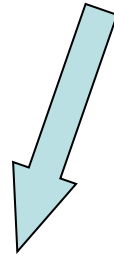


Fármacos Colinérgicos e Anticolinérgicos

Elisa M. Kawamoto

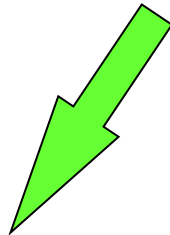
SISTEMA NERVOSO



SISTEMA NERVOSO CENTRAL



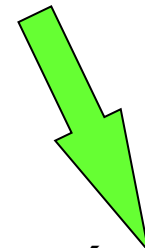
SISTEMA NERVOSO PERIFÉRICO



Somático



Sistema nervoso autônomo (SNA)



Entérico

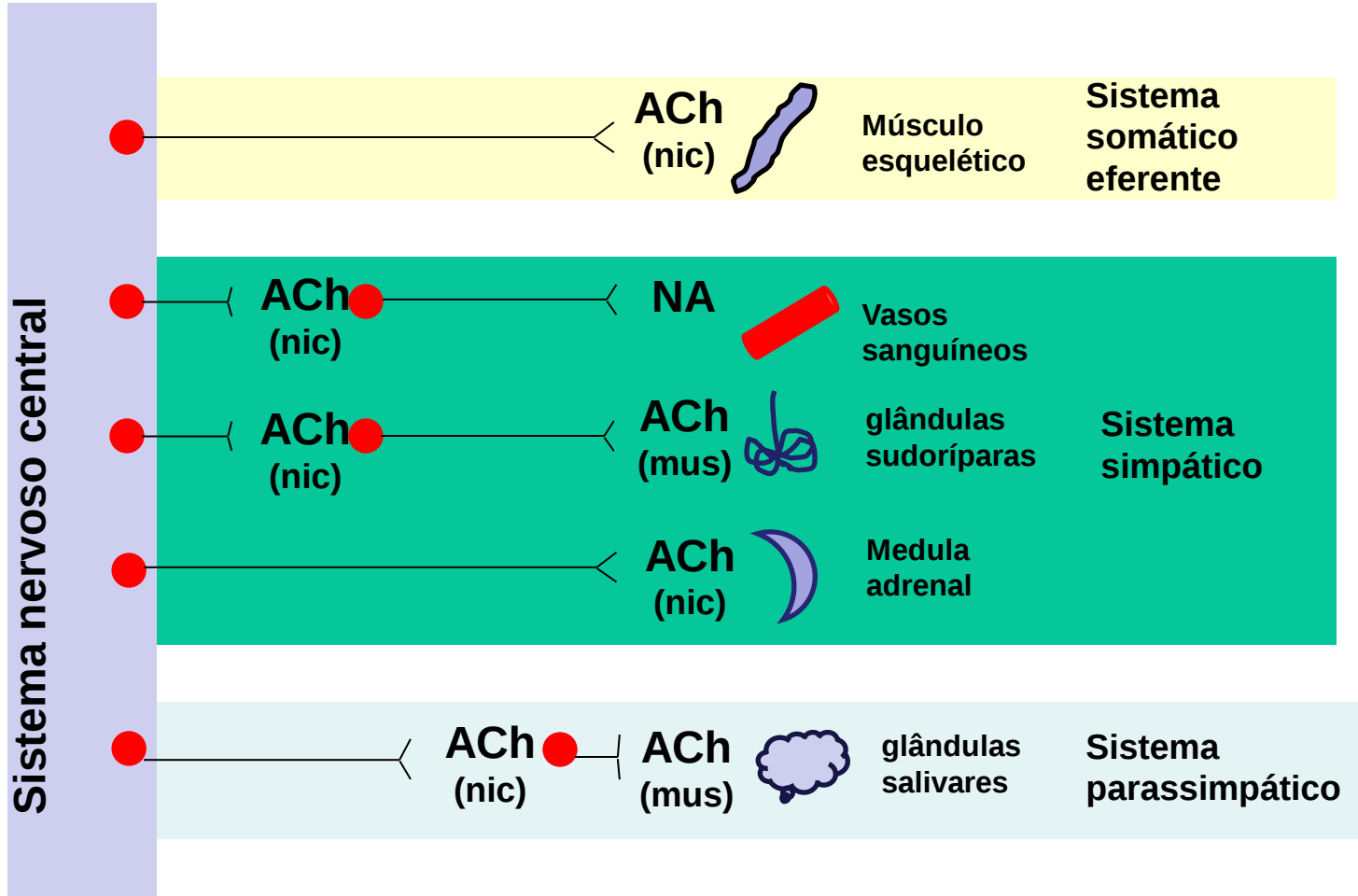


Simpático

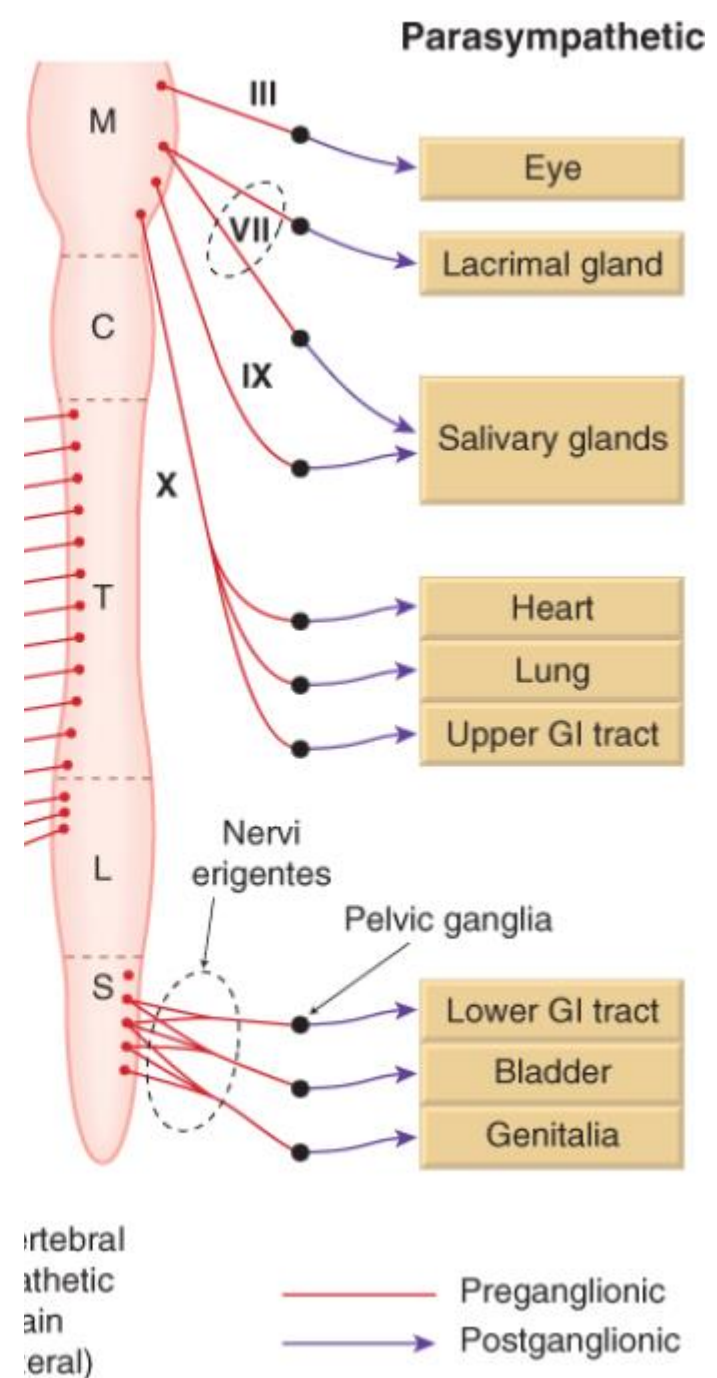
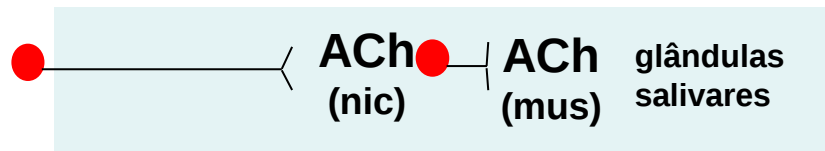


Parassimpático

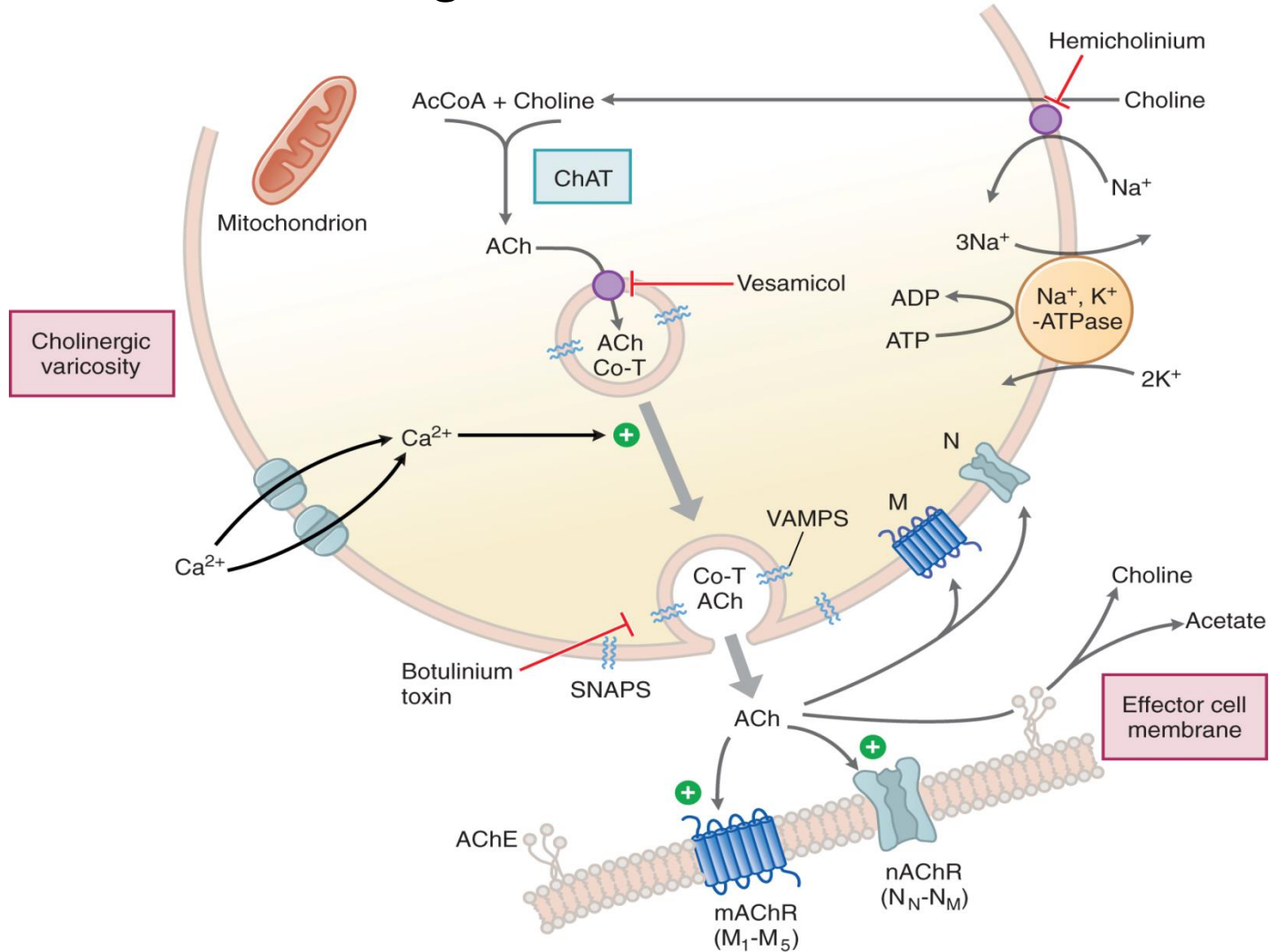
Sistema Nervoso Periférico



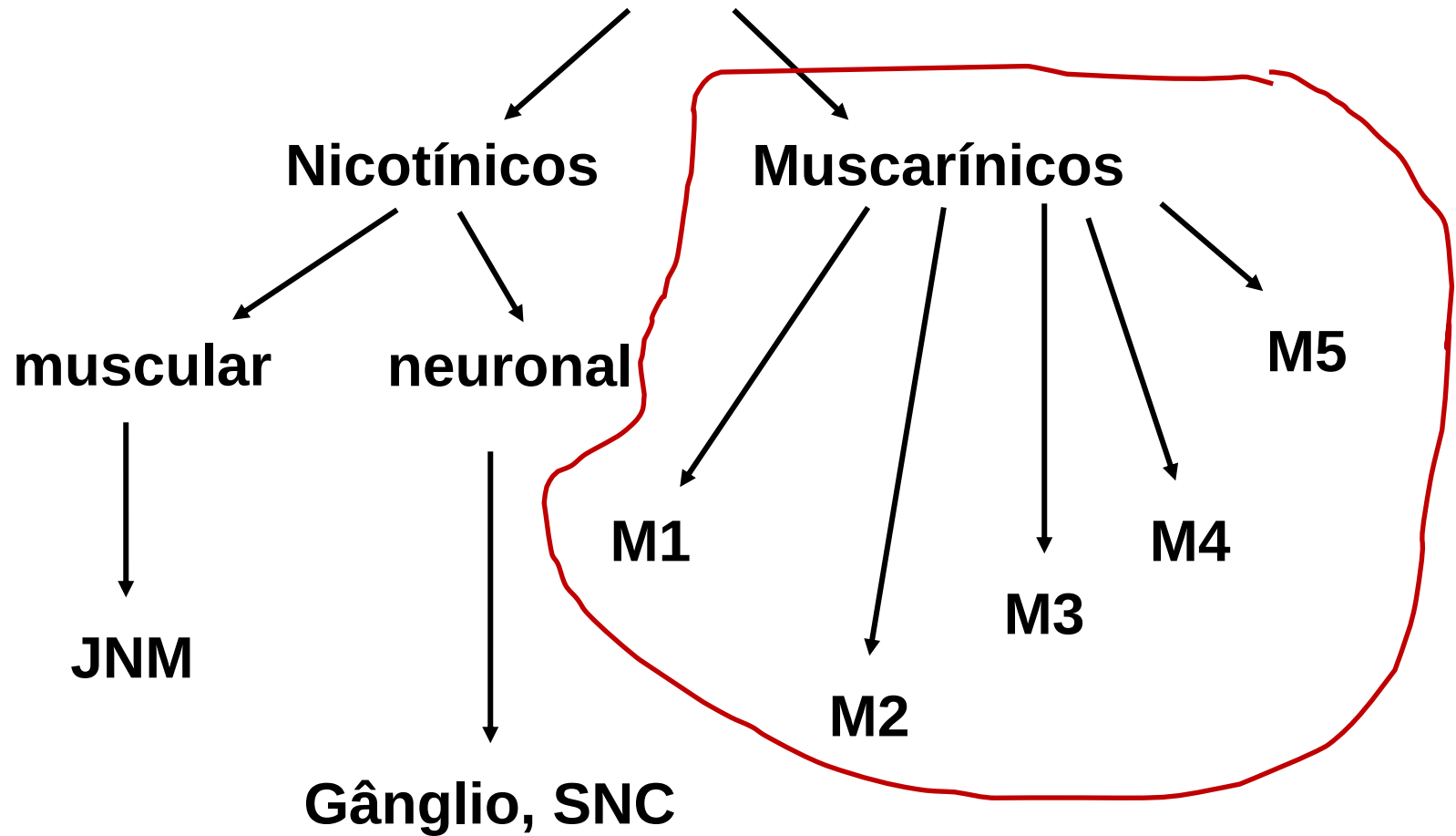
Sistema parassimpático



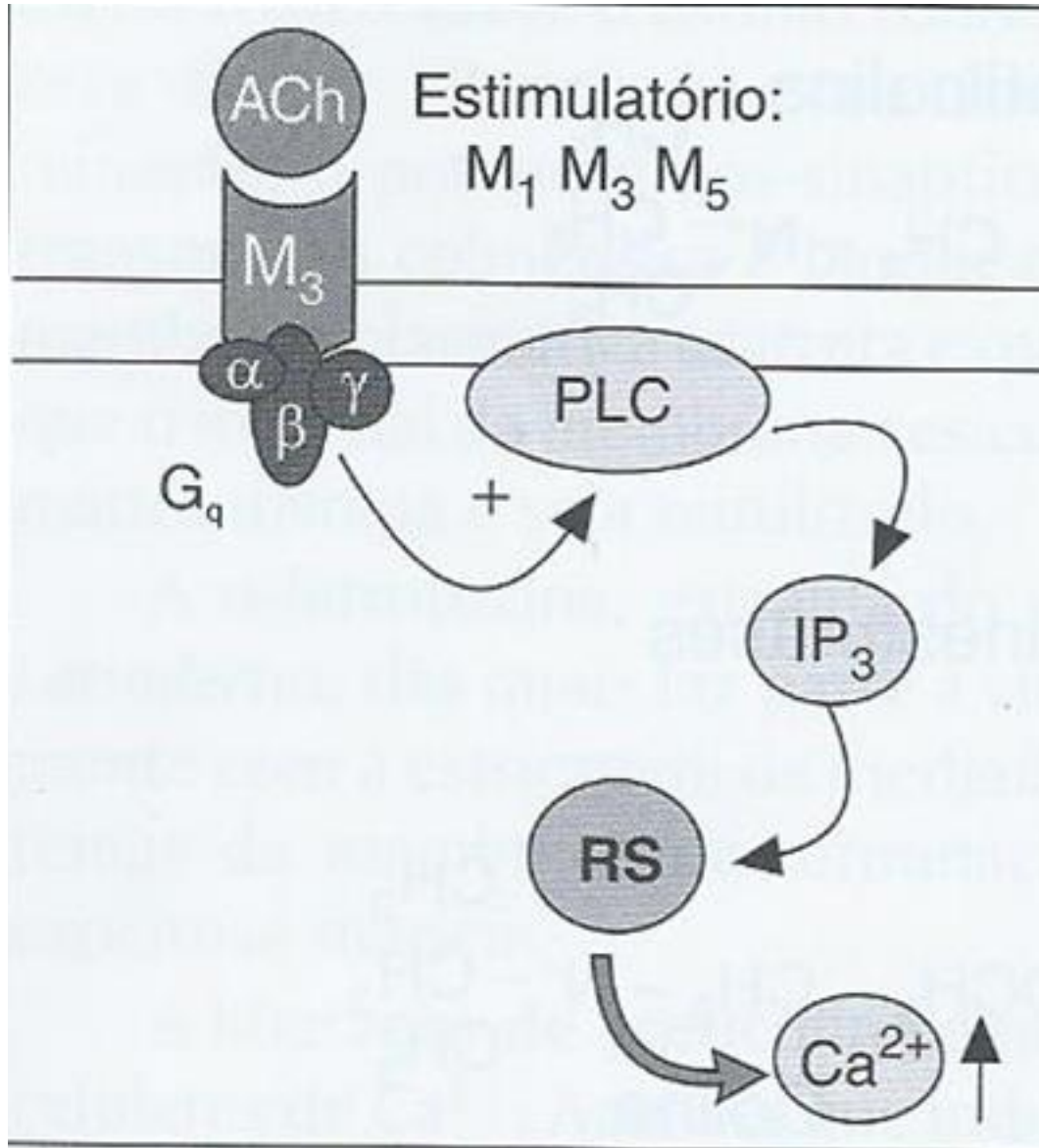
Transmissão Colinérgica



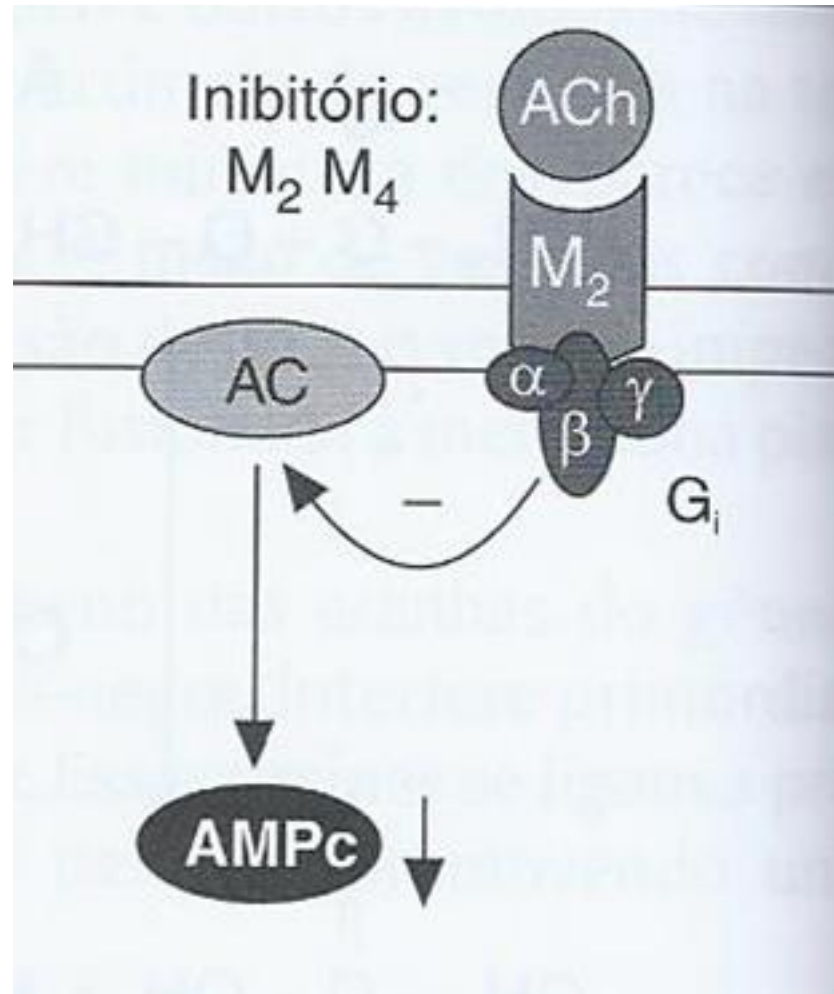
Receptores de Acetilcolina



Receptor Muscarínico (M1, M3, M5): excitação



Receptor Muscarínico (M₂, M₄): inibição

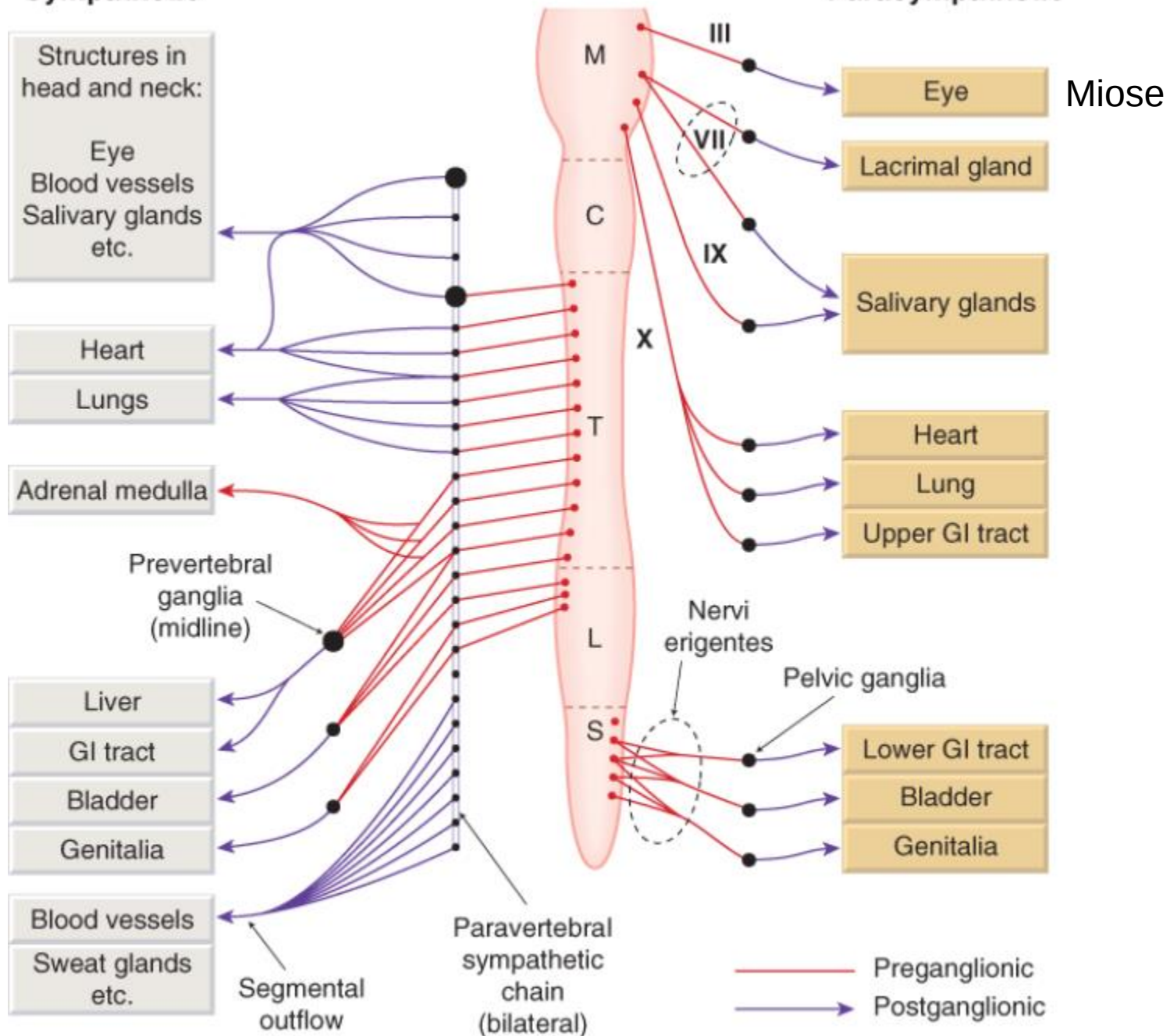


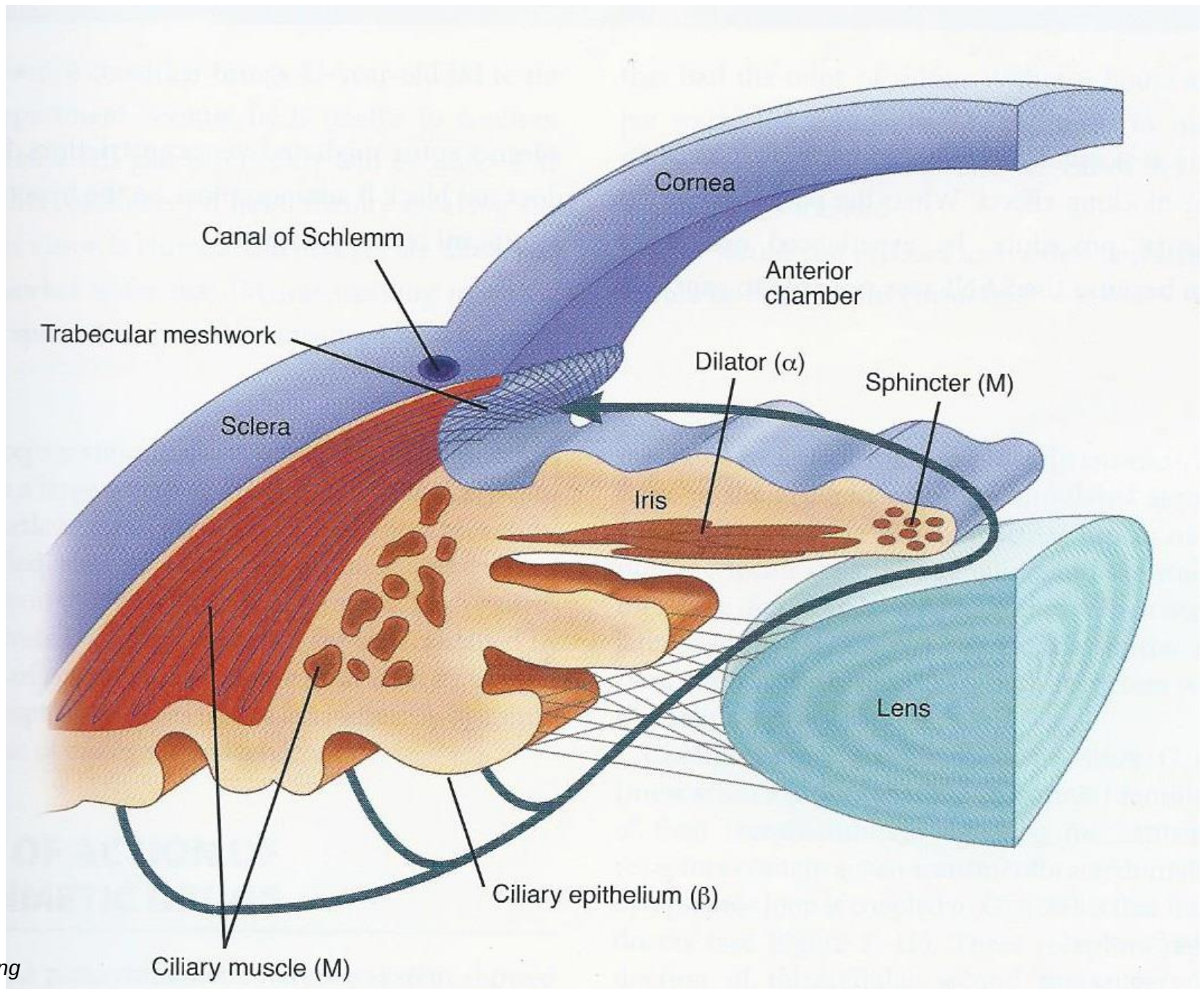
Receptores Muscarínicos

	M1 (“neurais”)	M2 (“cardíacos”)	M3 (“glandulares/ músculos lisos”)
Localização	Neurônios SNC e periféricos, células parietais gástricas	Coração Terminações pré-sinápticas dos neurônios centrais e periféricos	Glândulas exócrinas, musculatura lisa, endotélio vascular
Efeitos	Estimulação do SNC ↑ secreção de ácido gástrico	Inibitórios (aumento condutância do K ⁺ e inibição dos canais de Ca ²⁺) ↓ FC, ↓ DC	Excitatórios: <u>estimulação das secreções</u> (salivares, brônquicas, sudoríparas); <u>contração da musculatura lisa visceral</u> ; <u>relaxamento da musculatura lisa vascular</u> (NO).

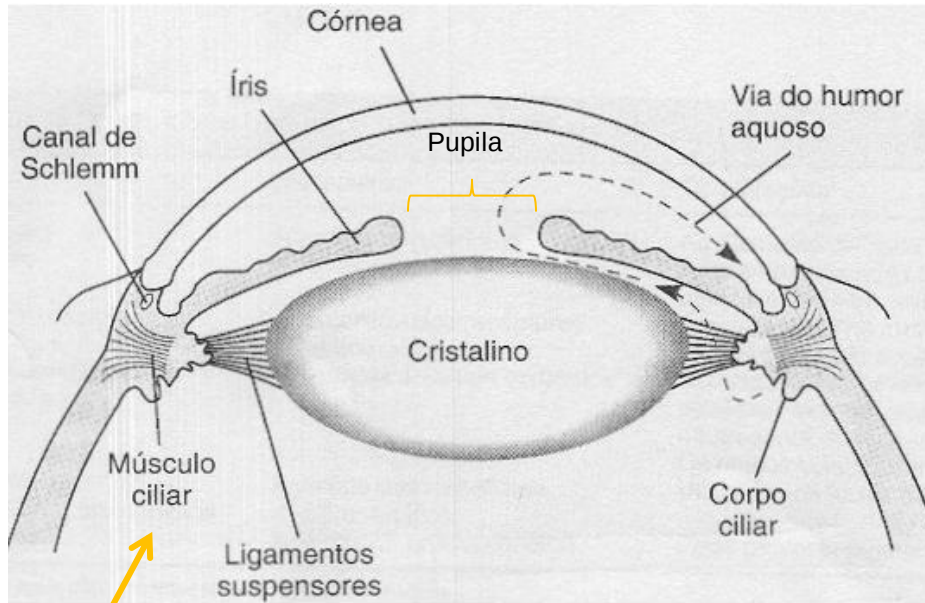
Sympathetic

Parasympathetic



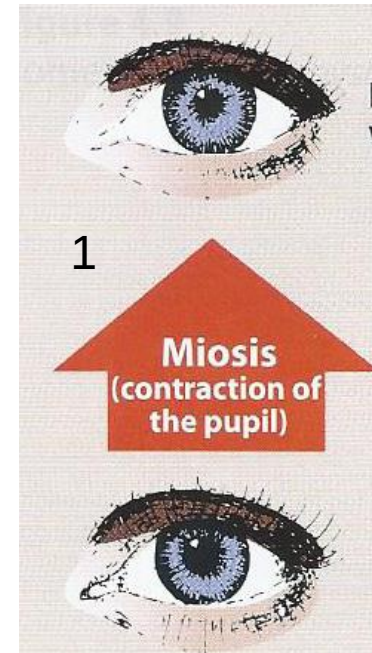


Aparelho Visual



acomodação para visão de perto

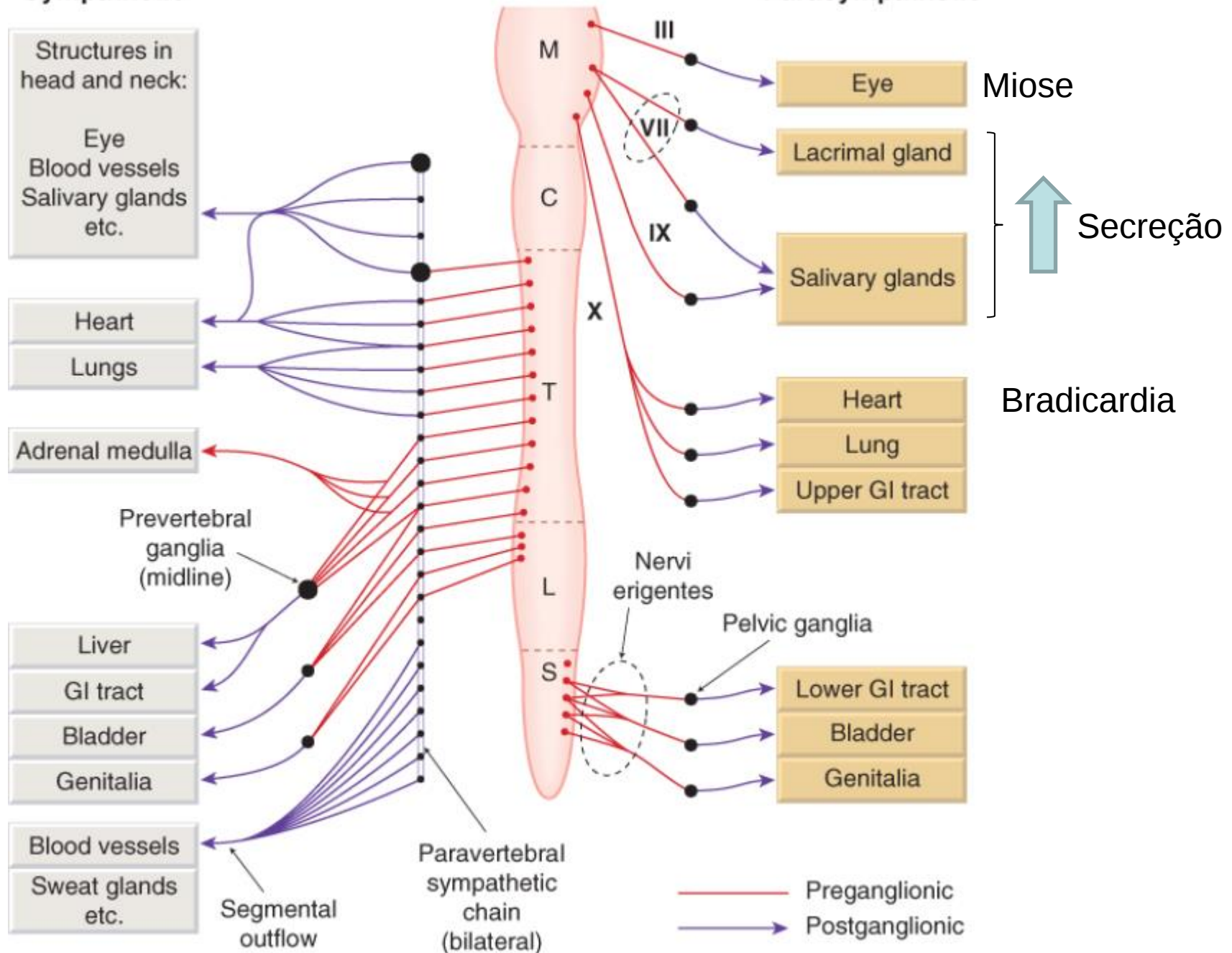
Músculo esfíncter da pupila



2 Regulação da PIO

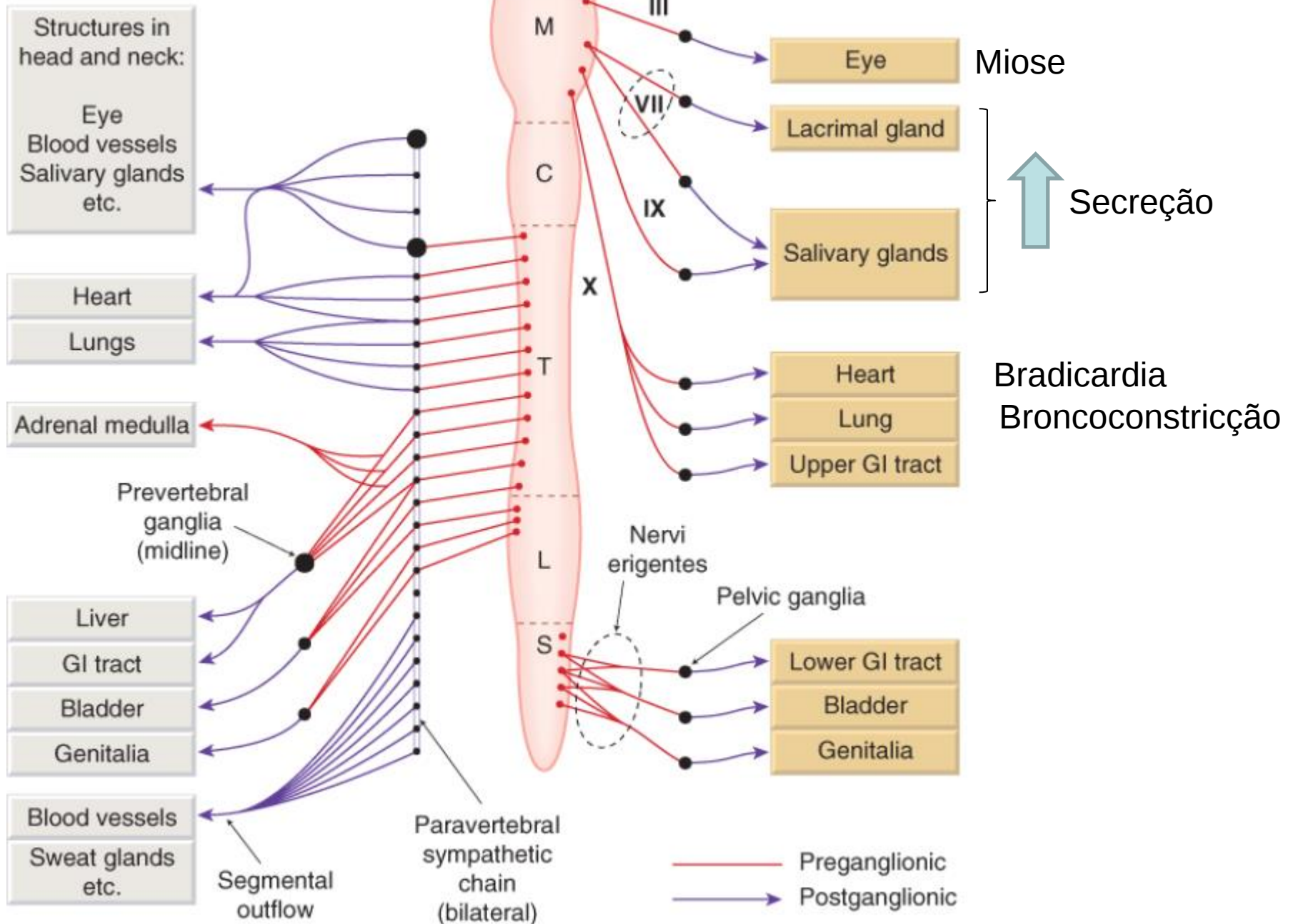
Sympathetic

Parasympathetic



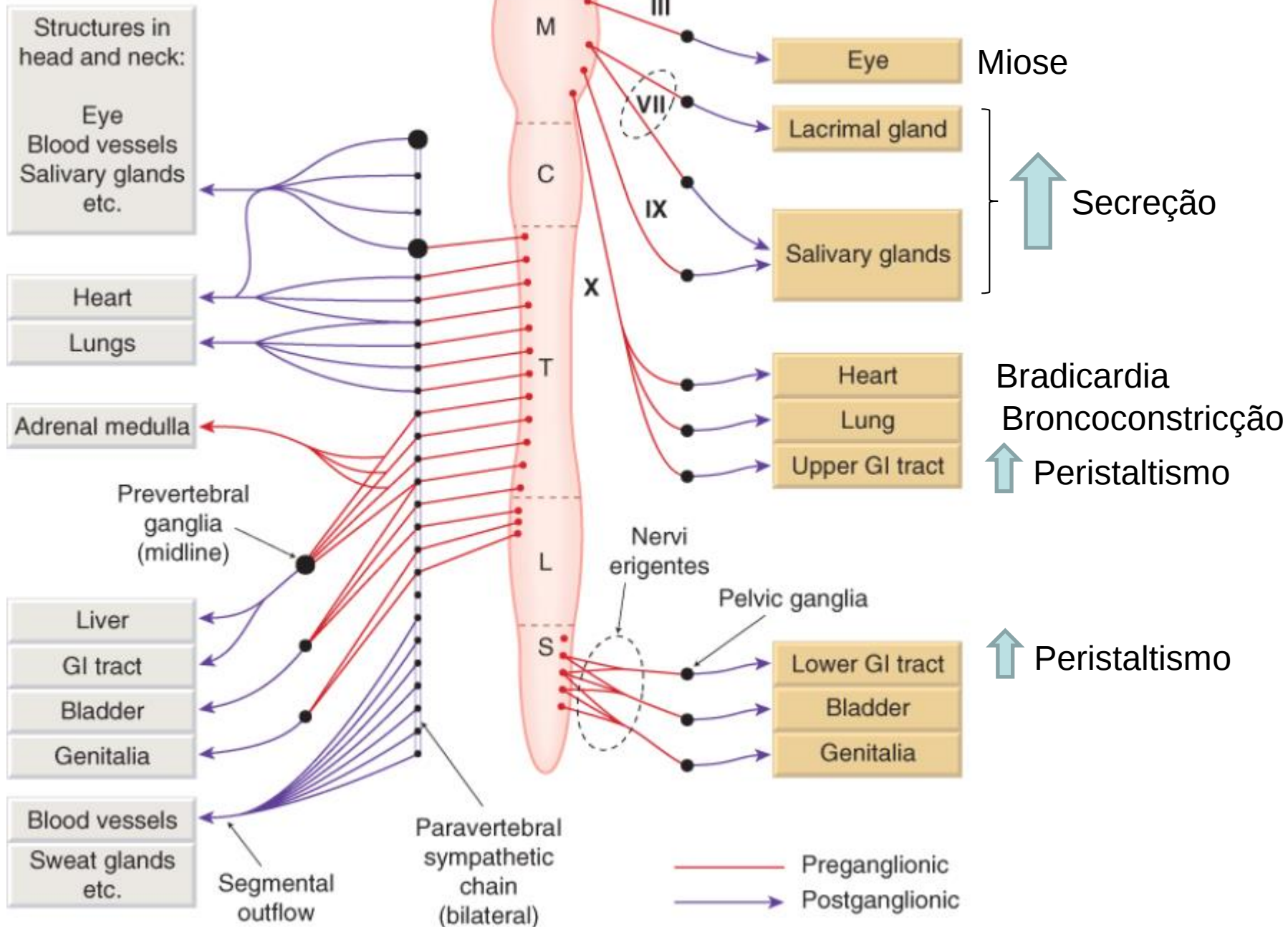
Sympathetic

Parasympathetic



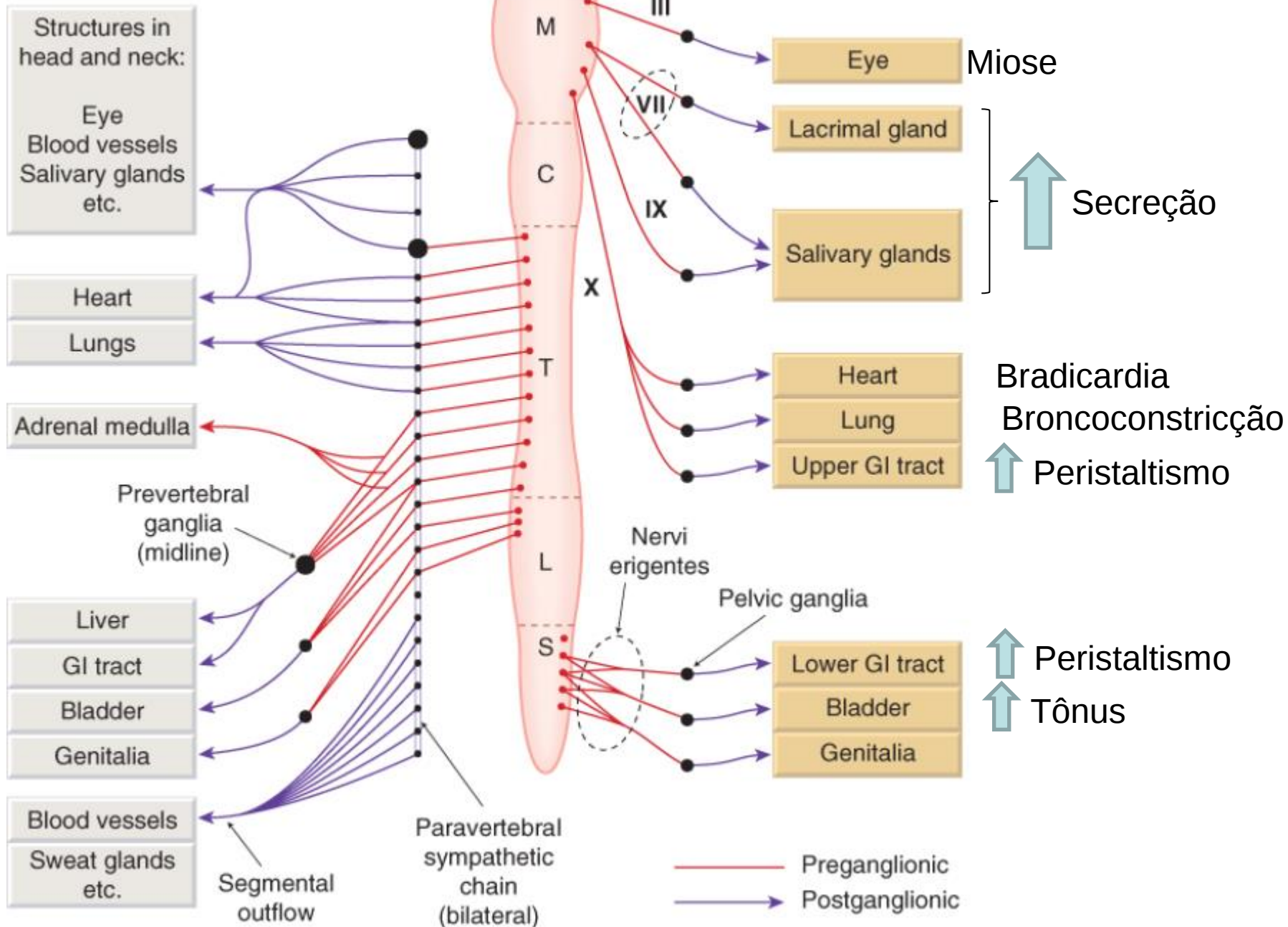
Sympathetic

Parasympathetic

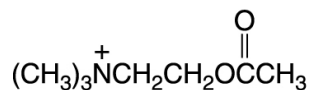


Sympathetic

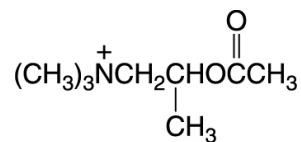
Parasympathetic



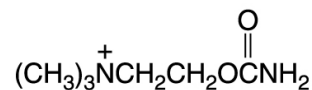
Colinérgicos de ação direta



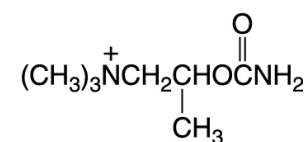
ACETYLCHOLINE



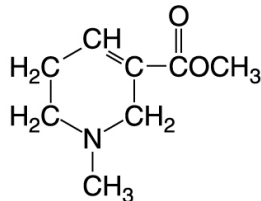
METHACHOLINE



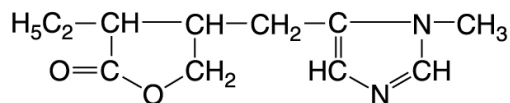
CARBACHOL



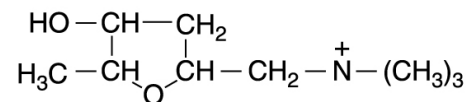
BETHANECHOL



ARECOLINE



PILOCARPINE



MUSCARINE

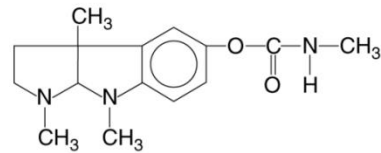
Quadro 9-1**Algumas propriedades farmacológicas dos ésteres de colina e alcaloides naturais**

	HIDRÓLISE PELAS COLINESTERASES	ATIVIDADE MUSCARÍNICA				Antagonismo pela atropina	ATIVIDADE NICOTÍNICA
		<i>Cardio-vascular</i>	<i>Gastrin-testinal</i>	<i>Bexiga</i>	<i>Olho (tópica)</i>		
Acetilcolina	+++	++	++	++	+	+++	++
Metacolina	+	+++	++	++	+	+++	+
Carbacol	—	+	+++	+++	++	+	+++
Detanecol	—	±	+++	+++	++	+++	—
Muscarina	—	++	+++	+++	++	+++	—
Pilocarpina	—	+	+++	+++	++	+++	—

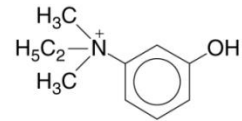
Metacolina: Respiratório

Pilocarpina: glândulas sudorípara e salivar

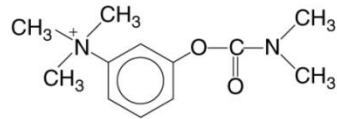
Colinérgicos de ação indireta: anticolinesterásicos



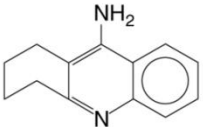
PHYSOSTIGMINE



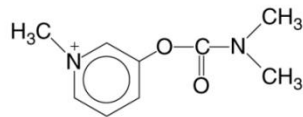
EDROPHONIUM



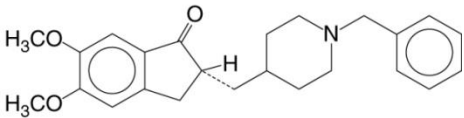
NEOSTIGMINE



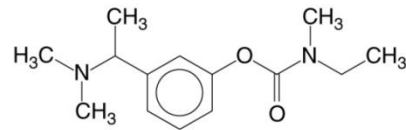
TACRINE



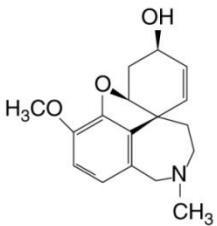
PYRIDOSTIGMINE



DONEPEZIL



RIVASTIGMINE



GALANTAMINE

Colinérgicos de ação indireta: anticolinesterásicos: organofosforados

Table 10-1

Chemical Classification of Representative Organophosphorus Compounds of Particular Pharmacological or Toxicological Interest

General formula			
$\begin{array}{c} \text{R}_1 \\ \\ \text{R}_2 - \text{P} - \text{X} \\ \\ \text{O} \end{array} \quad (\text{S})$			
Group A, X = halogen, cyanide, or thiocyanate leaving group; group B, X = alkylthio, arylthio, alkoxy, or aryloxy leaving group; group C, thionophosphorus or thio-thionophosphorus compounds; group D, quaternary ammonium leaving group. R₁ can be an alkyl (phosphonates), alkoxy (phosphorates) or an alkylamino (phosphoramidates) group.			
GROUP	STRUCTURAL FORMULA	COMMON, CHEMICAL, AND OTHER NAMES	COMMENTS
A		DFP; Isoflurophate; diisopropyl fluorophosphate	Potent, irreversible inactivator
		Tabun Ethyl N-dimethylphosphoramidocyanidate	Extremely toxic "nerve gas"
		Sarin (GB) Isopropyl methylphosphonofluoridate	Extremely toxic "nerve gas"
		Soman (GD) Pinacolyl methylphosphonofluoridate	Extremely toxic "nerve gas"; greatest potential for irreversible action/rapid aging
		Paraoxon (MINTACOL), E 600 O,O-Diethyl O-(4-nitrophenyl)-phosphate	Active metabolite of parathion
B		Malaoxon O,O-Dimethyl S-(1,2-dicarboxyethyl)-phosphorothioate	Active metabolite of malathion
		Parathion O,O-Diethyl O-(4-nitrophenyl)-phosphorothioate	Agricultural insecticide, resulting in numerous cases of accidental poisoning; phased out in 2003.
C		Diazinon, Dimpylate O,O-Diethyl O-(2-isopropyl-6-methyl-4-pyrimidinyl) phosphorothioate	Insecticide; use limited to non-residential agricultural settings
		Chlorpyrifos O,O-Diethyl O-(3,5,6-trichloro-2-pyridyl) phosphorothioate	Insecticide; use limited to non-residential agricultural settings
C		Malathion O,O-Dimethyl S-(1,2-dicarboethoxyethyl) phosphorodithioate	Widely employed insecticide of greater safety than parathion or other agents because of rapid detoxification by higher organisms
		Echothiophate (PHOSPHOLINE IODIDE), MI-217 Diethoxyphosphinylthiocholine iodide	Extremely potent choline derivative; administered locally in treatment of glaucoma; relatively stable in aqueous solution

Sympathetic

Structures in head and neck:

Eye
Blood vessels
Salivary glands
etc.

Heart

Lungs

Adrenal medulla

Prevertebral ganglia (midline)

Liver

GI tract

Bladder

Genitalia

Blood vessels

Sweat glands
etc.

Segmental outflow

Paravertebral sympathetic chain (bilateral)

Parasympathetic

Eye

Lacrimal gland

Salivary glands

Heart

Lung

Upper GI tract

Nervi erigentes

Pelvic ganglia

Lower GI tract

Bladder

Genitalia

Preganglionic

Postganglionic

Miose

M3

↑
Secreção M3

Bradicardia M2

Broncoconstricção

↑
Peristaltismo M3

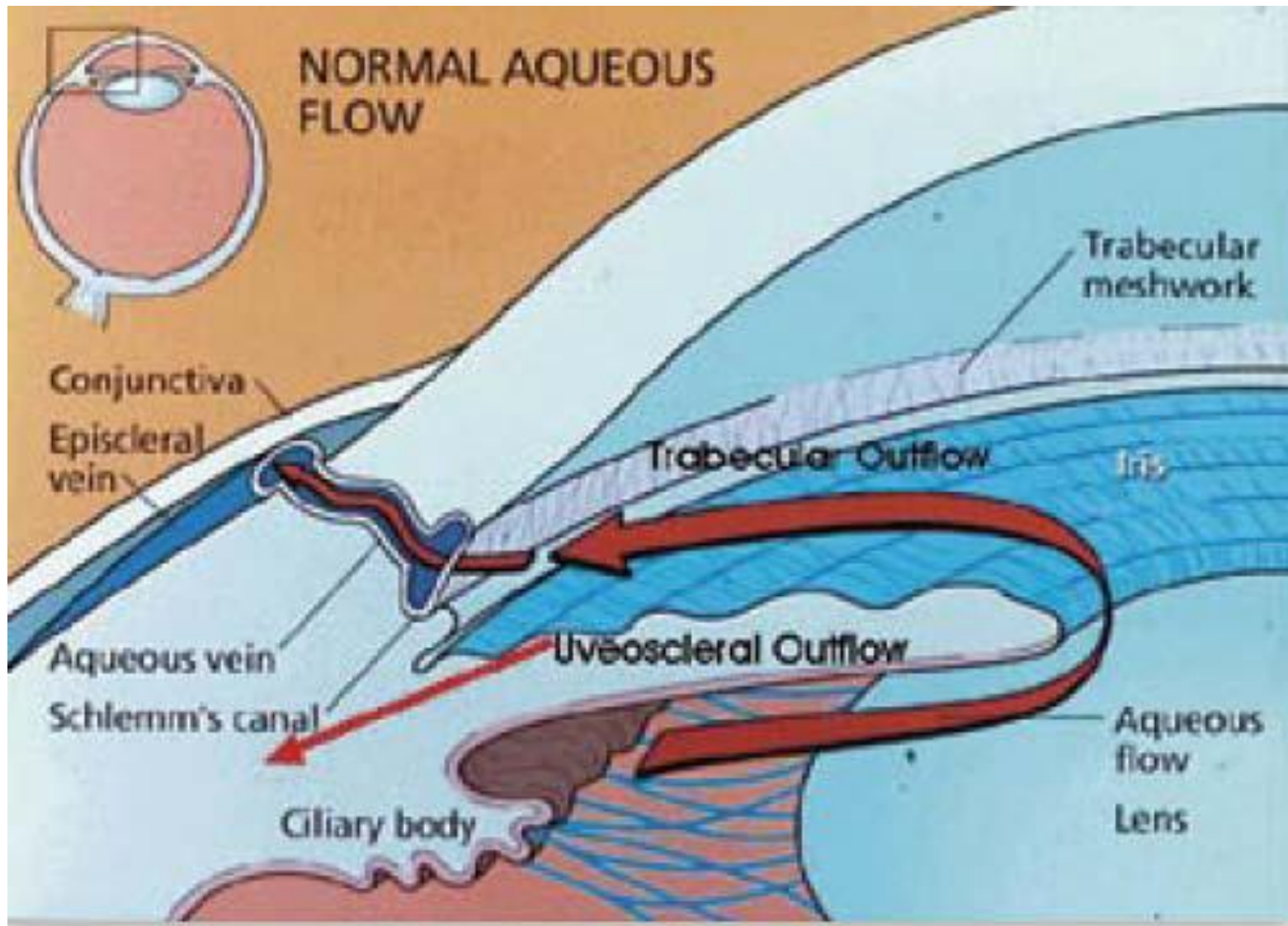
↑
Peristaltismo

↑
Tônus M3

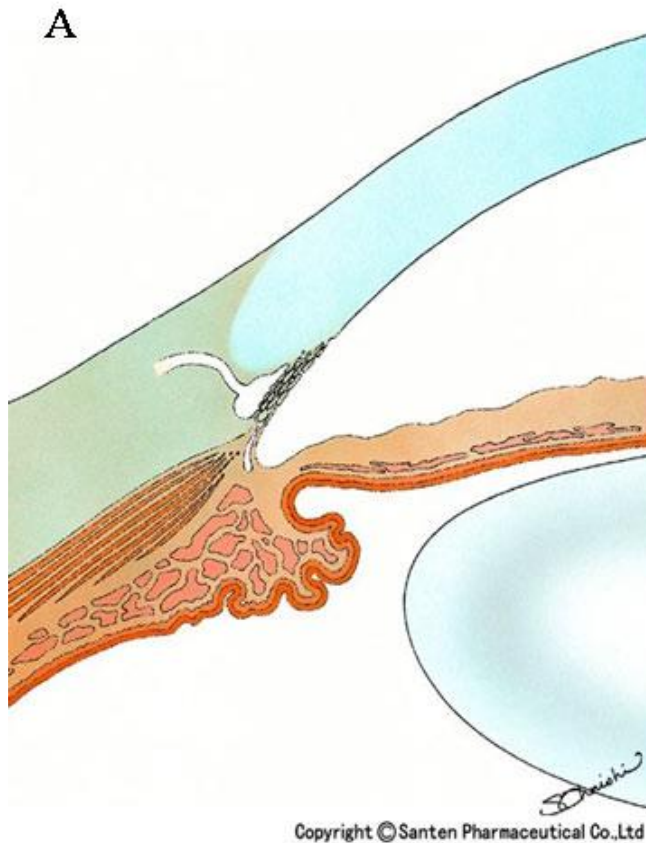
Usos clínicos

Aparelho	Patologia/Uso	Fármaco
Visual	Glaucoma	Pilocarpina, Ecotiopato
Digestório	Xerostomia (boca seca) Síndrome de Sjögren (boca e olhos secos)	Pilocarpina
	Atonia intestinal	Betanecol, neostigmina
Urinário	Atonia vesical	Betanecol, neostigmina

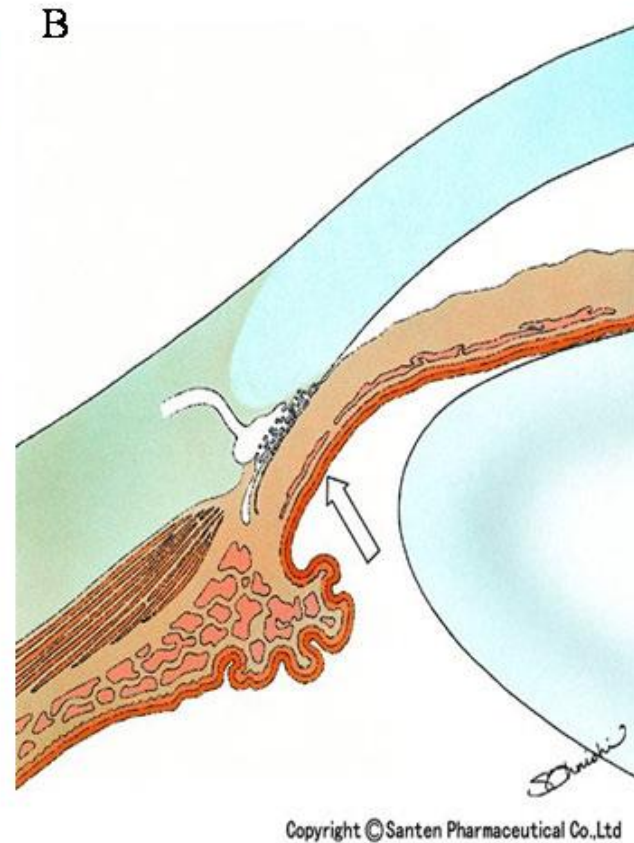
Aparelho visual:



GLAUCOMA



ÂNGULO ABERTO



ÂNGULO FECHADO

GLAUCOMA

Aparelho Visual

Elevação anormal da pressão intra-ocular: lesão, cegueira

**Redução
do humor
aquoso**

- β -bloqueador (timolol), agonista α_2 (apraclonidina)

**Aumento
da
drenagem**

- agonista muscarínico (Pilocarpina)

Aparelho	Patologia/Uso	Fármaco
Visual	Glaucoma	Pilocarpina, Ecotiopato
Digestório	Xerostomia (boca seca) Síndrome de Sjögren (boca e olhos secos)	Pilocarpina
	Atonia intestinal	Betanecol, neostigmina
Urinário	Atonia vesical	Betanecol, neostigmina

Glândulas exócrinas

- **Xerostomia – Boca seca (diversas causas: doenças, medicamentos)**
- **Síndrome de Sjögren: doença autoimune caracterizada pela infiltração de linfócitos das glândulas exócrinas (salivares e lacrimais)**

Aparelho	Patologia/Uso	Fármaco
Visual	Glaucoma	Pilocarpina, Ecotiopato
Digestório	Xerostomia (boca seca) Síndrome de Sjögren (boca e olhos secos)	Pilocarpina
	Atonia intestinal	Betanecol, neostigmina
Urinário	Atonia vesical	Betanecol, neostigmina

Intoxicações

Micetismo: intoxicação por fungo contendo muscarina

Sinais e sintomas: efeitos do reforço muscarínico

Tratamento: anticolinérgico (atropina)

Organofosforados

Sinais e Sintomas: efeitos do reforço muscarínico
efeitos do reforço nicotínico

Tratamento: anticolinérgico (atropina) + reativadores enzimáticos (oximas)

Intoxicação por anticolinesterásicos

Efeitos muscarínicos exacerbados

MIOSE

ESPASMO DA ACOMODAÇÃO

PERDA DA VISÃO DE LONGE

BRONCOCONSTRICÇÃO

AUMENTO SECREÇÃO RESPIRATÓRIA

BRADICARDIA

HIPOTENSÃO

DEFECAÇÃO INCONTROLÁVEL

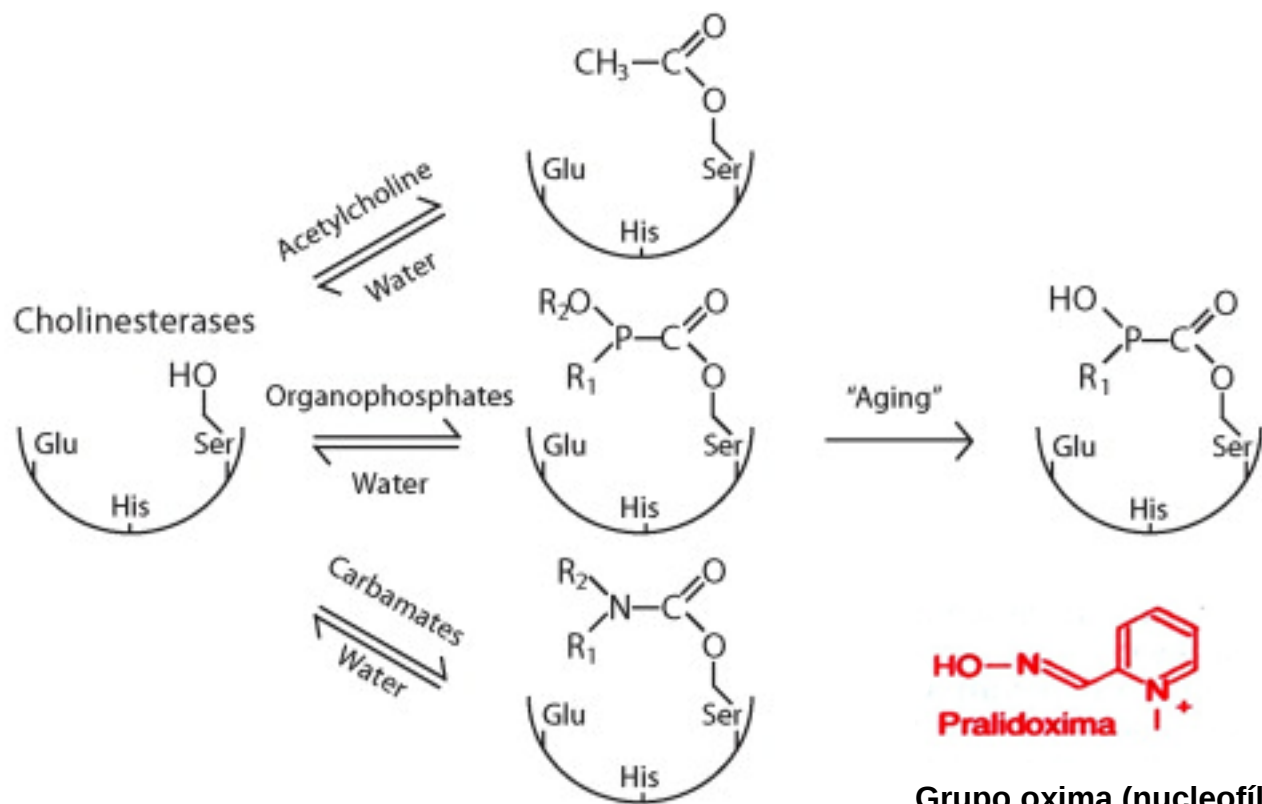
MICÇÃO INCONTROLÁVEL

Efeitos nicotínicos exacerbados

BLOQUEIO DA JNM POR DESPOLARIZAÇÃO PROLONGADA

Reativação da colinesterase

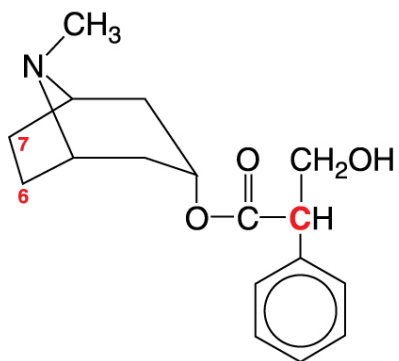
Pralidoxima



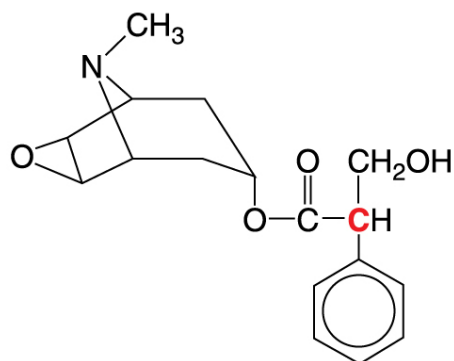
Grupo oxima (nucleofílico)
atrai o grupo fosfato
removendo- do sítio
catalítico da enzima.

Anticolinérgicos

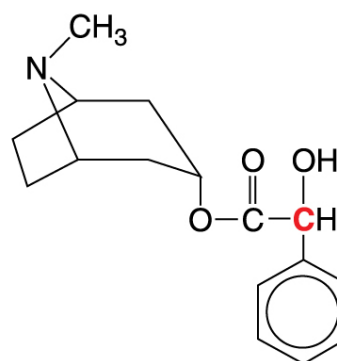
Anticolinérgicos



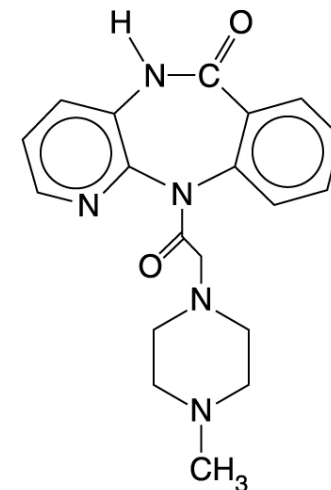
ATROPINE



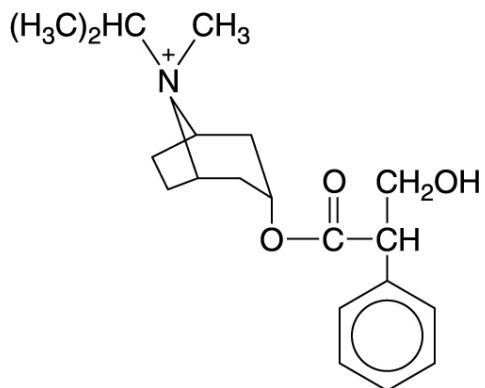
SCOPOLAMINE



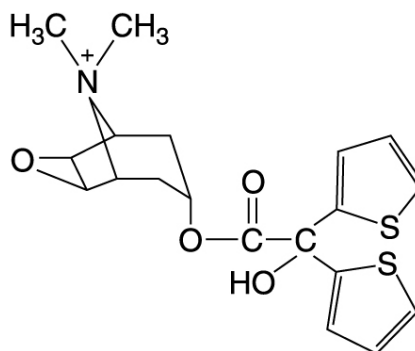
HOMATROPINE



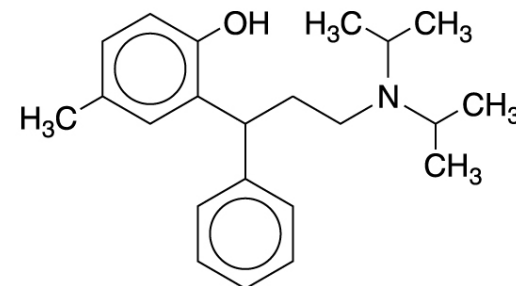
PIRENZEPINE



IPRATROPIUM



TIOTROPIUM



TOLTERODINE

Sympathetic

Structures in head and neck:

Eye
Blood vessels
Salivary glands
etc.

Heart

Lungs

Adrenal medulla

Prevertebral ganglia (midline)

Liver

GI tract

Bladder

Genitalia

Blood vessels
Sweat glands
etc.

Segmental outflow

Paravertebral sympathetic chain (bilateral)

Parasympathetic

Eye

Lacrimal gland

Salivary glands

Heart

Lung

Upper GI tract

Nervi erigentes

Pelvic ganglia

Lower GI tract

Bladder

Genitalia

— Preganglionic
— Postganglionic

~~Miose~~ Midríase

~~Secreção~~

~~Bradycardia~~

Taquicardia

~~Broncoconstricção~~

Broncodilatação

~~Peristaltismo~~

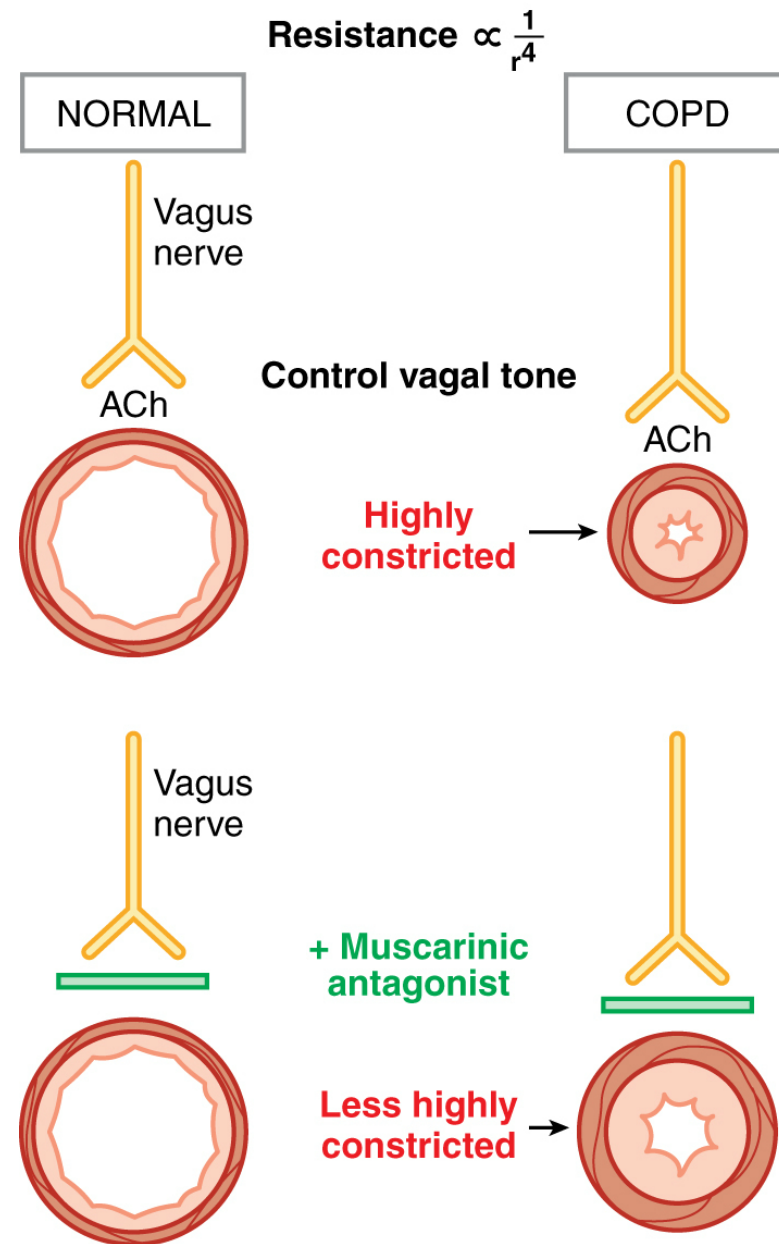
~~Peristaltismo~~

~~Tônus~~

Usos clínicos

Aparelho	Patologia/Uso	Fármaco
Visual	Midriático (exame de fundo de olho)	Tropicamida, ciclopentolato
Cardiovascular	Bradicardia (pós infarto do miocárdio)	Atropina
Respiratório	Asma e DPOC	Ipratrópio
Digestório	Anti-espasmódico	Escopolamina
	Úlcera Péptica	Pirenzepina (anti-M₁)
Urinário	Bexiga hiperativa/incontinência urinária	Darifenacina (anti-M₃)

Tratamento da DPOC



Aparelho	Patologia/Uso	Fármaco
Visual	Midriático (exame de fundo de olho)	Tropicamida, ciclopentolato
Cardiovascular	Bradicardia (pós infarto do miocárdio)	Atropina
Respiratório	Asma e DPOC	Ipratrópio
Digestório	Anti-espasmódico	Escopolamina
	Úlcera Péptica	Pirenzepina (anti-M₁)
Urinário	Bexiga hiperativa/incontinência urinária	Darifenacina (anti-M₃)

Intoxicação Atropínica

Sinais e sintomas: midríase parálitica (fotofobia), rubor, taquicardia, febre (inibição da sudorese), pele e mucosas secas, atonia intestinal, atonia vesical, distensão abdominal, bexigoma, agitação

Tratamento: anticolinesterásico (fisostigmina)

**Medidas
adjuvantes**

**{ benzodiazepínico (controlar agitação)
compressas frias (abaixar a temperatura)
sondas vesical e retal**

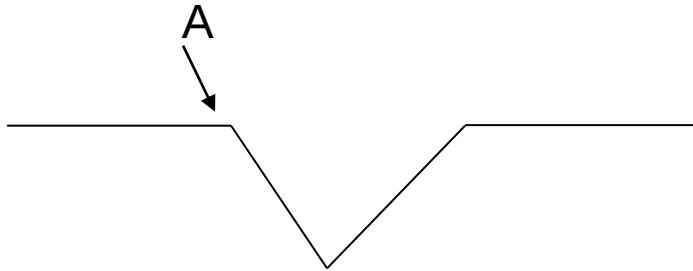
Referências Bibliográficas

- 1. Goodman & Gilman's. The pharmacological basis of therapeutics**
- 2. Rang & Dale's Pharmacology.**

Curvas de PA

M3: relaxamento músculo liso vascular (NO)

M2: diminuição contração músculo cardíaco, bradicardia



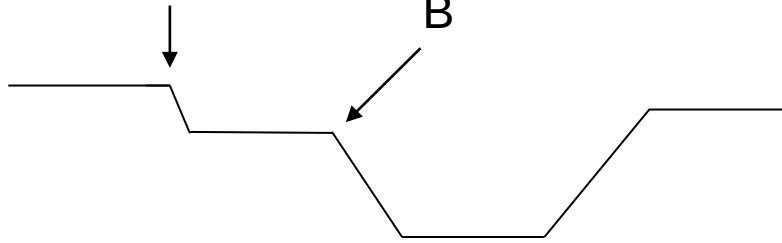
A=acetilcolina

$$PA=FC \times VS \times R_p$$

anticolinesterásico

B=acetilcolina

Neostigmina



C= pilocarpina

