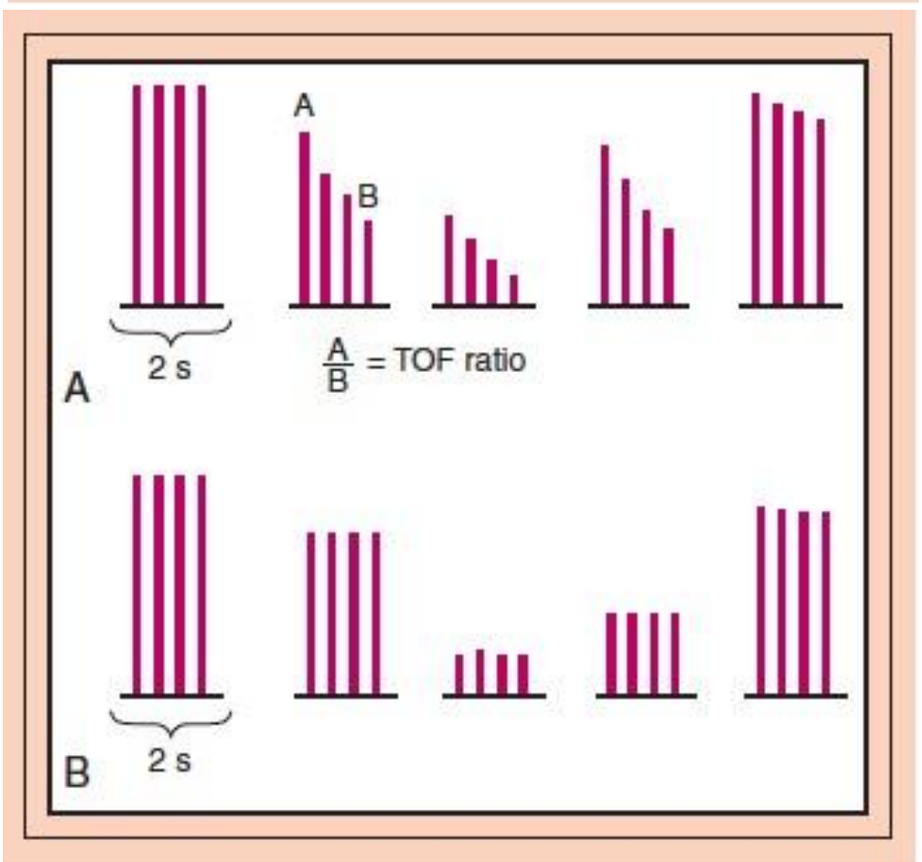
Non depolarising

* Histamine release
* Respiratory side effects

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Neuromuscular transmission





Neuromuscular blockade reversal

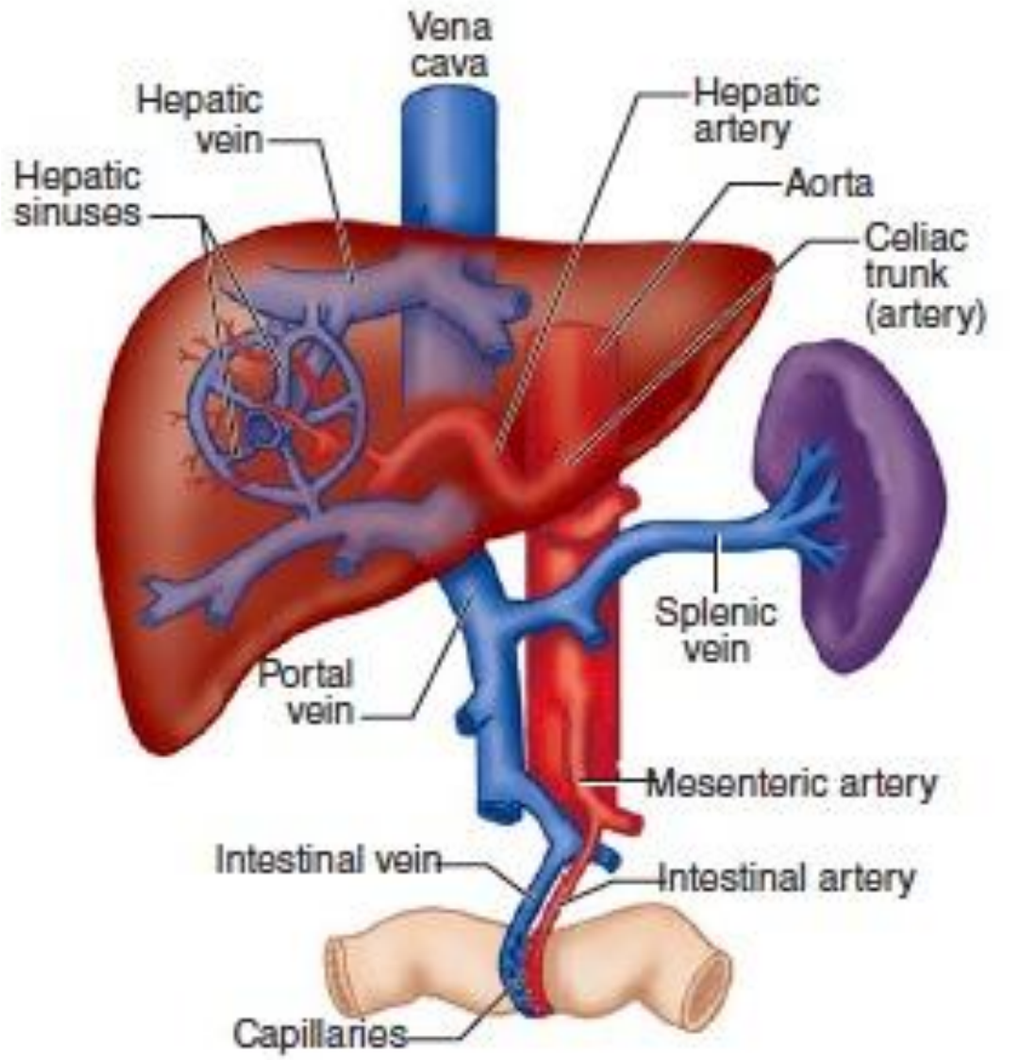
➡ There are not specific antidotes for depolarising neuromuscular blocking drugs

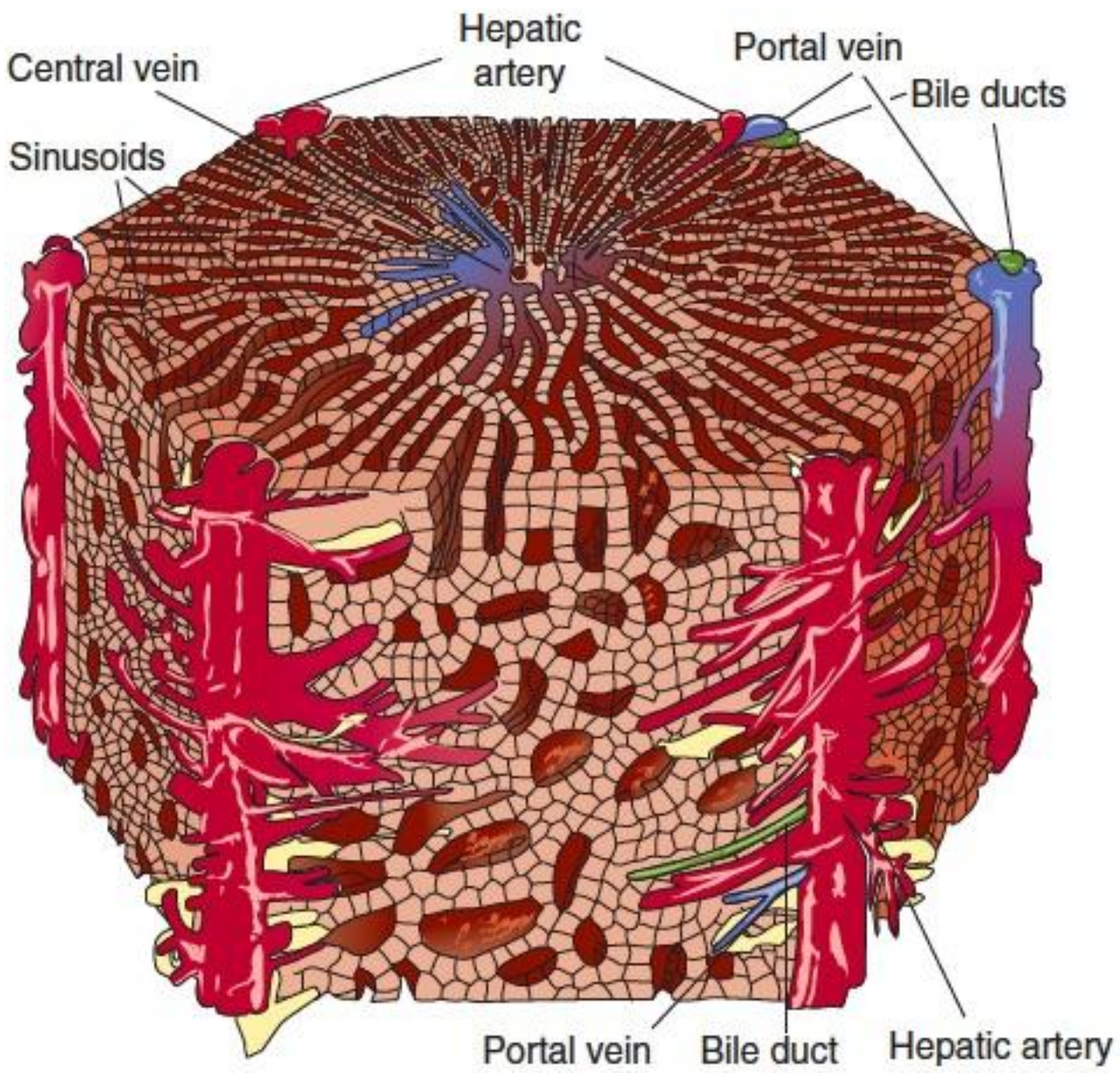
➡ Cholinesterase inhibitors used to reverse the block of non depolarising blocking drugs

➡There is specific antidote for rocuronium (sugammadex)

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Liver





ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Liver

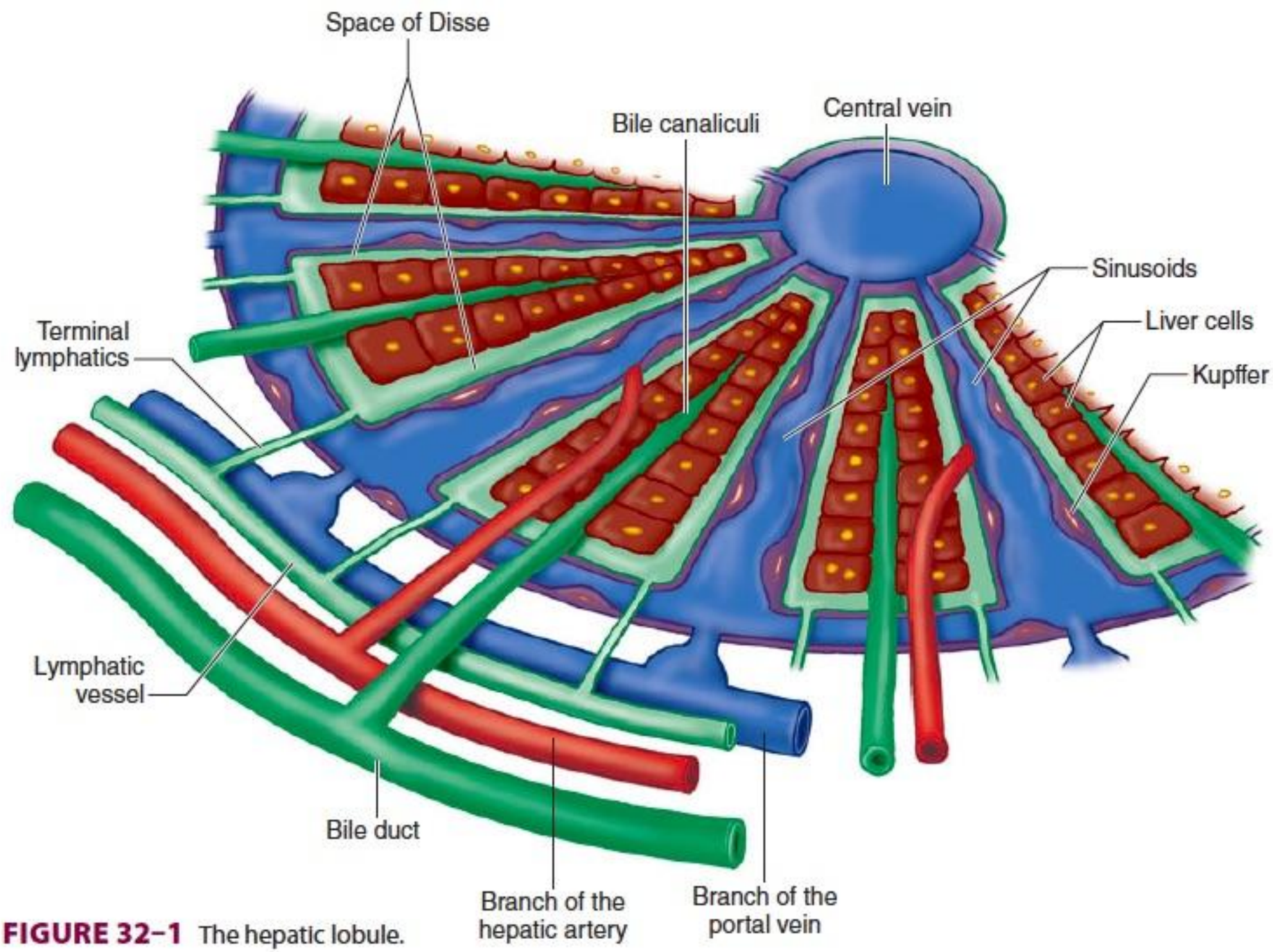


FIGURE 32–1 The hepatic lobule.

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Liver

- ☆ Hepatic blood flow is 25% to 30% of the C.O
- ☆ It is provided by the hepatic artery and portal vein.
- ☆ The hepatic artery supplies about 45% to 50% of the liver' s oxygen requirements
- ☆ Hepatic arterial flow dependent on metabolic demand (autoregulation)
- ☆ The hepatic artery has α_1 & β_2 -adrenergic receptors, dopaminergic (D_1), and cholinergic vasodilator receptors.
- ☆ The portal vein has only α_1 -adrenergic and dopaminergic (D_1) receptors
- ☆ Has a central role in metabolism of nutrients & drugs, synthesis of many coagulant factors & other proteins & secretion of bile

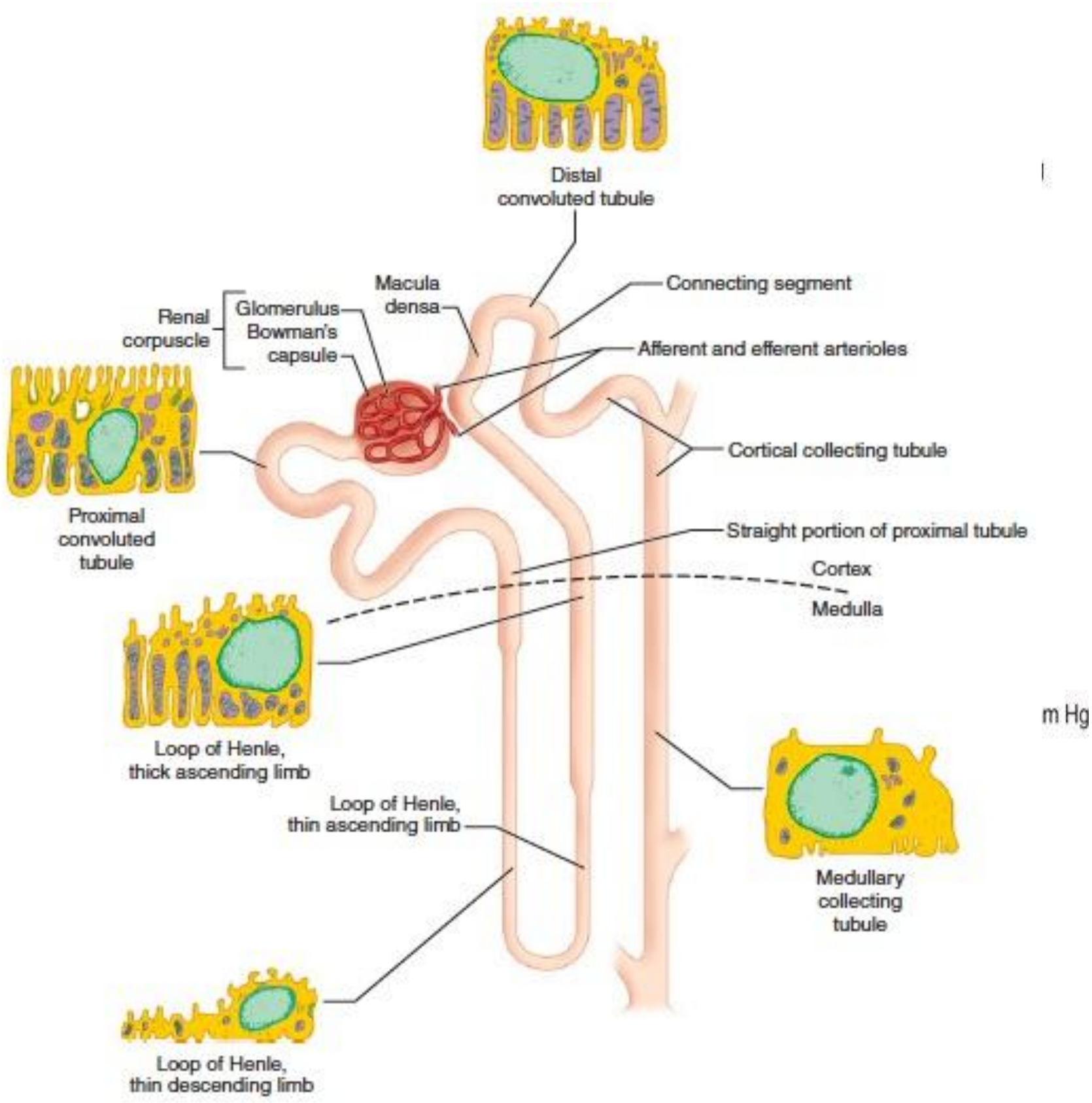
Liver

Effects of anaesthesia on liver function

* Indirect effects because of cardiovascular changes
* Metabolic effects because of stress
* Opioids cause Oddi's sphincter spasm
* Modern volatile anesthetic agents have no direct effects upon hepatocytes

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

ΝΕΦΡΟΙ



m Hg

Segment	Function
Renal corpuscle (glomerulus, Bowman's capsule)	Ultrafiltration of blood
Proximal tubule	Reabsorption Sodium[2] chloride Water Bicarbonate Glucose, protein, amino acids Potassium, magnesium, calcium Phosphates,[3] uric acid, urea Secretion Organic anions Organic cations Ammonia production
Loop of Henle	Reabsorption Sodium, chloride Water Potassium, calcium, magnesium Countercurrent multiplier
Distal tubule	Reabsorption Sodium[4] chloride Water Potassium Calcium[5] Bicarbonate Secretion Hydrogen ion[4] Potassium[4] Calcium
Collecting tubule	Reabsorption Sodium[4,6] chloride Water[6,7] Potassium Bicarbonate Secretion Potassium[4] Hydrogen ion[4] Ammonia production
Juxtaglomerular apparatus	Secretion of renin

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ
ΝΕΦΡΟΙ

- Renal function is intimately related to renal blood flow (RBF). The kidneys are the only organs for which oxygen consumption is determined by blood flow.
- The blood flow through both kidneys normally accounts for 20–25% of C.O. Approximately 80% of RBF normally goes to cortical nephrons.
- The renal cortex extracts relatively little oxygen, having an oxygen tension of about 50 mm Hg.
- The renal medulla maintains high metabolic activity because of solute reabsorption and requires low blood flow to maintain high osmotic gradients. The medulla has an oxygen tension of only about 15 mm Hg and is relatively vulnerable to ischemia.
- Redistribution of RBF away from cortical nephrons with short loops of Henle to larger juxtamedullary nephrons with long loops occurs under certain conditions.
- Sympathetic stimulation, increased levels of catecholamines and angiotensin II, and heart failure can cause redistribution of RBF to the medulla and is associated with sodium retention

Control Mechanisms of RBF

- Intrinsin regulation
- Tubuloglomelural feedback
- Hormonal
- Neuronal and paracrine stimulation

Effects of Anesthesia on Renal Function

* Reversible decreases in RBF, GFR, urinary flow, and sodium excretion occur during both regional and general anesthesia

* Most of these changes are indirect and are mediated by autonomic and hormonal responses to surgery and anesthesia.

* AKI is less likely when an adequate intravascular volume and a normal blood pressure are maintained.

* There is no evidence that currently utilized vapor anesthetic agents cause AKI

- **Cardiovascular effects**
- **Neurogenic mechanisms**
- **Endocrine changes**
- **Other drugs**

Type of Injury	Drug or Toxin
Decreased renal perfusion	Nonsteroidal antiinflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors, radiocontrast agents, amphotericin B, cyclosporine, tacrolimus
Direct tubular injury	Aminoglycosides, radiocontrast agents, amphotericin B, methotrexate, cisplatin, foscarnet, pentamidine, heavy metals, myoglobin, hemoglobin, intravenous immunoglobulin, HIV protease inhibitors
Intratubular obstruction	Radiocontrast agents, methotrexate, acyclovir, sulfonamides, ethylene glycol, uric acid, cocaine, lovastatin
Immunological–Inflammatory	Penicillin, cephalosporins, allopurinol, NSAIDs, sulfonamides, diuretics, rifampin, ciprofloxacin, cimetidine, proton pump inhibitors, tetracycline, phenytoin

Αναισθησιολογία
Ακαδ. έτος 2018-19

ΣΑΣ ΕΥΧΑΡΙΣΤΩ

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ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Questions

Ποια από τα παρακάτω είναι λάθος:

1. Η ηπατική αιμάτωση γίνεται από την πυλαία φλέβα και την ηπατική αρτηρία

2. Η νευρομυϊκή διαβίβαση γίνεται με τους μουσκαρινικούς υποδοχείς

3. Η ρύθμιση της νεφρικής αιματικής ροής μεταξύ άλλων γίνεται και με ορμονικούς μηχανισμούς

4. Η επινεφρίνη είναι ένας εκλεκτικός α1 αγωνιστής

Which is the wrong statement:

1. Hepatic blood perfusion is provided by the hepatic artery and portal vein

2. Neuromuscular transmission is achieved through muscarinic receptors

3. Hormonal mechanisms may play role in the regulation of the renal blood flow

4.Epinephrine is a selective α1 agonist

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Questions

Ποιό από τα παρακάτω είναι αληθές

1. Η νορεπινεφρίνη είναι ένας προγαγγλιακός νευροδιαβιβαστής του παρασυμπαθητικού

2.Η νορεπινεφρίνη είναι ένας μεταγαγγλιακός νευροδιαβιβαστής του συμπαθητικού

3.Η ακετυλοχολίνη είναι ένας μεταγαγγλικός νευροδιαβιβαστής του του συμπαθητικού

4.Η ακετυλοχολίνη είναι ένας αγονιστής των α1 αδρενεργικών υποδοχέων

Which of the following is true

1. Norepinephrine is a pregagglionic neutotransmitter of the parasympathetic nervous system

2. Norepinephrine is a postgaglionic neurotransmitter of the sympathetic nervous system

3. Acetylocholine is a postgaglionic neurotransmitter of the sympathetic nervous system

4. Acetylocholine is an agonist of the a1 adrenergic receptors

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Questions

What of the following are potential adverse outcomes from residual neuromuscular blockade.

1. Αναπνευστικές επιπλοκές
2. Καρδιολογικές επιπλοκές
3. Υπόταση
4. Νεφρική βλάβη

What of the following are potential adverse outcomes from residual neuromuscular blockade.

1. Respiratory complications
2. Cardiac complications
3. Hypotension
4. Renal injury

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Questions

Ποιός από τους παρακάτω παράγοντες μπορεί να ευθύνεται για την πρόκληση νεφρικής βλάβης περιεγχειρητικά:

1.NSAID's

2.Ενδοφλέβια αναισθητικά

3.Εισπνεόμενα αναισθητικά

4.Η χορήγηση ντοπαμίνης

Which of the following factors may cause kidney injury perioperatily

1. NSAID'S

2. Intravenous anesthetics

3. Inhaled anaesthetics

4. Dopamine infusion

ΦΥΣΙΟΛΟΓΙΑ ΚΑΤΑ ΤΗΝ ΑΝΑΙΣΘΗΣΙΑ

Questions

Ποιο από τα παρακάτω είναι λάθος:

1. Τα σύγχρονα αναισθητικά προκαλούν ηπατική βλάβη

2. Το ήπαρ δέχεται περίπου το 25% της καρδιακής παροχής

3. Το ήπαρ συμμετέχει στη παραγωγή παραγόντων πήξης

5. Η ηπατική αρτηρία έχουν α1 υποδοχείς

Which of the following is wrong:

1. Currently utilised aesthetics cause liver injury

2. Liver blood flow is almost 25% of cardiac output

3. Liver produce some of the coagulation factors

4. The hepatic artery has α 1 -adrenergic receptors