The Autonomic Nervous System and Toxic Syndromes

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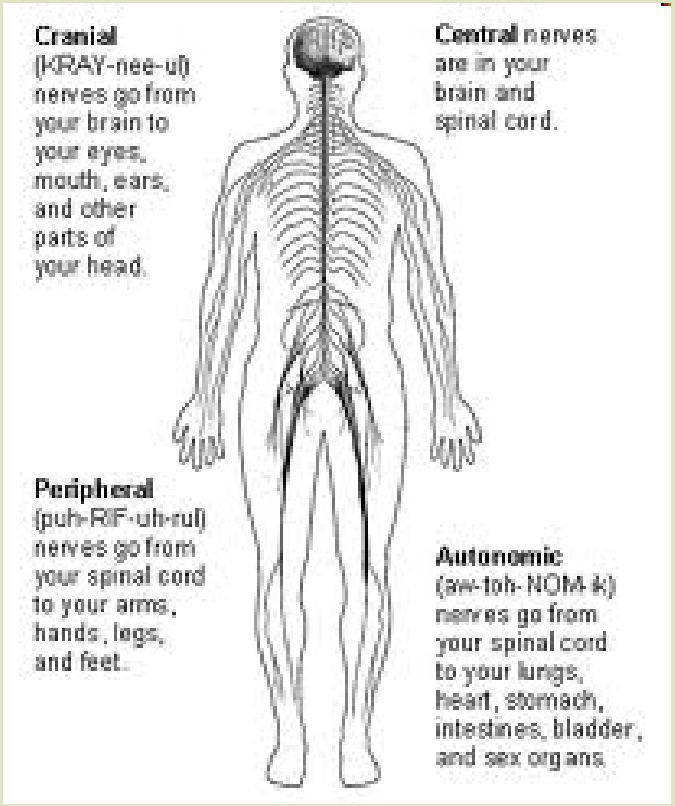


Objectives

VCU Medical Center
Every Day, A New Discovery.

- Review the anatomy and physiology of the autonomic nervous system
- Improve understanding of medications that affect the autonomic nervous system
- Use clinical findings to predict potential causes of toxic syndromes
- Go over a bunch of tox cases and make this lecture slightly more enjoyable than a hernia

Key:
- = Structure
- = Function

Central Nervous System (CNS)
- Brain and spinal cord
- Integrative and control centers

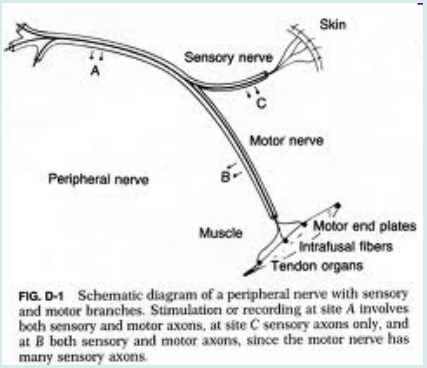


FIG. D-1 Schematic diagram of a peripheral nerve with sensory and motor branches. Stimulation or recording at site *A* involves both sensory and motor axons, at site *C* sensory axons only, and at *B* both sensory and motor axons, since the motor nerve has many sensory axons.

Peripheral Nervous System (PNS)
- Cranial nerves and spinal nerves
- Communication lines between the CNS and the rest of the body

Sensory (afferent) division
- Somatic and visceral sensory nerve fibers
- Conducts impulses from receptors to the CNS

Motor (efferent) division
- Motor nerve fibers
- Conducts impulses from the CNS to effectors (muscles and glands)

Sympathetic division
- Mobilizes body systems during activity ("fight or flight")

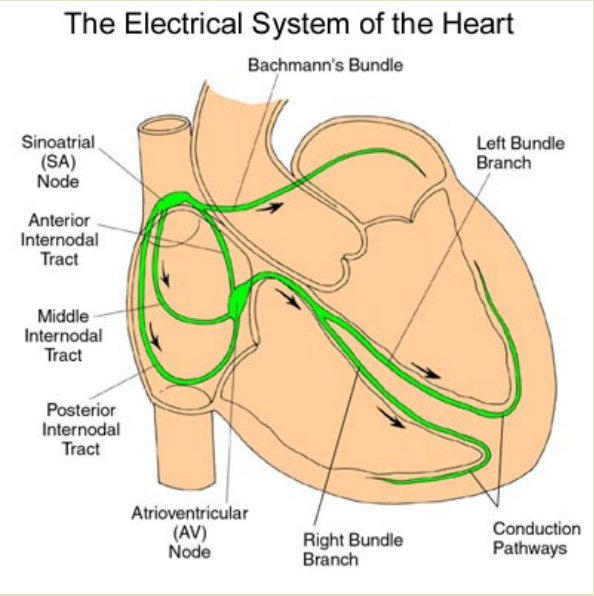
Parasympathetic division
- Conserves energy
- Promotes "housekeeping" functions during rest

Autonomic nervous sytem (ANS)
- Visceral motor (involuntary)
- Conducts impulses from the CNS to cardiac muscles, smooth muscles, and glands

Somatic nervous sytem
- Somatic motor (voluntary)
- Conducts impulses from the CNS to skeletal muscles

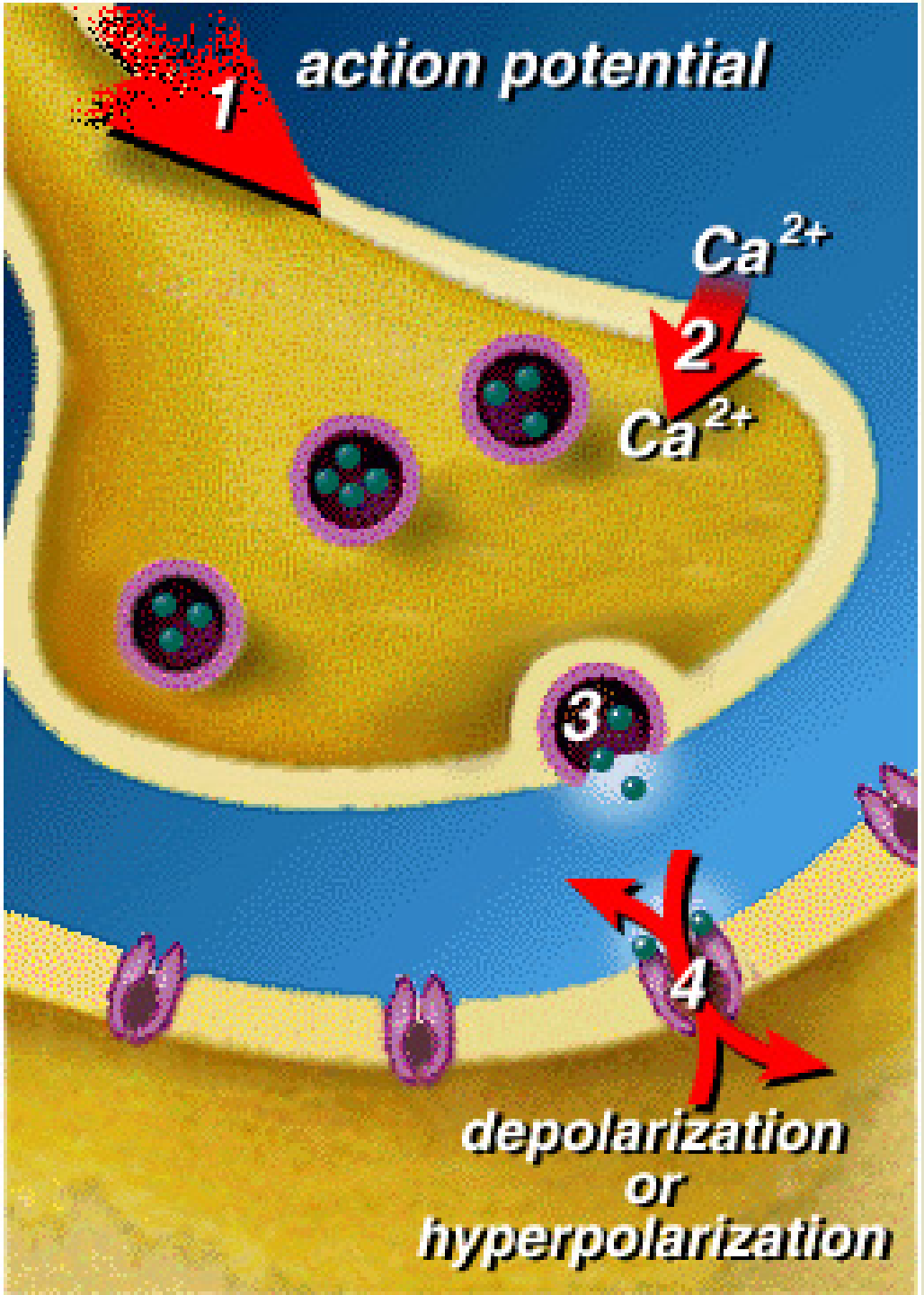
Autonomic Nervous System

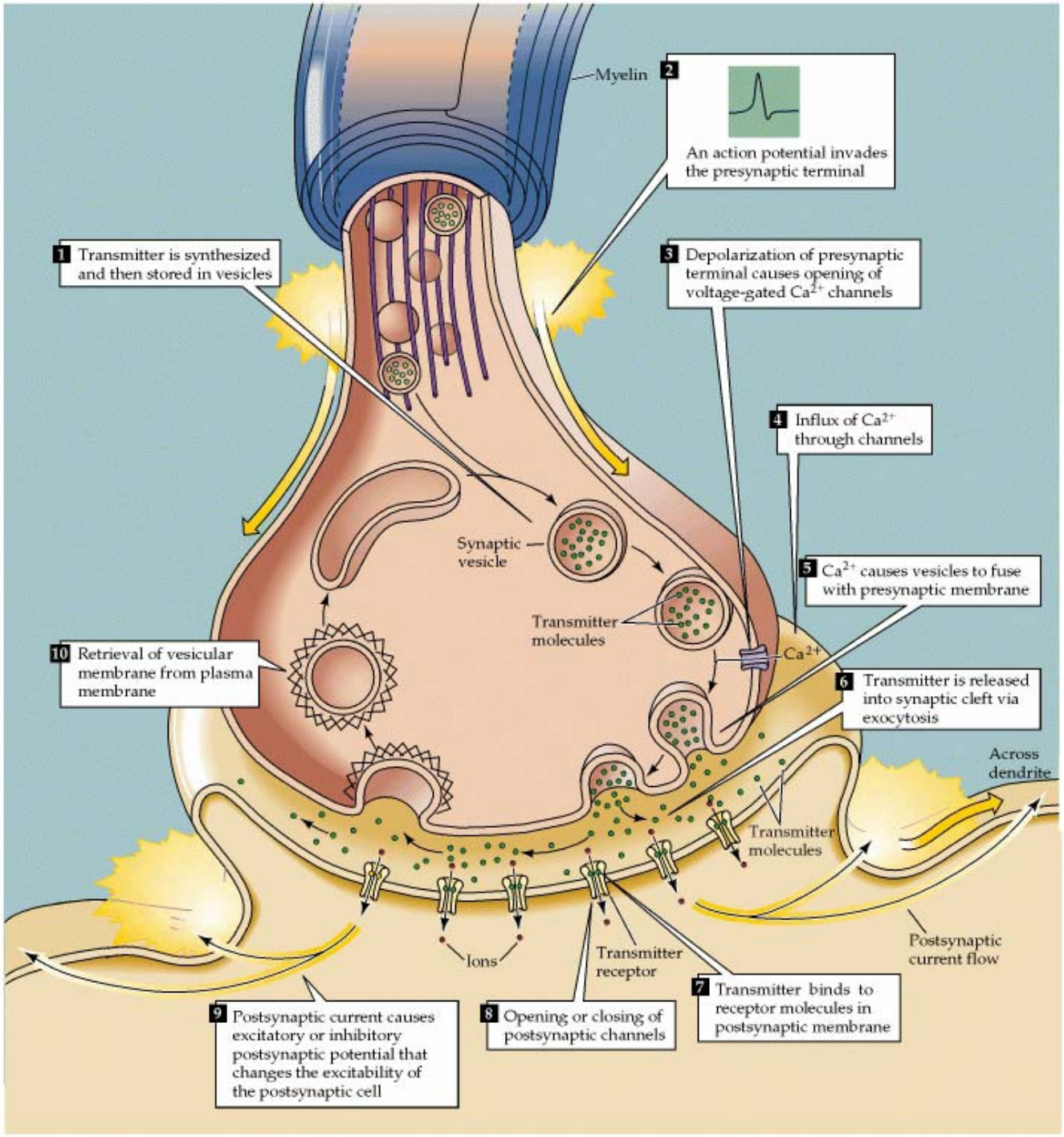
- Temperature regulation
- Fluid and electrolyte balance
- Metabolism rate
- Digestion and excretion
- Cardiovascular function



Autonomic Nervous System

- Responsible for control of involuntary responses
- Two functional divisions:
  - Sympathetic (adrenergic)
  - Parasympathetic (cholinergic)
- Preganglionic fibers – from spinal cord to ganglia
- Postganglionic fibers – from ganglia to target organs
- Synapses – space between nerve cells (endings)
- Neurotransmitters – chemical messengers
  - Norepinephrine (NE)
  - Acetylcholine (Ach)


action potential
1
Ca 2+
2
Ca 2+
3
4
depolarization
or
hyperpolarization


Myelin
2 An action potential invades the presynaptic terminal
1 Transmitter is synthesized and then stored in vesicles
3 Depolarization of presynaptic terminal causes opening of voltage-gated Ca^{2+} channels
4 Influx of Ca^{2+} through channels
Synaptic vesicle
5 Ca^{2+} causes vesicles to fuse with presynaptic membrane
Transmitter molecules
Ca^{2+}
10 Retrieval of vesicular membrane from plasma membrane
6 Transmitter is released into synaptic cleft via exocytosis
Across dendrite
Transmitter molecules
Ions
Transmitter receptor
Postsynaptic current flow
9 Postsynaptic current causes excitatory or inhibitory postsynaptic potential that changes the excitability of the postsynaptic cell
8 Opening or closing of postsynaptic channels
7 Transmitter binds to receptor molecules in postsynaptic membrane

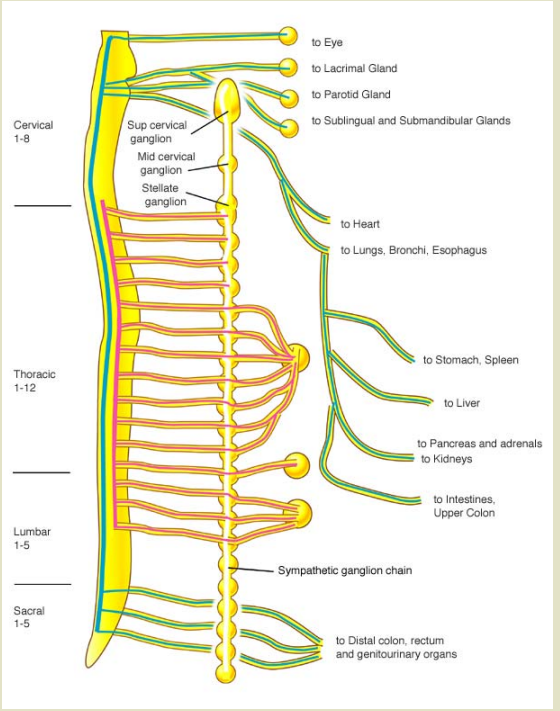
Autonomic Nervous System

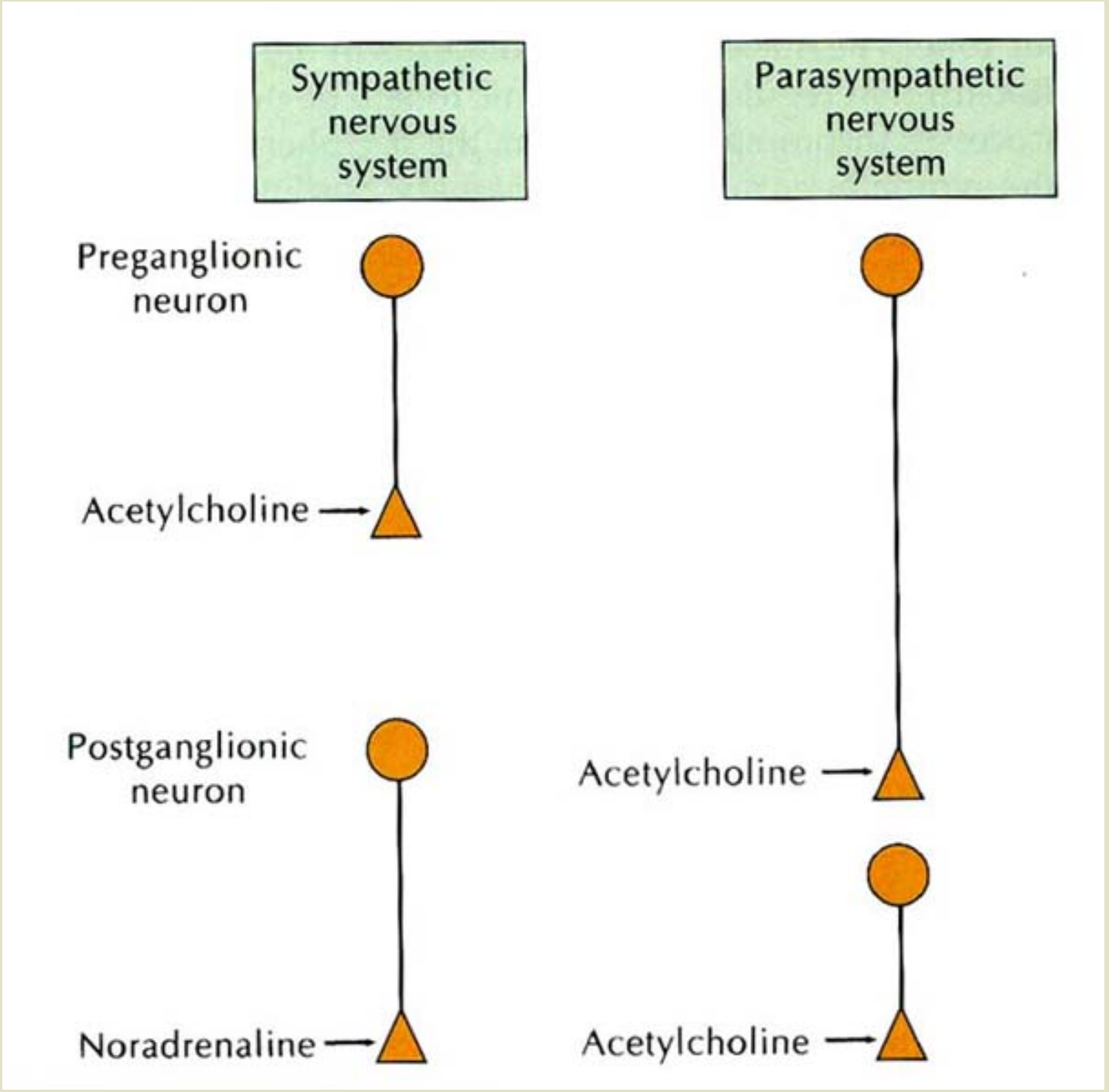
A. Sympathetic (thoracolumbar)

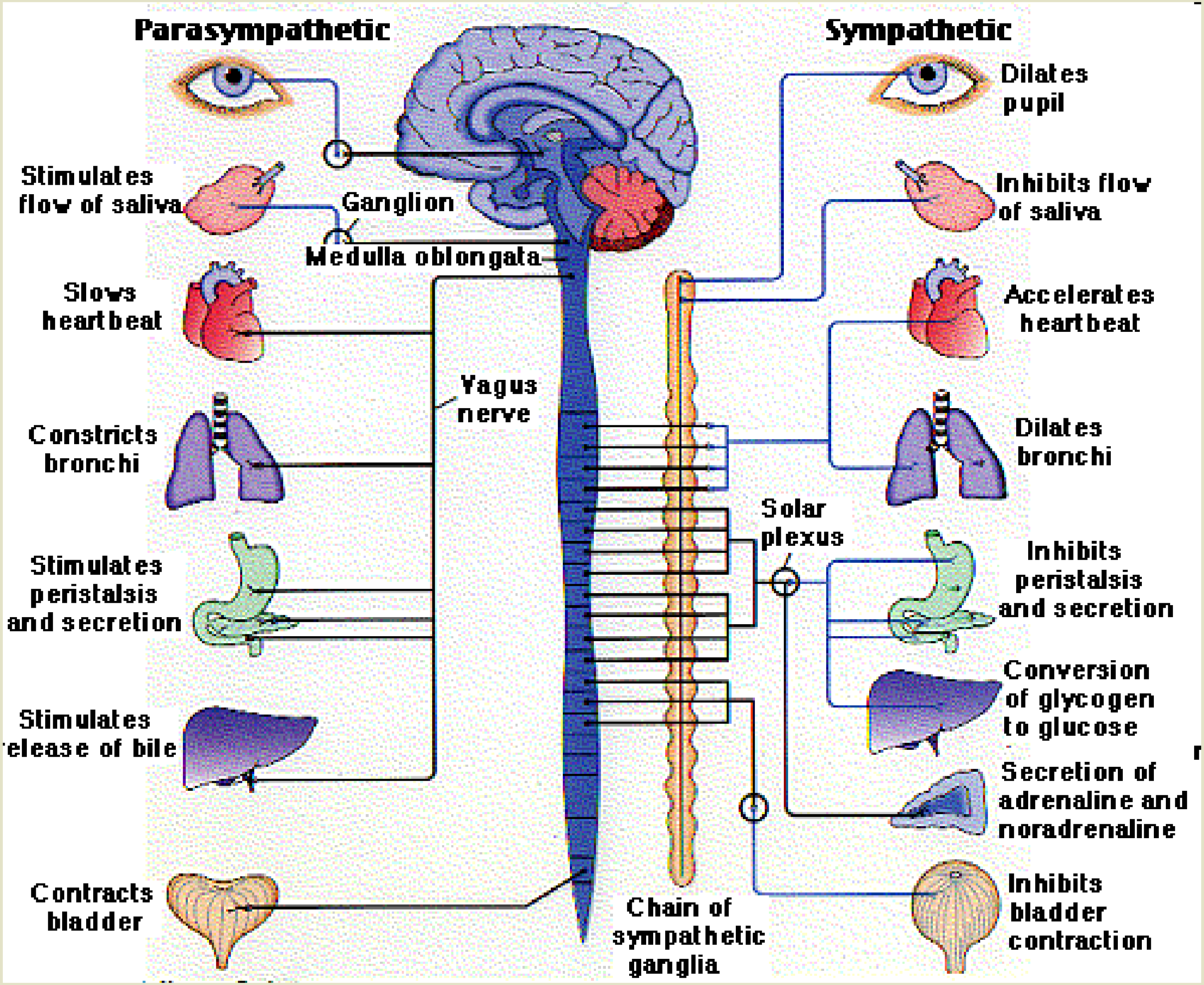
- Peripheral neurotransmitter = norepinephrine
- Receptors: alpha (1 and 2) & beta (1 and 2)

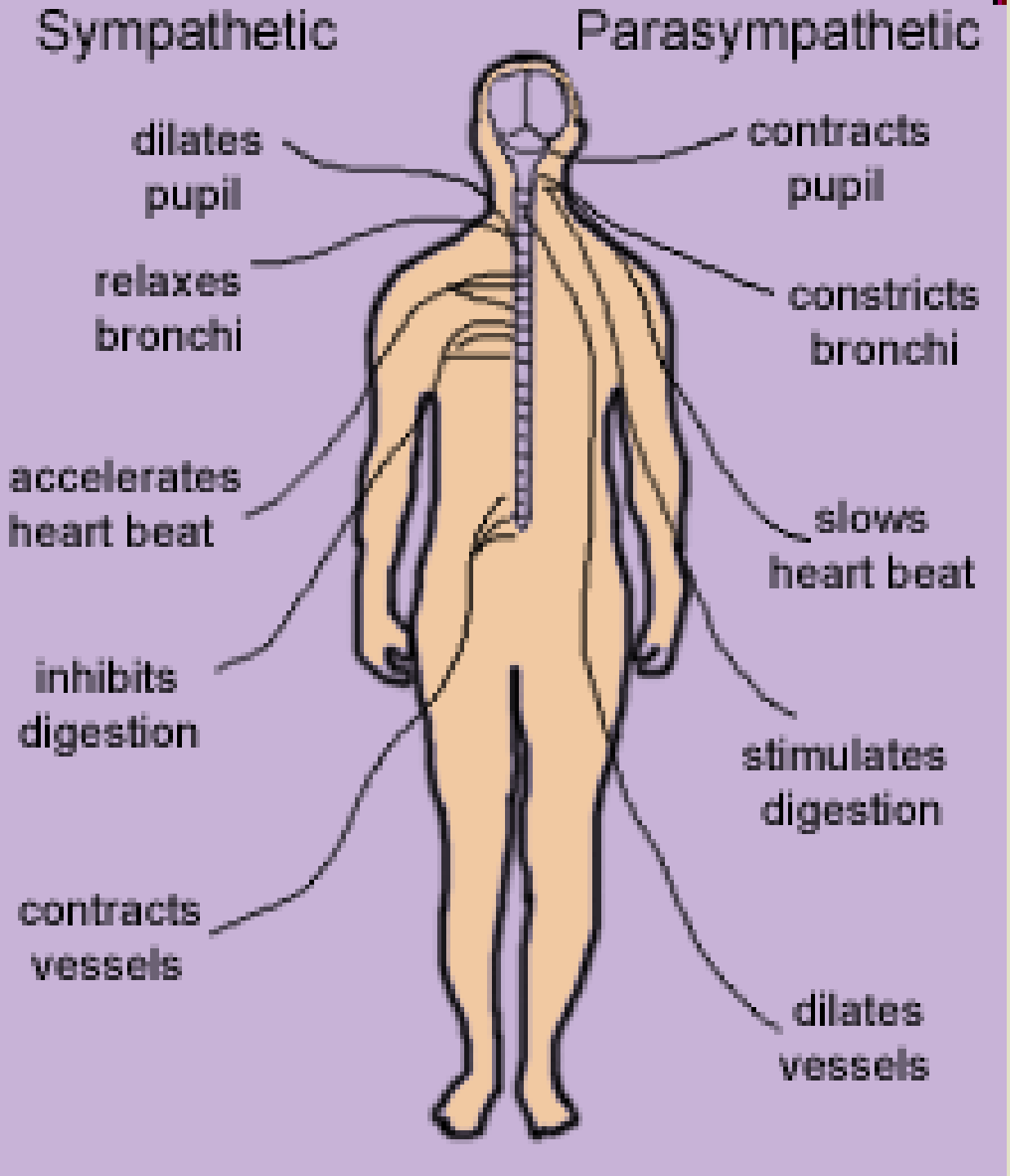
B. Parasympathetic (craniosacral)

- Peripheral neurotransmitter = acetylcholine
- Cholinergic receptors: muscarinic and nicotinic




Sympathetic nervous system
Parasympathetic nervous system
Preganglionic neuron
Acetylcholine
Postganglionic neuron
Noradrenaline
Acetylcholine
Acetylcholine


Parasympathetic
Sympathetic
Dilates pupil
Stimulates flow of saliva
Ganglion
Medulla oblongata
Inhibits flow of saliva
Slows heartbeat
Accelerates heartbeat
Vagus nerve
Constricts bronchi
Dilates bronchi
Solar plexus
Stimulates peristalsis and secretion
Inhibits peristalsis and secretion
Conversion of glycogen to glucose
Stimulates release of bile
Secretion of adrenaline and noradrenaline
Contracts bladder
Chain of sympathetic ganglia
Inhibits bladder contraction


Sympathetic
Parasympathetic
dilates pupil
contracts pupil
relaxes bronchi
constricts bronchi
accelerates heart beat
slows heart beat
inhibits digestion
stimulates digestion
contracts vessels
dilates vessels

Physiologic Receptors in the Autonomic Nervous System

CHOLINERGIC (Acetylcholine)

Nicotinic: autonomic ganglia, adrenal medulla, striated muscle

Muscarinic: heart, smooth muscle, glands

ADRENERGIC (epinephrine, norepinephrine)

Alpha – 1: blood vessels, eyes, reproductive organs

Alpha – 2: regulate neurotransmitter release

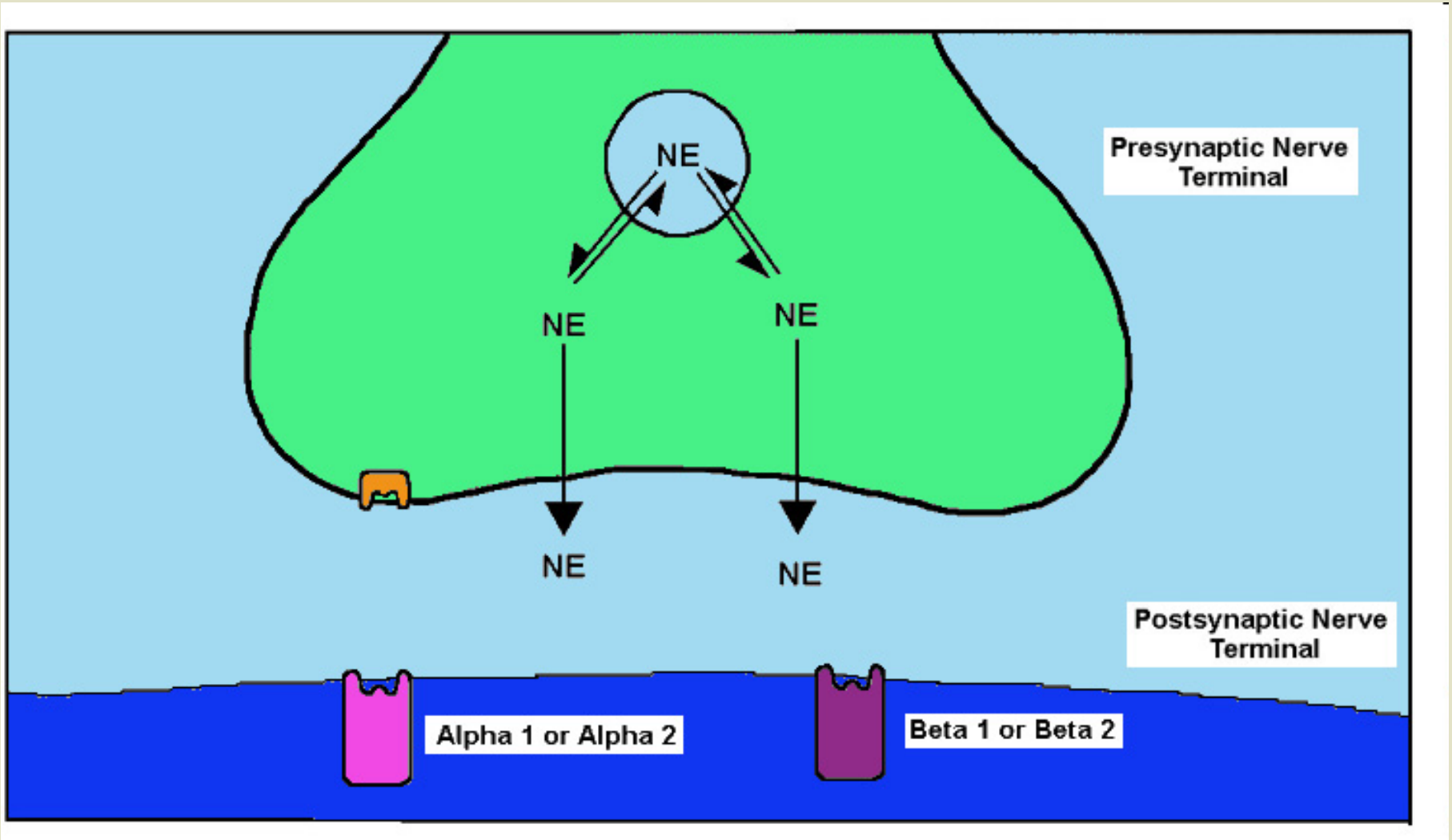
Beta – 1: heart and kidneys

Beta – 2: salivary glands, eyes, lungs, GI tract, arterioles of hear, lungs, skin, skeletal muscle

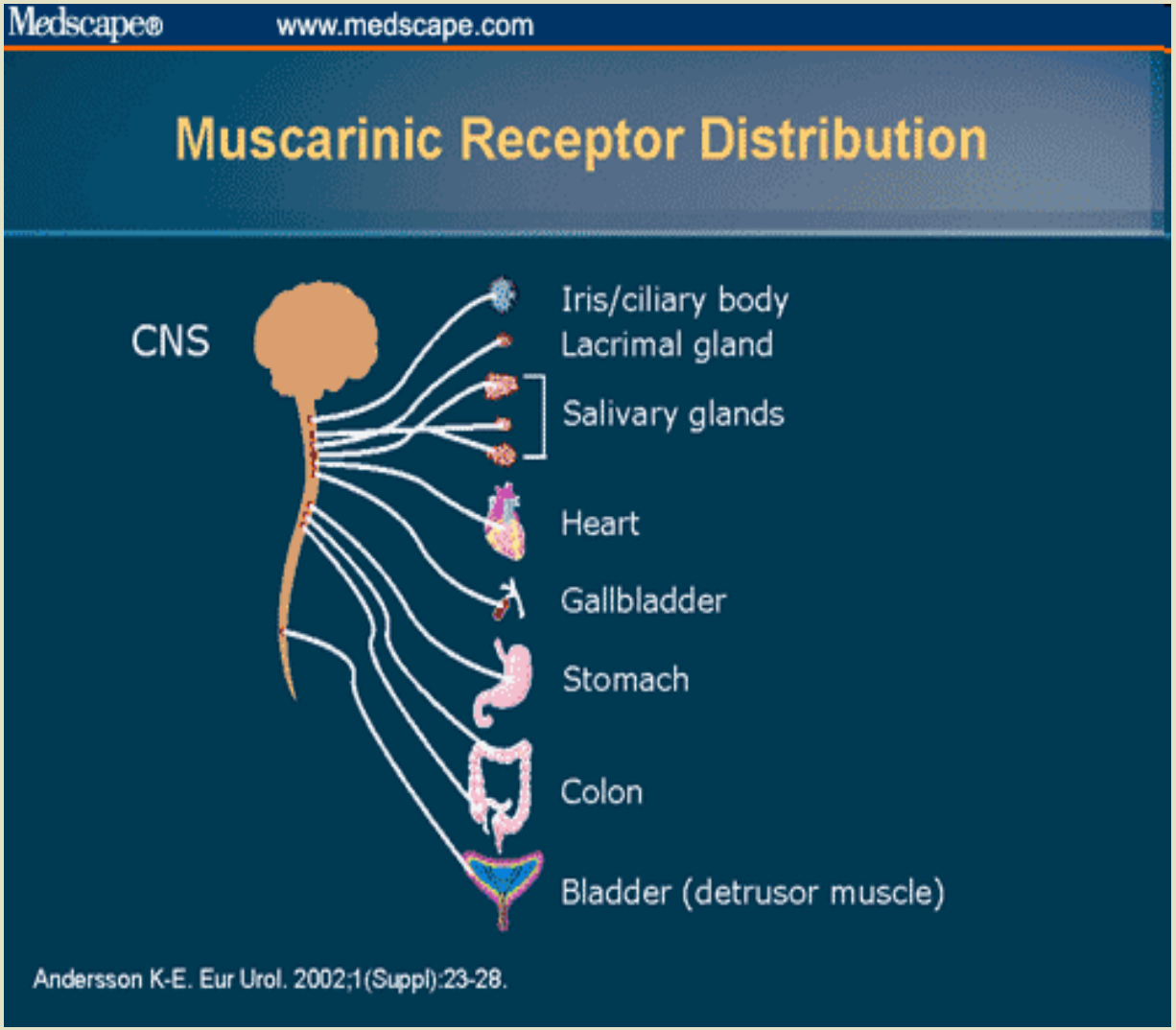
DOPAMINERGIC

CNS and renal vasculature

Adrenergic Transmission



Parasympathetic Receptors



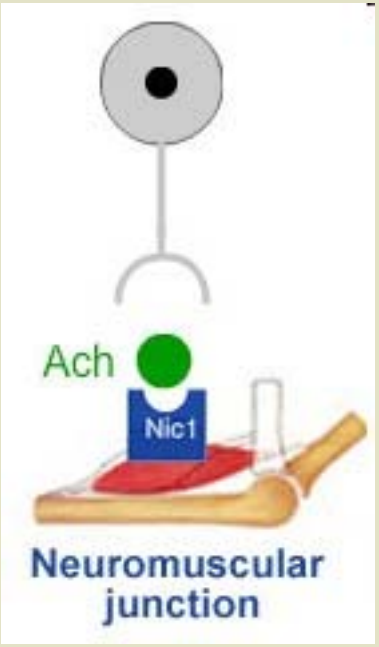


TABLE 2.
Location and Function of Muscarinic Receptors[18-21,23,24,35-44]

	Location	Cellular Function	Systemic Function	Changes in Schizophrenia
M_1	Striatum, cortex, hippocampus	Gq; Postsynaptic, modulate fast transmission and metabotropic function	Learning, memory, possible role in some types of epilepsy, cleave amyloid precursor protein, IL-2 production	Down in hippocampus, stratum, PFC, NAc
M_2	Basal forebrain, thalamus, heart, brainstem, pupil, exocrine glands, spinal cord	Gi; Presynaptic inhibitory auto/heteroreceptor	Salivation, akinesia, bradycardia, smooth muscle contractility, bronchoconstriction, tremor, hypothermia, analgesia, axonal growth	Down in striatum
M_3	Brain (evenly distributed), pupil, hypothalamus, exocrine glands, peripheral arteries	Like M_1	Salivation, smooth muscle contractility, vasorelaxation, NO release, appetite	Unknown
M_4	Striatum, cortex, hippocampus, spinal cord	Like M_2 plus inhibitory postsynaptic	Regulate striatal DA release, modulate PPI, analgesia, keratinocyte migration	Down in hippocampus, stratum, PFC, NAc
M_5	DA neurons, basal ganglia, brain vasculature	Like M_1	Cerebral arterial vasorelaxation	Unknown

M=muscaranic; Gq=G protein that activates phospholipase C; Gi=inhibitory G protein; PFC=prefrontal cortex; DA=dopaminergic; NAc=nucleus accumbens; PPI=pre-pulse inhibition.

Sellin AK, Shad M, Tamminga C. *CNS Spectr*. Vol 13, No 11. 2008.

Autonomic NS Receptors

Ach

Nicotinic (Opens Na+/K+ gate)
- synaptic communication
- excites brain
- at neuromuscular junction

Muscarinic (Second messengers)
- watery saliva
- slows heart rate
- constricts bronchioles
- stimulates digestive processes
- increases insulin release

See Figure 11-5 in Silverthorn

NE (& E)

α_1 (Activates phospholipase C)
- mucous in saliva
- constricts arteries
- constricts bronchioles

α_2 (Decreases cAMP)
- inhibits digestive processes
- inhibits insulin secretion

β_1 (Increases cAMP)
- increases heart rate

β_2 (Decreases cAMP)
- dilates veins
- inhibits digestive processes
- dilates bronchioles

β_3 (Increases cAMP)
- fat breakdown

Autonomic Pharmacology

- Sympathetic
  - Agonist: sympathomimetic / adrenergic (epinephrine)
  - Antagonist: sympatholytic
    - Alpha receptor blockers (phentolamine)
    - Beta blockers (propranolol, metoprolol)
- Parasympathetic
  - Agonist: cholinergic (acetylcholine)
  - Antagonist: parasympatholytic, anticholinergic
    - Muscarinic receptor blocker (atropine)
    - Nicotinic antagonist (neuromuscular blockers, ganglionic blockers)

Toxic Syndromes

- Physical signs
- Patient symptoms
- Characteristic odors, color
- Laboratory findings
- Suggests, but does not confirm, a diagnosis

TOXIC SYNDROMES – CASE 1

A 34 y/o female presents with confusion, disorientation and somnolence

HR	140	BP	130/80
RR	16	T	101.6

Pupils widely dilated, reactive

Skin hot, dry

Bowel sounds decreased

Mouth dry

Speech slurred

CLUE: depressed, took “sleeping pills”

Diagnosis ???


Benadryl®
ALLERGY
Diphenhydramine Hydrochloride
Antihistamine
For Allergy Relief
Sneezing
Runny Nose
Itchy, Watery Eyes
Itchy Throat
Easy to Swallow
24 ULTRATAB TABLETS


From the makers of
TYLENOL® PM
Fall Asleep Fast, Wake Up Refreshed
Simply Sleep™
Nighttime Sleep Aid
Contains Diphenhydramine HCl
Does NOT Contain Pain Reliever
Safe, Non-habit Forming
OTC SLEEP
PHARMACIST PREFERRED
INGREDIENT
48 Sleep Caps
48 CAPLETS 25 mg each
THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN

ANTICHOLINERGIC SYNDROME

- Antihistamines: pyrilamine, doxylamine, diphenhydramine, dimenhydrinate
- Phenothiazines, cyclic antidepressants
- Antiparkinson agents: benztropine, trihexiphenidyl
- Plants
  - Jimson weed (*Datura stramonium*)
  - Deadly nightshade (*Atropa belladonna*)
- Some Mushrooms (muscimol, ibotenic acid)
- Atropine, scopalamine
- Antispasmodics (belladonna, hyoscamine)

ANTICHOLINERGIC SYNDROME

Blind as a bat

Dry as a bone

Red as a beet

Hot as Hades

Mad as a hatter

TOXIC SYNDROMES – CASE 2

A 24 y/o male presents with seizures and coma.

HR	160
BP	190/100
RR	24
T	102

Pupils, dilated, reactive Marked diaphoresis

Bowel sound hypoactive

CLUE 1: EKG – narrow complex sinus tach

CLUE 2: Drug abuser

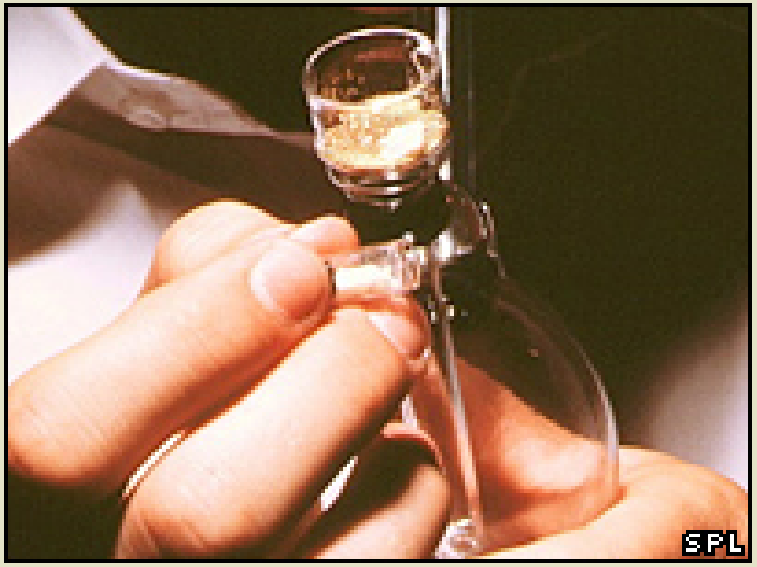
CLUE 3: HR & BP return to normal within 60 minutes

SYMPATHOMIMETIC SYNDROME

- Mixed alpha and beta adrenergic effects
- Clinical effects:
  - Tachycardia
  - Hypertension
  - CNS stimulation
  - Diaphoresis
  - Decreased GI motility
  - Miosis/Mydriasis

SYMPATHOMIMETIC SYNDROME

Dx: **cocaine toxicity**



Other agents:

- Amphetamines
- Ephedrine
- Pseudoephedrine
- Anoretics (Fen-Phen)
- Propylhexadrine
- Tyramine

FIGURE 1

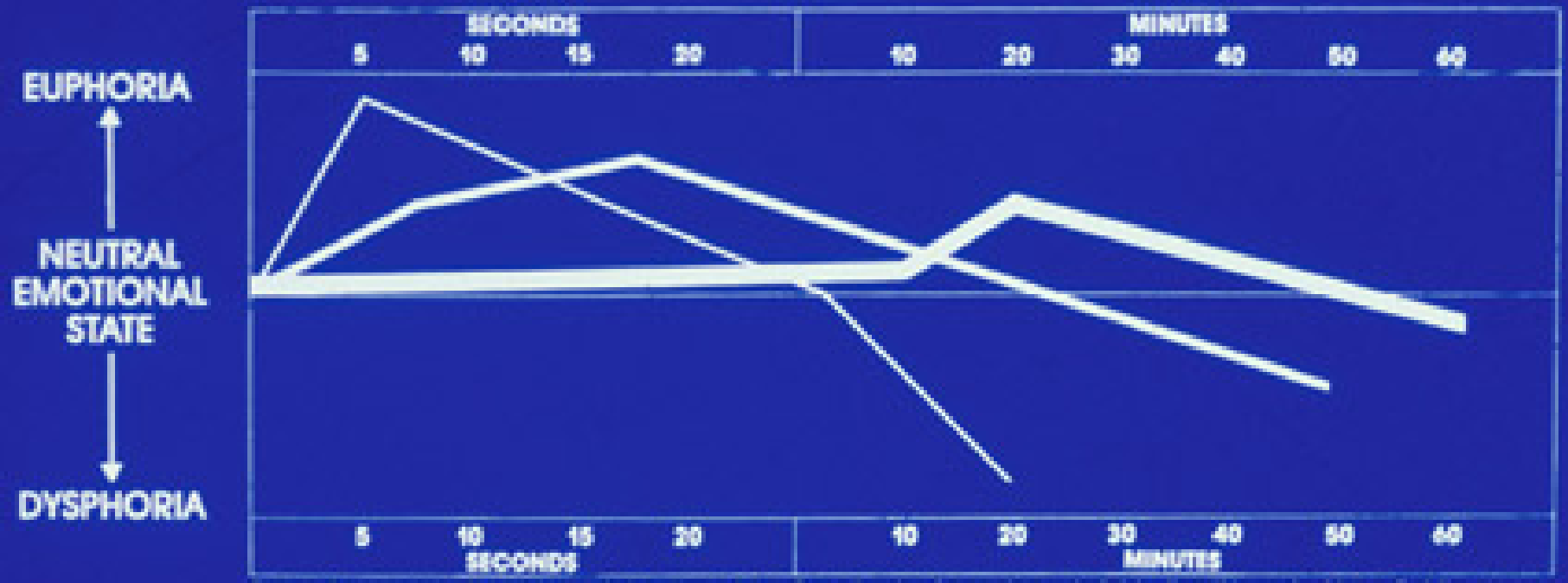


Figure 1 compares intensity and duration of the 3 methods of cocaine administration if ingested by a first time user.

SMOKING — Smoking results in a faster, more intense high but also a shorter one with the most marked crashing effect.

SHOOTING — Shooting has an almost immediate effect and slower decline but the dysphoria is also substantial.

SNORTING — Snorting results in a longer intense high and a less abrupt decline with fewer crashing symptoms.

TOXIC SYNDROMES – CASE 3

A 22 y/o male presents with lethargy, confusion, and complaining of severe crampy abdominal pain, vomiting and severe diarrhea.

HR	60
BP	110/70
RR	28, labored
T	99

Diaphoretic, cyanotic, drooling

Marked respiratory distress with rales

Bowel sounds hyperactive

Incontinent of bowel and bladder

CLUE: depressed Orkin Man recently broke up with his girlfriend

CHOLINERGIC SYNDROME

- Excess acetylcholine at muscarinic and nicotinic receptors
- Dx: Organophosphate insecticide
- Other Agents:
  - Carbamate insecticides
  - Physostigmine
  - Nicotine insecticides
  - Tobacco
  - Mushroom (Clitocybe, Inocybe)

CHOLINERGIC SYNDROME

D	diarrhea, diaphoresis
U	urination
M	miosis
B	bradycardia
B	bronchorrhea
E	emesis
L	lacrimation
S	salivation, sweating

TOXIC SYNDROMES – CASE 4

A 19 y/o male presents with headache and lethargy. No history of vomiting or diarrhea.

HR	60	BP	210/120
RR	16	T	99.9

Pupils dilated, sluggishly reactive

Skin slightly moist

Bowels sounds decreased

CLUE: 30 min later he develops ↓ LOC and hemiparesis. Hx of “street speed”.

ALPHA ADRENERGIC SYNDROME

- Dx: Phenylpropanolamine (PPA) Overdose

- Other agents:
  - Phenylephrine
  - Methoxamine
  - Imidazolines
    - Tetrahydrozaline (Visine)
    - Oxymetazoline
    - Naphazoline
    - Xylometazoline

Alpha Adrenergic Drugs

ALPHA AGONISTS

- Dobutamine
- Dopamine
- Ephedrine
- Epinephrine
- Ergot alkaloids
- Methoxamine (Vasoxyl)
- Phenylephrine (Neo-synephrine)
- Phenylpropanolamine (PPA)
- Pseudoephedrine (Sudafed)

ALPHA ANTAGONISTS

- Doxazosin (Cardura)
- Prazosin (Minipress)
- Terazosin (Hytrin)
- Phentolamine (Regitine)
- Phenoxybenzamine
- Tolazoline (Priscoline)
- Induramine (Baratol)
- Urapidil
- Labetalol (alpha & beta)

TOXIC SYNDROMES – CASE 5

A 2 y/o male presents with agitation and bizarre behavior.

HR	190
BP	80/60
RR	24
T	99.8

Tremulous, irritable

Pupils normal size, reactive

Skin and bowel sounds normal

CLUE: older sibling takes liquid medicine for asthma

BETA-ADRENERGIC SYNDROME

- Dx: Albuterol overdose

- Other agents:
  - Terbutaline
  - Metaproterenol
  - Isoproterenol
  - Theophylline
  - Caffeine

Beta Adrenergic Drugs

BETA AGONISTS

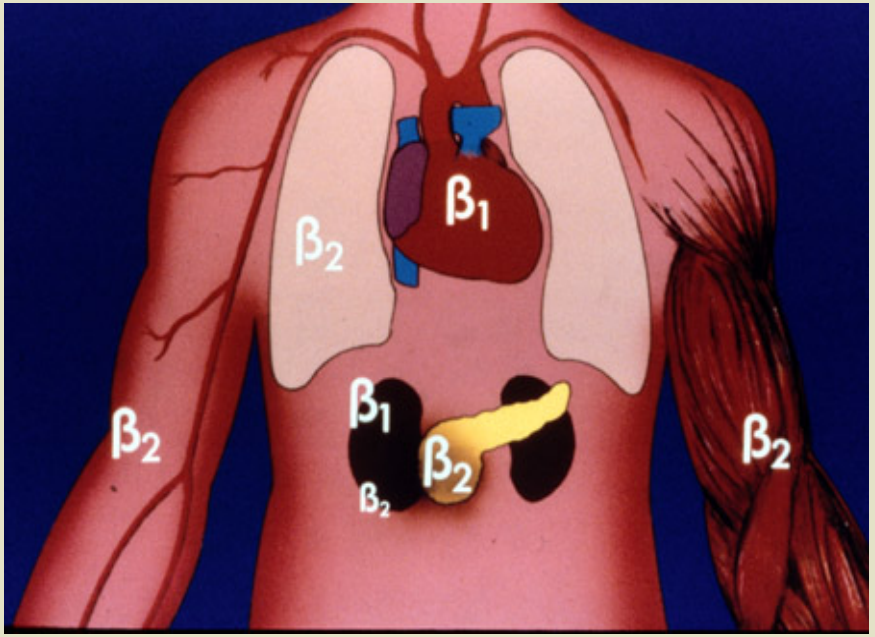
- Albuterol (Proventil, Ventolin)
- Bitolterol (Tornalate)
- Dobutamine
- Dopamine
- Epinephrine
- Isoetharine (Bronkosol)
- Isoproterenol (Isuprel)
- Metaproterenol (Alupent)
- Norepinephrine
- Ritodrine (Yutopar)]
- Salmeterol (Serevent)
- Terbutaline (Bricanyl, Brethrine)

BETA BLOCKERS

- Acebutolol (Sectral)
- Atenolol (Tenormin)
- Betaxolol (Kerlone)
- Bisoprolol (Zebeta)
- Esmolol (Brevibloc)
- Metoprolol (Lopressor)
- Carteolol (Cartrol)
- Nadolol (Corgard)
- Penbutolol (Levatol)
- Pindolol (Visken)
- Propranolol (Inderal)
- Sotalol (Betapace)
- Timolol (Blocadren)
- Labetalol (Normodyne, Trandate)

Beta Blocker Toxicity

- **Bradycardia**
- **Hypotension**
- A-V block
- Heart failure
- CNS depression
- Seizures



TOXIC SYNDROMES – CASE 6

A 2 y/o female presents with extreme lethargy.

HR	72	Dusky appearance
BP	70/50	Lips cyanotic
RR	10	Shallow respirations
T	98	Skin Dry

Bowel sounds decreased, present

CLUE 1: The child improves somewhat after a 2mg dose of naloxone

CLUE 2: Grandfather, visiting at child's house, takes blood pressure medicine

SYMPATHOLYTIC SYNDROME

- Clonidine
- Methyldopa
- Guanabenz
- Sedative / hypnotics
- Opioids
- Alcohol

Imidazolines

- **Antihypertensives:**
  - **Guanfacine (Tenex)**
  - **Guanabenz (Wytensin)**

- **Decongestants**
  - **Tetrahydrozoline (Visine)**
  - **Oxymetazoline (Afrin)**
  - **Naphazoline (Clear Eyes)**

TOXIC SYNDROMES – CASE 7

A 45 y/o male presents comatose and cyanotic.

HR	68	BP	110/60
RR	8, shallow	T	97.8

Pupils constricted

Needle marks on left arm

Bowel sounds decreased

CLUE: wakes up after IV naloxone

OPIOID SYNDROME

- Dx: Heroin Overdose
- Triad: coma, respiratory depression, miosis
- Other agents
  - Opiates
  - Clonidine
  - GHB or analogue

TOXIC SYNDROMES – CASE 8

A 35 y/o female presents with confusion and lethargy. No nausea or vomiting.

HR	110
BP	120/80
RR	32
T	99

PE unremarkable except for drowsy, confusion and tachypnea.

Labs:	Na	142	Cl 96	BUN	27	Glucose 100
	K	4.1	Bicarb 8	Cr	2.2	

Other labs?

ABG: 7.02 / 96 / 25 Measured osmolality = 380. ETOH = 0.

CLUE 1: Ca oxylate crystals in urine

CLUE 2: Empty container of radiator antifreeze found in trash can at home.

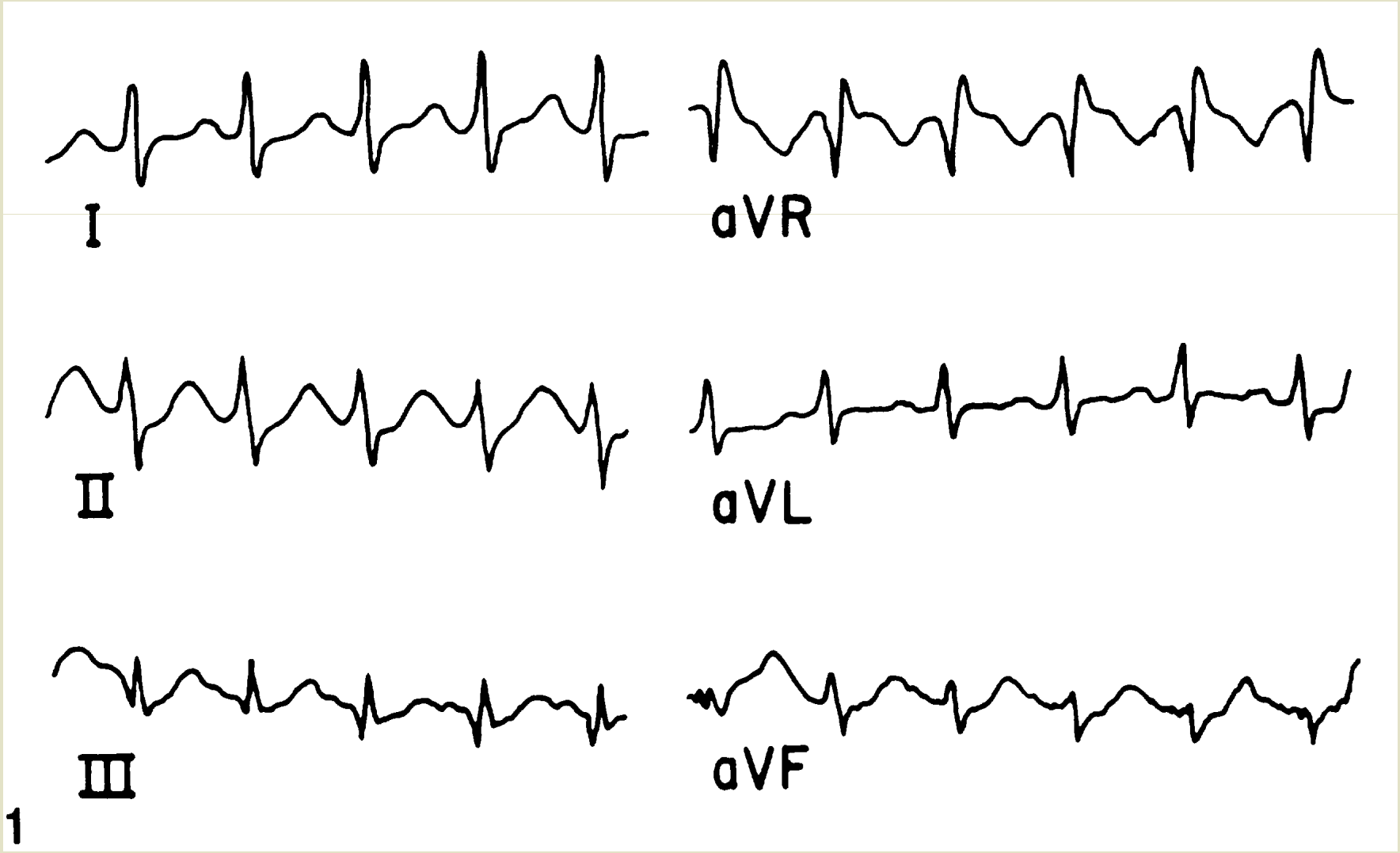

TRAK AUTO
ANTIFREEZE
COOLANT
DEX-COOL™ Antifreeze

TOXIC SYNDROMES- CASE 9

The police bring in a 28 y/o female with drowsiness who says she just wants to die. There is a suicide note.

HR	130	Skin warm and dry
BP	120/80	Bowel sounds decreased
RR	16	Pupils slightly,reactive
T	98	

15 minutes later:



TOXIC SYNDROMES- CASE 9

The police bring in a 28 y/o female with drowsiness who says she just wants to die. There is a suicide note.

HR	130	Skin warm and dry
BP	120/80	Bowel sounds decreased
RR	16	Pupils slightly,reactive
T	98	

CLUE: 15 minutes later she has a seizure lasting 2 minutes, after which she is deeply comatose with agonal respirations. Cardiac monitor shows wide complex tachycardia with a rate of 160. BP 60/40.

TCA Clinical Toxicity

- Lethargy ± agitation
- Sinus tachycardia

- Then:
- Seizures, hypotension, ventricular dysrhythmias

Cyclic Antidepressants

- Inhibit catecholamine reuptake
  - NE, 5-HT, DA
- Block ACH_M receptors
- Block fast Na^+ cardiac channels
- Block alpha- adrenergic receptors
- Block K^+ efflux from cardiac cells
- Indirect GABA antagonist
- Block H_1 and H_2 receptors

TOXIC SYNDROMES – CASE 10

A 22 y/o female presents with a severe toothache for one week, and mild nausea and vomiting for 3 days. She is seeking pain medication for the persistent toothache. Her friends told her that her eyes were turning yellow.

Vital signs normal

Mild scleral icterus

Right upper quadrant tenderness

Severely abcessed tooth

CLUE: taking 4-5 OTC pain pills at a time every 3 – 4 hours.


VALUE SIZE
TYLENOL
TYLENOL
EXTRA
STRENGTH
Pain Reliever
Fever Reducer
Contains
Acetaminophen
Caplets
Contains
no aspirin
VALUE SIZE
225
CAPLETS

TOXIC SYNDROMES – CASE 11

A depressed 17 y/o female presents with acute onset of nausea, abdominal pain, hematemesis and diarrhea.

HR 115

BP initially normal but falls to 80/50

Anion gap metabolic acidosis is present

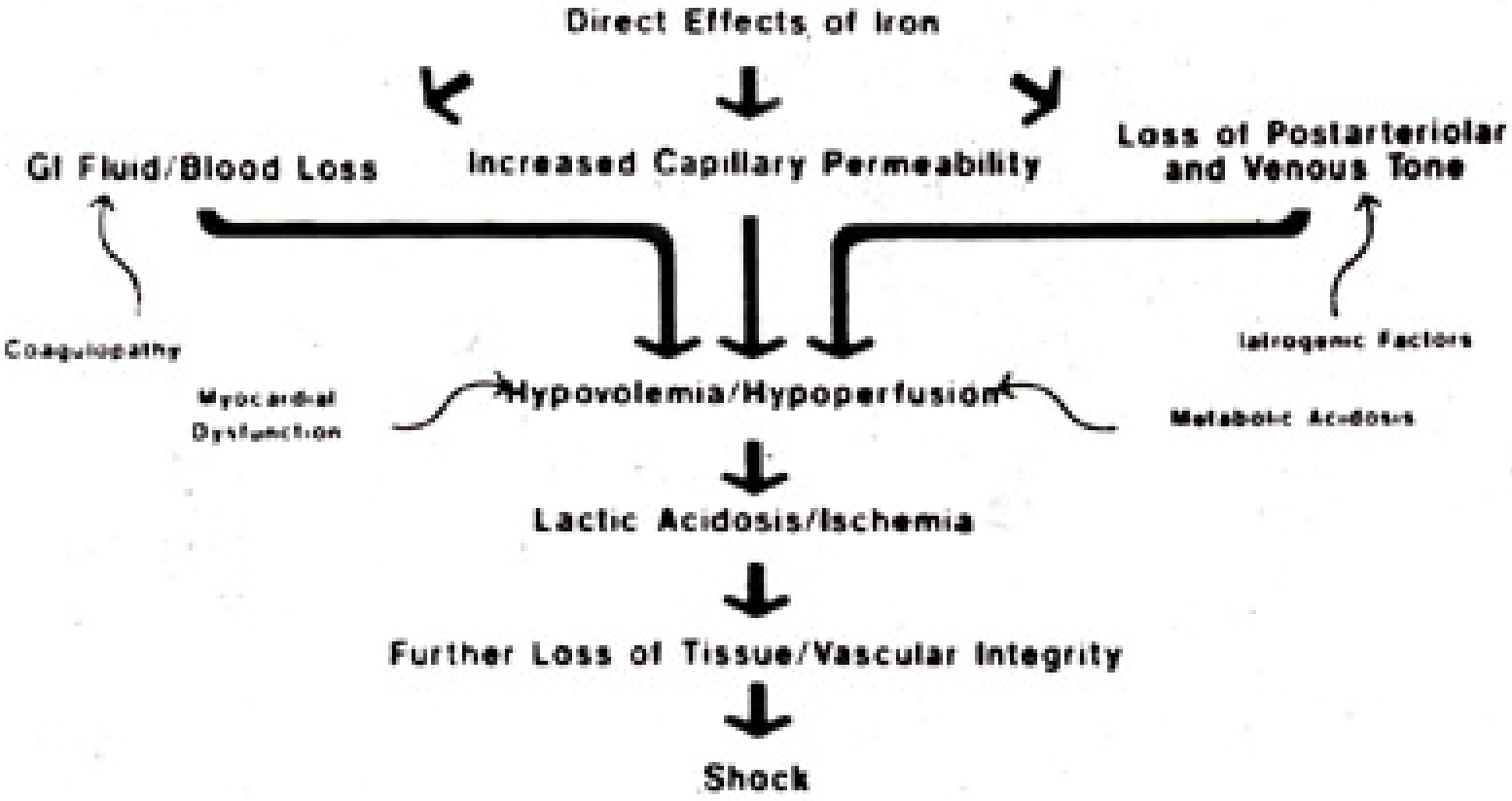
CLUE 1: pregnant

CLUE 2: X-ray shows radiopaque pills in stomach and proximal small bowel

Iron Poisoning

- Direct GI irritant → corrosive
- Decreased venous return → fall in CO
- Elevated lactate, release of protons as Fe++ converted to Fe+++
- Catalyzes free radical formation and lipid peroxidation (hepatotoxicity)
- Hyperglycemia, leukocytosis

The Pathophysiology of Shock in Iron Intoxication



TOXIC SYNDROMES – CASE 12

A 44 y/o female presents with dyspnea, nausea, vomiting and lethargy. It is difficult to obtain a history because the patient is hard of hearing.

HR	96	BP	130/90
RR	28	T	100.6

PE: consistent with advanced rheumatoid arthritis

CLUE:

ABG: 7.48 / 98 / 22

Na 142 Cl 106 Bicarb 14 K 3.5

Salicylates

- **Analgesics**
  - **ASA, Fiorinal**
  - **Goody, BC powders**
- **Pepto-Bismol**
- **Topical liniment analgesics (Ben Gay)**
- **Suppositories**
- **Chewing gum**
- **Flavorings (oil of wintergreen)**
- **Plants (acacia, hyacinth, calycanthus)**
- **Chinese / herbal products**

Salicylates

- GI irritant
- Stimulates respiratory center
  - Hyperventilation/respiratory alkalosis
- May alter capillary permeability
  - Cerebral/pulmonary edema
- Uncouples oxidative phosphorylation
  - Causing lactic acidosis, ketoacidosis
- Inhibits cyclo-oxygenase
  - Loss of gastric mucosal barrier
  - Platelet dysfunction

TOXIC SYNDROME – CASE 13

A 44 y/o female presents with severe nausea and vomiting.

HR	140, irregular	
BP	110/70	
RR	18	Agitated, tremulous
T	99	Skin, pupils, bowel sounds are normal

Cardiac monitor shows sinus tach with narrow QRS complex and occasional PADS and PVDS. Before any further information can be obtained the patient has a seizure which is not controlled with diazepam and phenytoin.

CLUE: husband had asthma

Hypokalemia

Theophylline

- Mechanism of Action
  - Inhibition of phosphodieterase
  - Adenosine receptor antagonism
  - Release of catecholamines

- Clinical Effects
  - Gastric acid and pepsin secretion
  - Stimulation of respiratory & vomiting centers in medulla
  - Positive inotropic and chronotropic effects
  - Reduction of peripheral arteriolar resistance
  - Relaxation of bronchial smooth muscle
  - Increase GFR and RBF
  - CNS stimulation

TOXIC SYNDROMES – CASE 14

A 48 y/o male alcoholic presents with confusion and blurred vision.

HR	100
BP	140/90
RR	32
T	99

Confused, lethargic, disoriented

Labs:	Na 144	Cl 100	Bicarb 10
	K 3.9	Glu 100	BUN 18
	Cr 1.2		

ETOH = 0 Measured osmolality = 350

CLUE: emesis has a bluish tint; urinalysis is normal


DANGER


READY TO USE
ALL-SEASON
Wiper Blue
WINDSHIELD WASHER
Antifreeze & Summer Cleaner
Protects to -20° F
DANGER POISON
COMBUSTIBLE - VAPOR HARMFUL.
MAY BE FATAL OR CAUSE BLINDNESS
IF SWALLOWED.
DIRECTIONS: POUR INTO WASHER TANK. In freezing temperatures, operate defrosters before use.
CONTAINS METHANOL. Cannot be made non-poisonous. Use with adequate ventilation. FIRST AID: If swallowed, induce vomiting by medically approved means. CALL A PHYSICIAN. If splashed in eyes, immediately flush with water for at least 15 minutes.
KEEP AWAY FROM OPEN FLAME.
KEEP OUT OF REACH OF CHILDREN.
DOUGLAS PRODUCTS AND PACKAGING
Liberty, Missouri 64068
1 U.S. GAL. (3.78L)
0 51223 00311 8


STERNO
Canned Heat
COOKING FUEL
STERNO


XXX

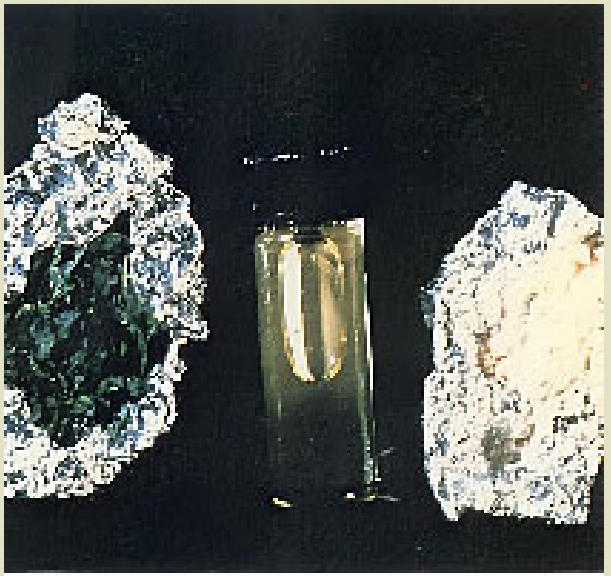
TOXIC SYNDROMES – CASE 15

A 19 y/o male is brought in by 6 policemen for severe agitation and disruptive behavior.

Hypertensive

Nystagmus

Severe agitation alternating with coma



PCP in both crystalline form and a vial of PCP dissolved in water

TOXIC SYNDROMES – CASE 16

A 55 y/o male alcoholic presents with lethargy, confusion, nausea, vomiting and abdominal pain.

HR 95 – remainder of vital signs normal

Mild epigastric tenderness

Labs:	Na 140	Cl 110	Bicarb 24
	K 3.8	BUN 21	Cr 1.2
	Glucose 100		

ETOH = 0

Measured osmolality = 372

CLUE: urine is positive for acetone

A 4 y/o girl is found comatose in a closet in her home. She is dressed in her mother's clothes, shoes and jewelry. Also in the closet are her doll, several suitcases and several cans of cleaning fluids and pesticides.

In the ED, she is comatose, with a regular HR of 108 bpm and BP 80 mm Hg by palpation. She has pinpoint pupils, dry skin and clear lungs. No bowel sounds are audible.

The parents are certain that all medications in the home are secured in a medicine cabinet, and all other toxic chemicals are locked under the kitchen sink

The child is stabilized in the ED. The HR decreases to 96 and the BP rises to 90 mm Hg. She becomes awake, alert and her pupils dilate to normal size after receiving a dose of 2 mg naloxone IV.

The parents still emphatically deny the use of any natural or synthetic opiates at home.

Upon returning home, the father, while searching through the closet, discovers an open bottle of Lomotil tablets in an open suitcase. The antidiarrheal medication had been left there after a foreign trip.

Lomotil

- Diphenoxylate 2.5mg + atropine 0.025mg
- Lethargy reported after ingestion of 1 tablet
- CNS depression may be delayed up to 18 hours
- Treatment is supportive
  - Naloxone for opioid effects
  - Physostigmine has been used for anticholinergic toxicity

A mother runs into your office with her 2 year-old son, anxiously stating that he is difficult to arouse. He awoke that morning and had breakfast as usual, then “fell asleep” two hours later. The child has now been “sleeping” for about an hour.

No one witnessed trauma.

Only medications in the house are APAP and ASA – both stored in the bathroom medicine cabinet.

No history of previous similar episodes.

No family history of metabolic disorders.

Pulse 110, BP 90/60, RR 8, T 36 (96.8)

Obtunded, responding only to painful stimuli by crying and moving purposelessly.

Skin cool, slightly diphoretic.

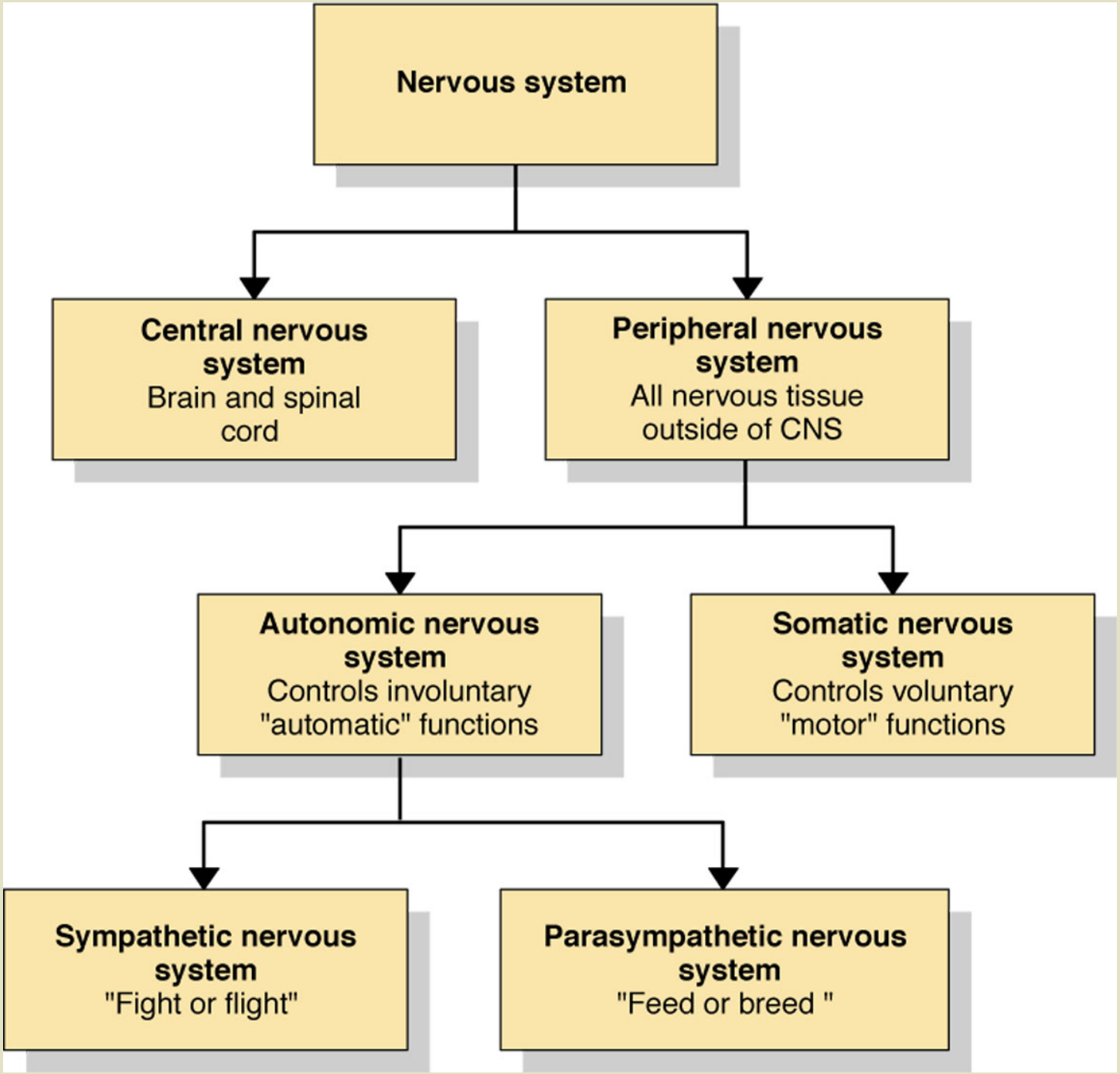
Pupils midsize, neuro exam non-focal and symmetric, with slight hyporeflexia in all extremities.

At the end of the exam the child has a generalized, tonic-clonic seizure.

Chem-strip blood sugar = 20 mg%

Further history reveals that the parents had hosted a party the night before that had continued late into the night.

Summary


Nervous system
Central nervous system
Brain and spinal cord
Peripheral nervous system
All nervous tissue outside of CNS
Autonomic nervous system
Controls involuntary "automatic" functions
Somatic nervous system
Controls voluntary "motor" functions
Sympathetic nervous system
"Fight or flight"
Parasympathetic nervous system
"Feed or breed "

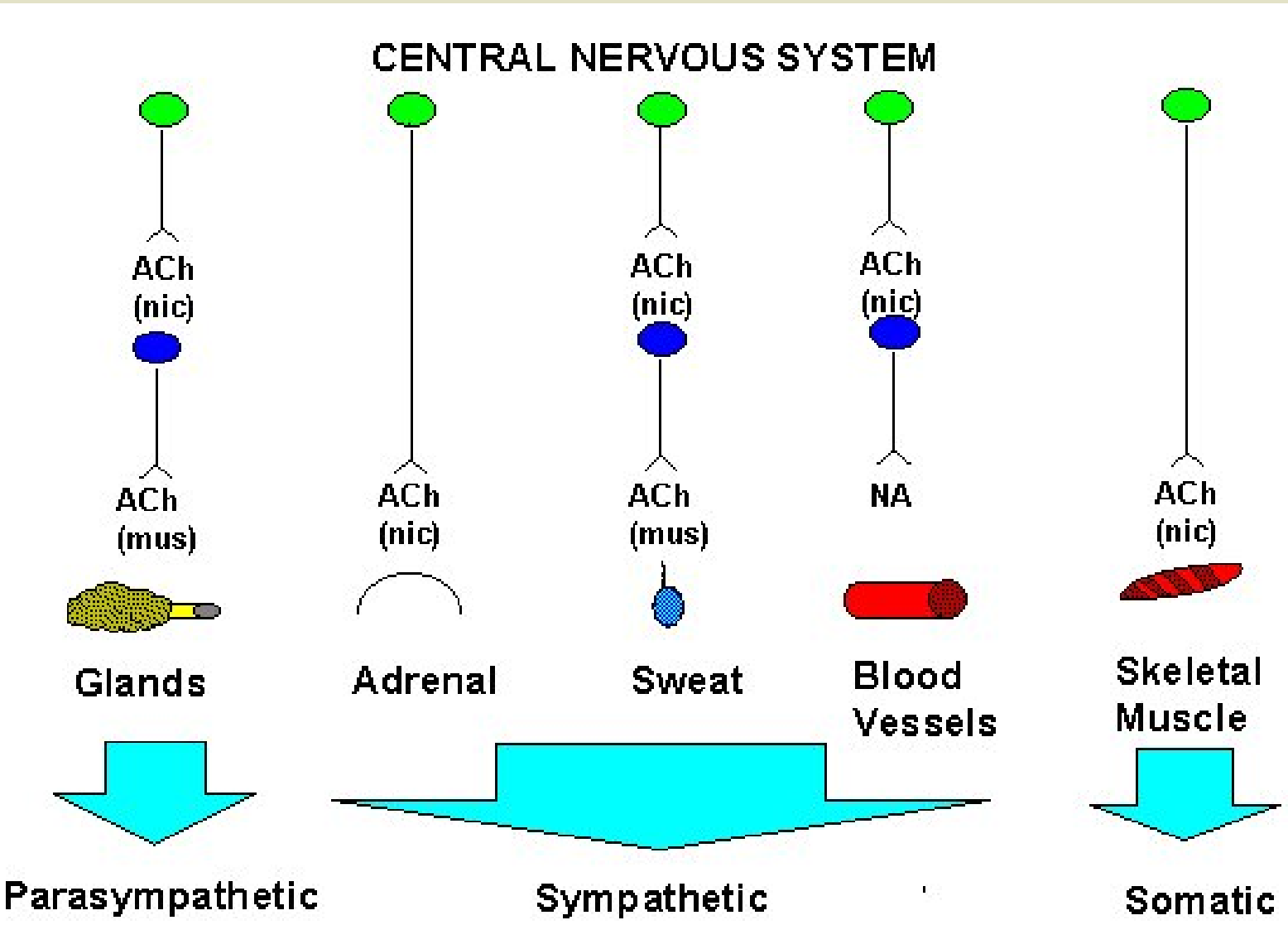

CENTRAL NERVOUS SYSTEM
ACh (nic)
ACh (mus)
ACh (nic)
ACh (nic)
ACh (mus)
ACh (nic)
NA
ACh (nic)
Glands
Adrenal
Sweat
Blood Vessels
Skeletal Muscle
Parasympathetic
Sympathetic
Somatic

TABLE 1-17
CLINICAL EFFECTS OF ADRENOCEPTOR BLOCKAGE AND STIMULATION[a]

α	β_1	β_2
Stimulation		
Mydriasis	Miosis	Miosis
Vasoconstriction	Tachycardia	Vasodilatation
Coronary dilatation	Increased cardiac contractility	Bronchodilatation
Decreased GI motility	Accelerated AV conduction	Hyperglycemia
Bladder contraction	Renin release	Decreased GI motility
		Bladder relaxation
		Renin release
Blockade		
Miosis	Hypotension[b]	Hypoglycemia with hypertension
Postural hypotension	Cardiac arrhythmias	Bronchospasm
Reflex tachycardia	Bradycardia[b]	Raynaud's phenomenon
Angina (uncommon)	Pulmonary edema	Hyperkalemia (uncommon)
Gastric hyperacidity	Hyperkalemia (uncommon)	

Abbreviations: AV, atrioventricular; GI, gastrointestinal.

[a] Additional effects not mediated by these adrenergic receptors, largely central nervous system and sympathomimetic, may also be seen.

[b] May be obliterated, or hypertension and tachycardia may occur if drug has intrinsic sympathomimetic effects.

Adapted from Done AK: The toxic emergency. Autonomics unraveled. II. Adrenergics. Emerg Med 1983;15(21):115. Used with permission.

Conclusions

- Safe use of cardiovascular and other resuscitation drugs requires understanding of autonomic nervous system
- Assessment for “toxidromes” can assist in diagnosis of intoxication when lab testing is not available
- Call the Poison Center – it’s a free call and not a sign of weakness!!