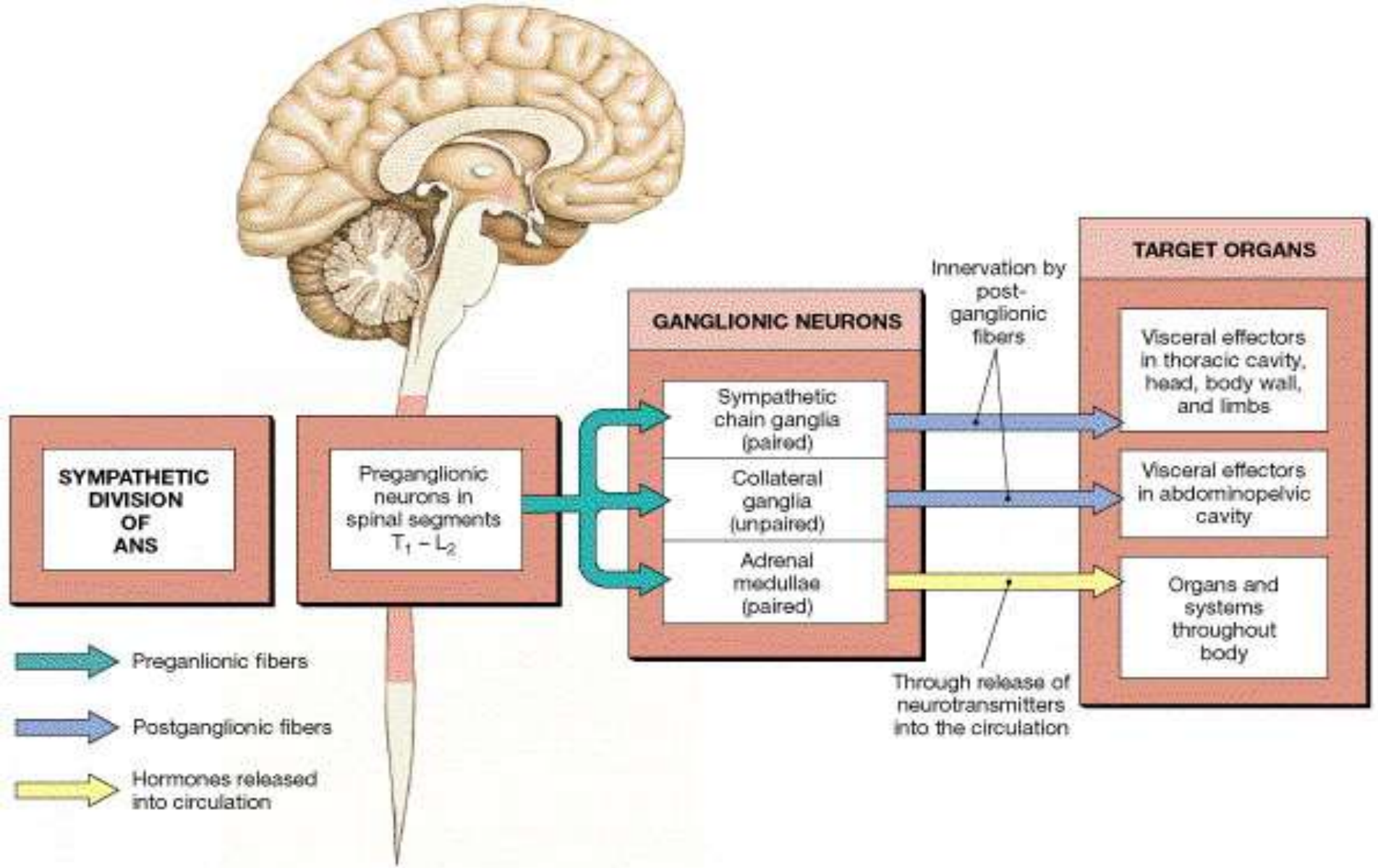
FARMAKOLOGI SSO

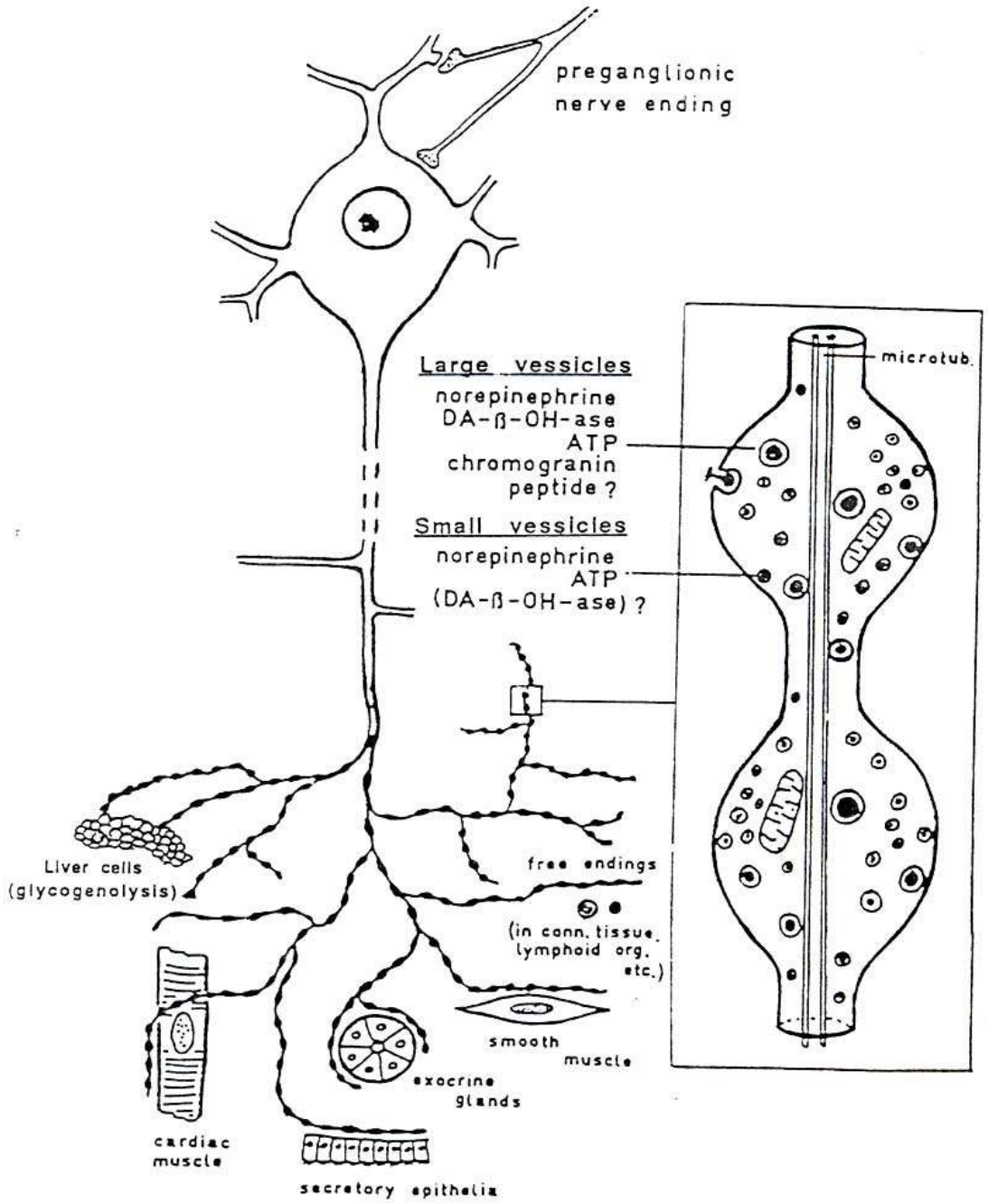
SISTEM ADRENERGIK

Fathiyah Safithri

Laboratorium Farmakologi
Fakultas Kedokteran
Univ. Muhammadiyah Malang
2020

Organisasi Divisi Simpatis





Neuron Adrenergik Perifer

Sintesa Katekolamin

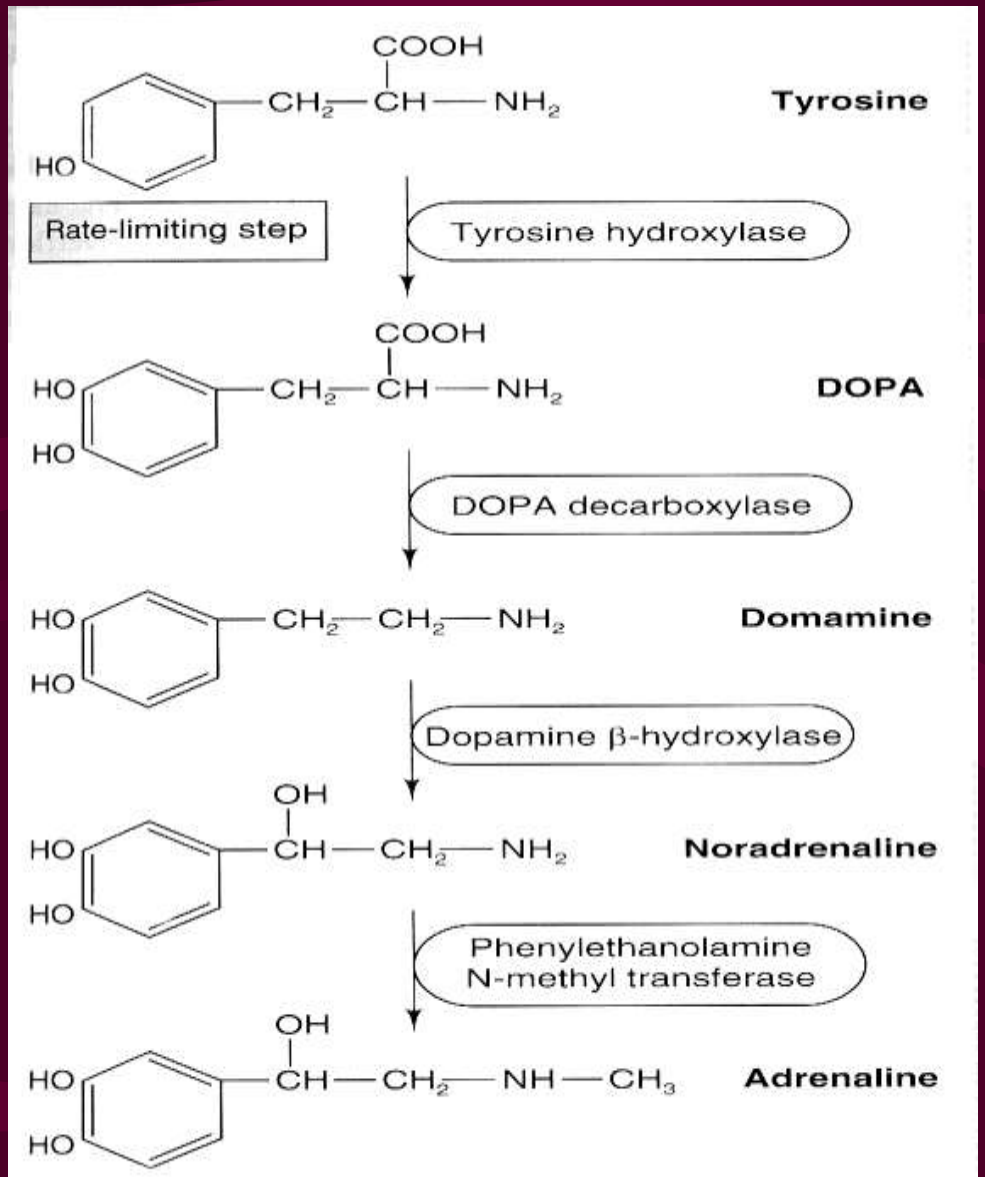
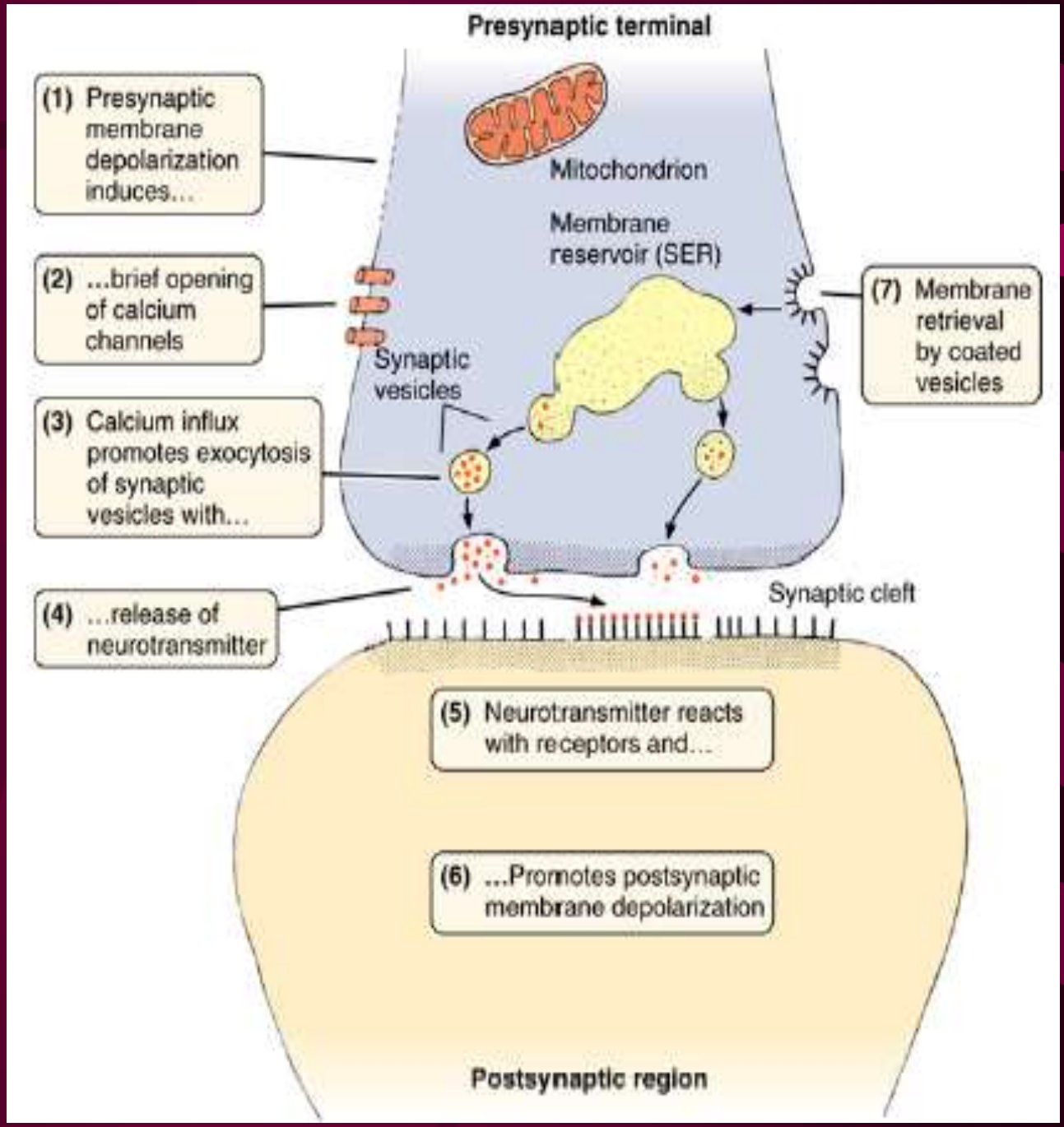


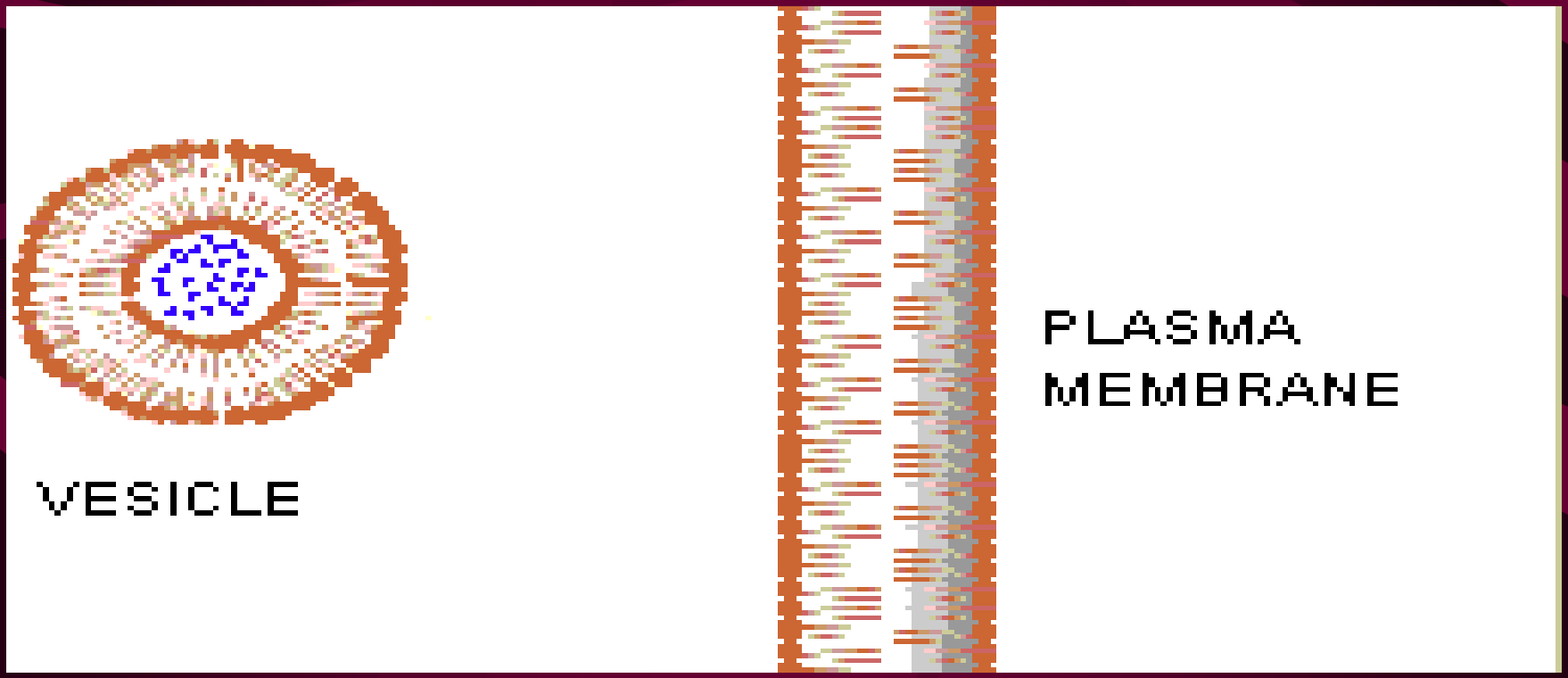
Fig. 8.2 **Biosynthesis of catecholamines**

TRANSMISI SINYAL

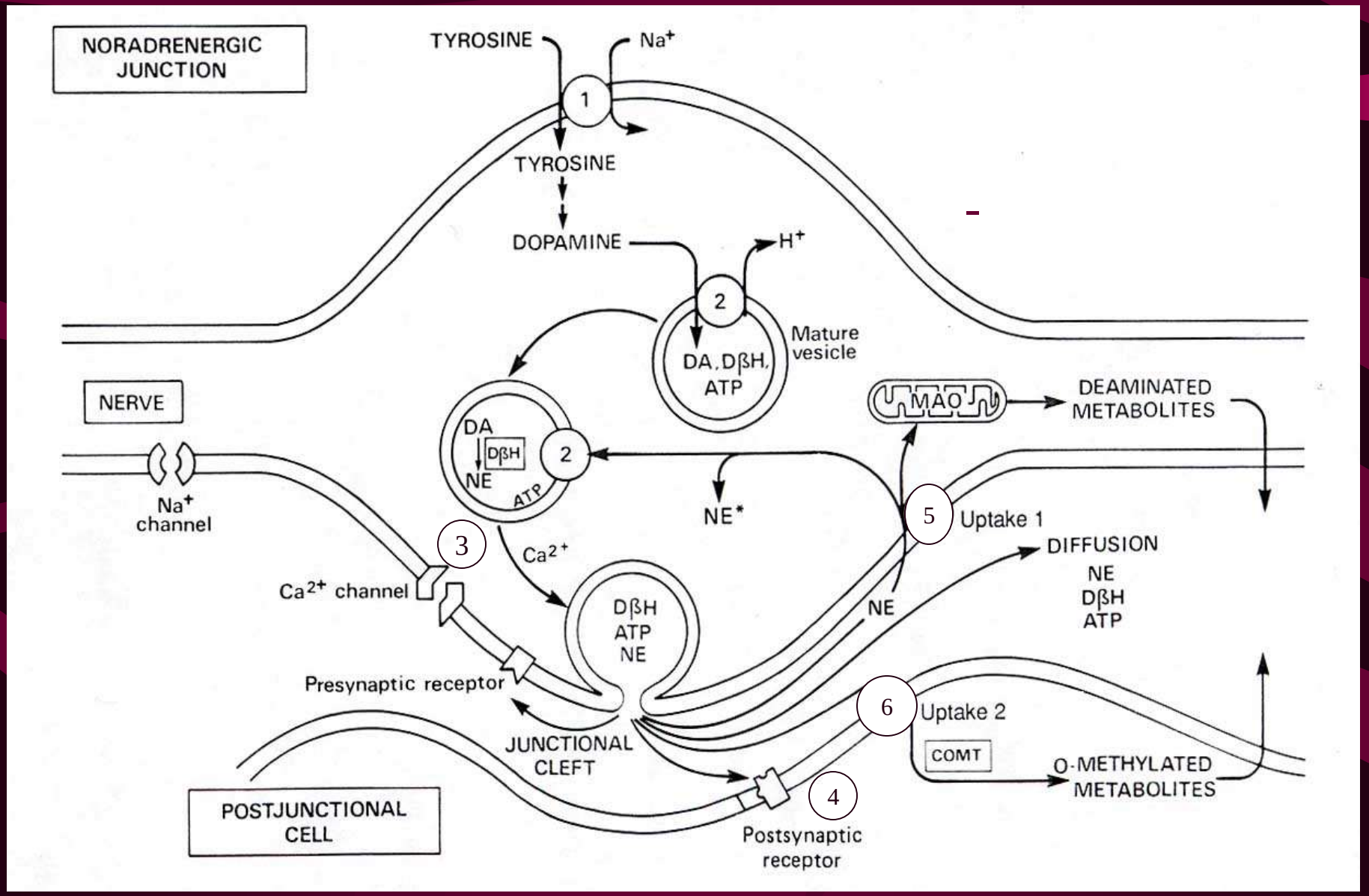


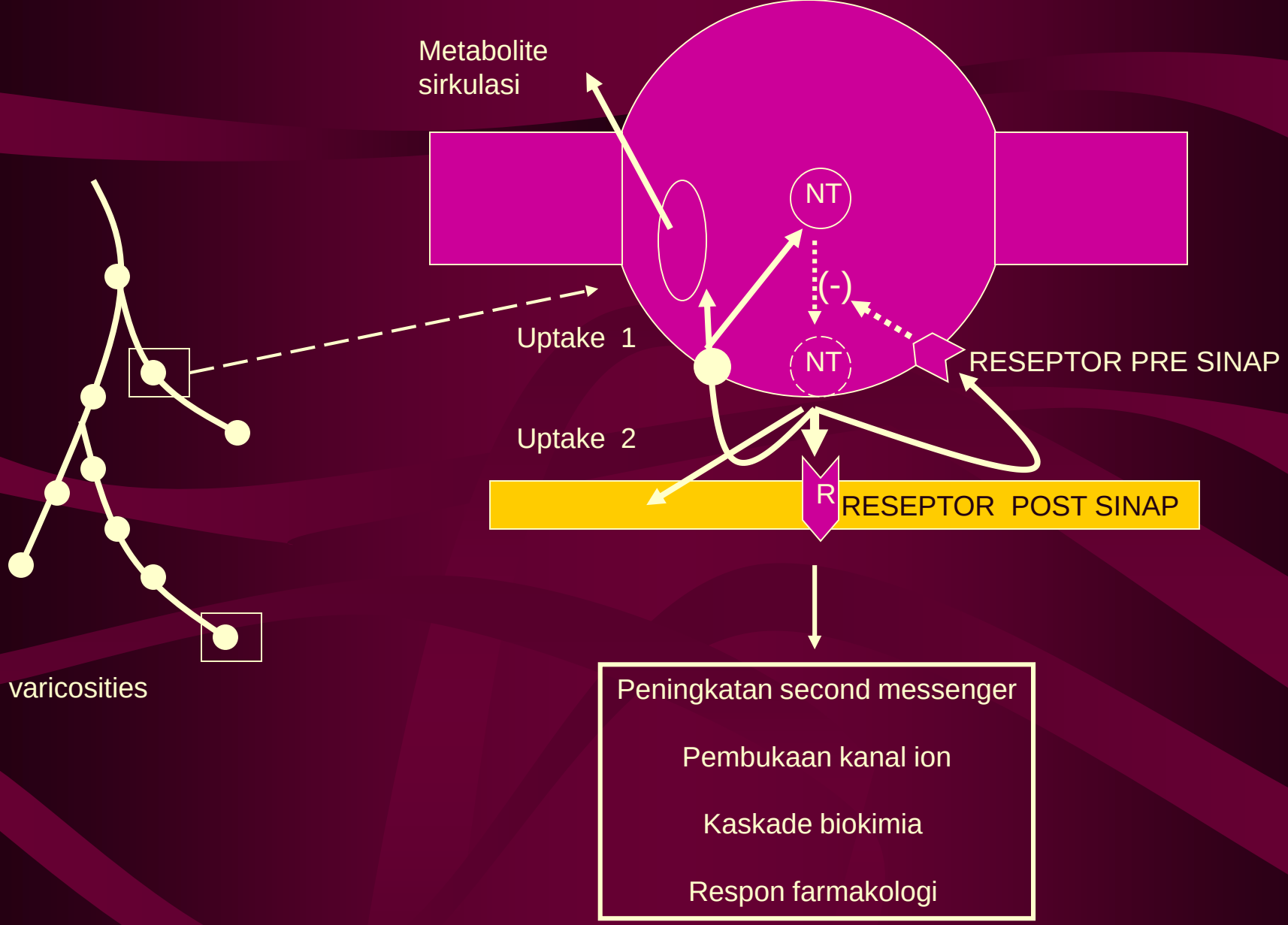
Release Norepineprine

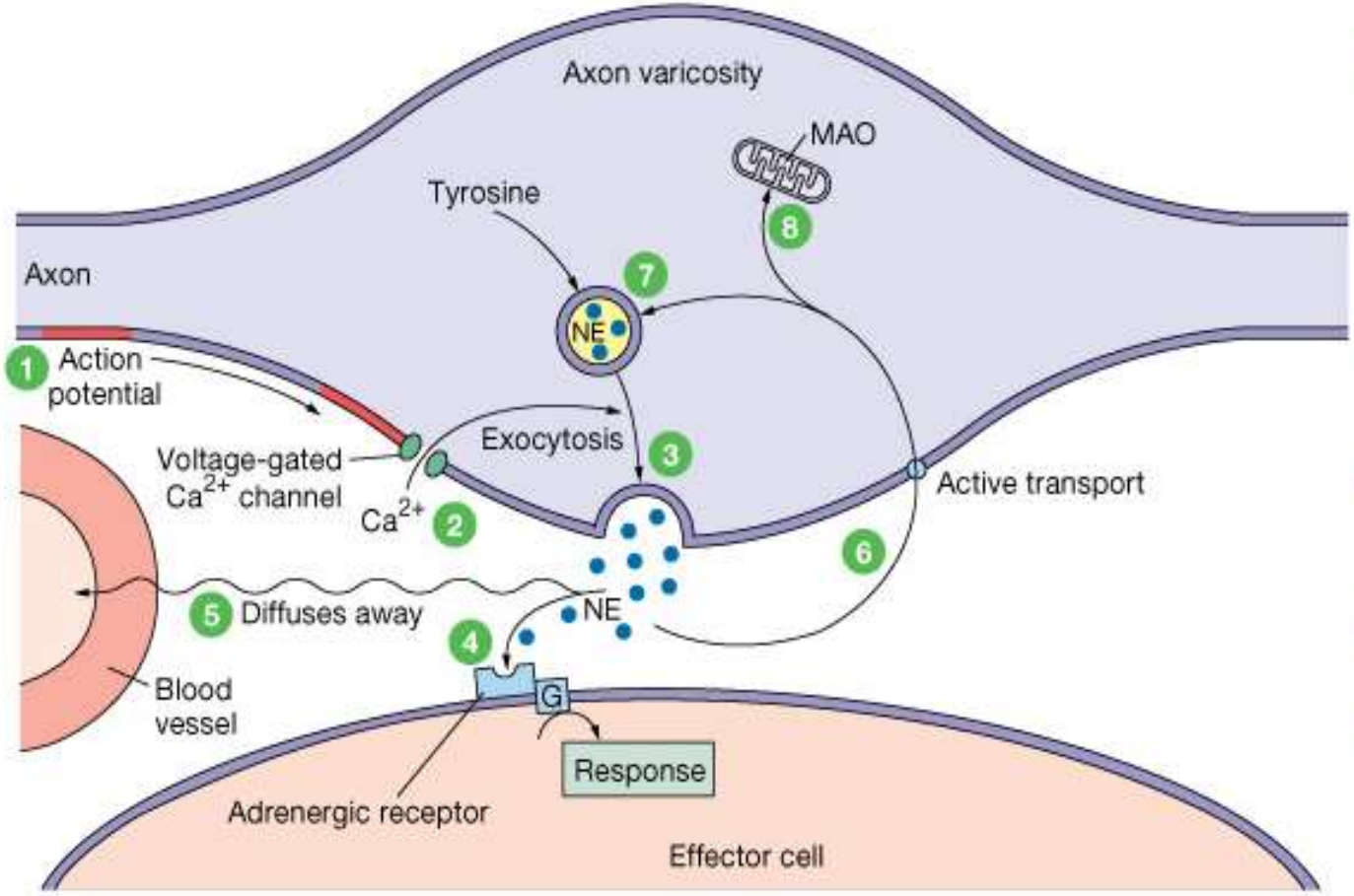
- aksi potensial pada membran saraf →depolarisasi → kanal ion Na terbuka → kanal Ca terbuka → ion calsium masuk ke dalam neuron → Peningkatan ion Ca intrasel → vesicle kontak dengan membran saraf → release NE secara eksositosis . Diduga release melibatkan mekanisme kontraktil dari sitoskeleton dan protein tubulin.



NEUROTRANSMISI ADRENERGIK




Metabolite
sirkulasi
NT
(-)
NT
RESEPTOR PRE SINAP
Uptake 1
Uptake 2
R
RESEPTOR POST SINAP
varicosities
Peningkatan second messenger
Pembukaan kanal ion
Kaskade biokimia
Respon farmakologi



KEY

- NE (norepinephrine)

1. Action potential arrives at the varicosity.
2. Depolarization opens voltage-gated Ca^{2+} channels.
3. Ca^{2+} entry triggers exocytosis of synaptic vesicles.
4. NE binds to adrenergic receptor on target.
5. Activity ceases when NE diffuses away from the synapse.
6. NE is transported back into the axon.
7. NE can be taken back into synaptic vesicles for re-release.
8. NE is metabolized by monoamine oxidase (MAO).

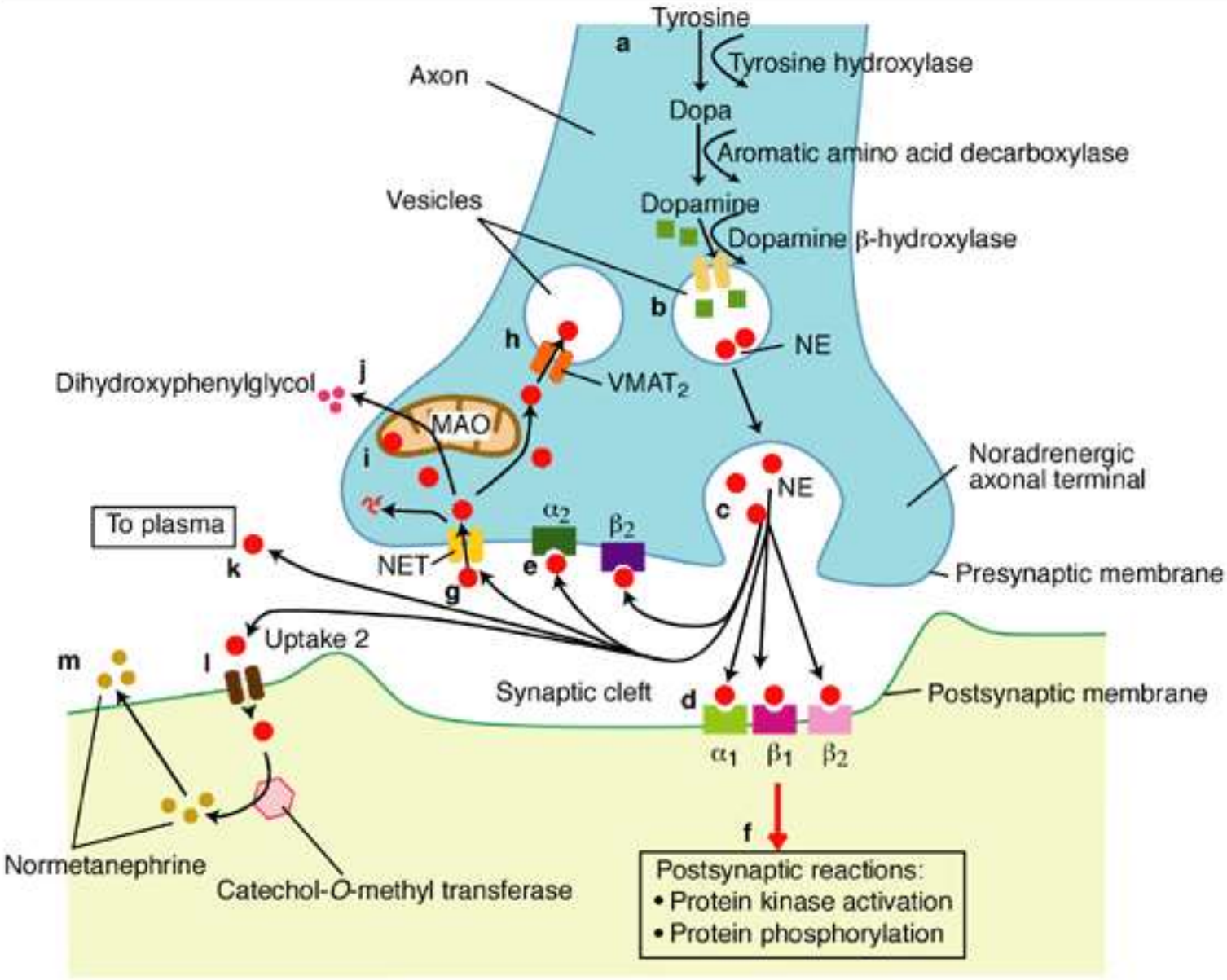
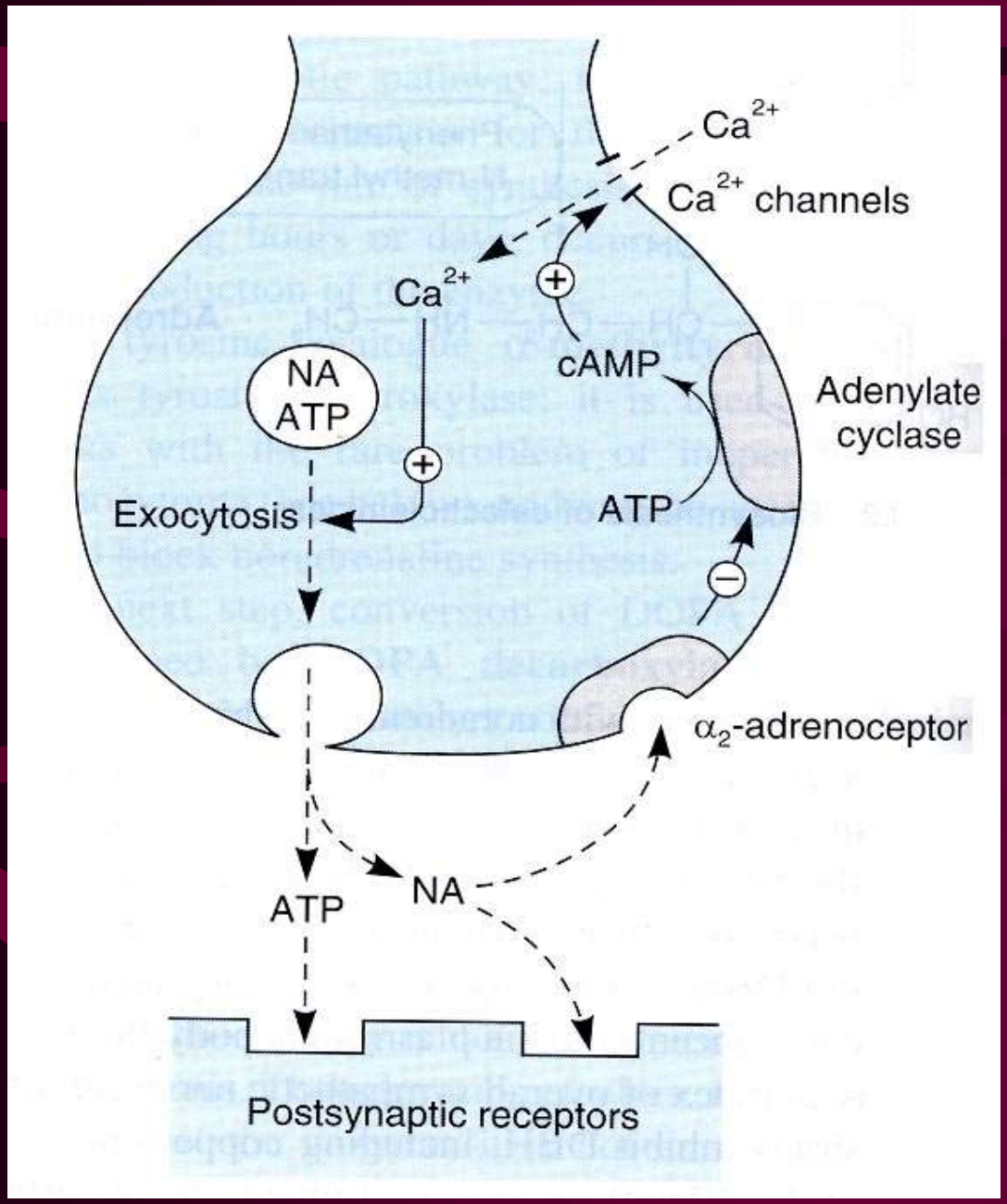


Diagram of a noradrenergic axonal terminal showing the release and re-uptake of norepinephrine



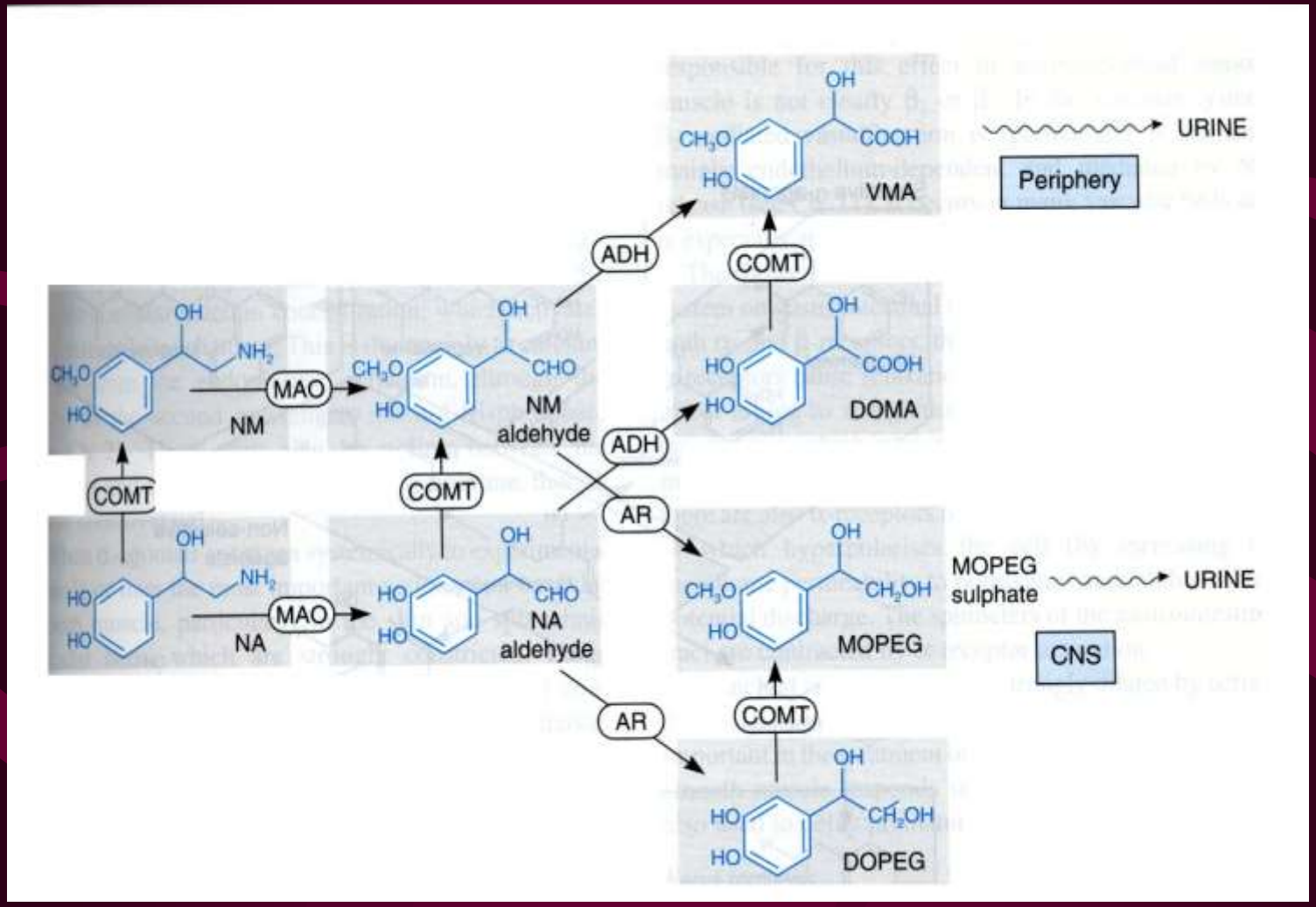
Feedback control Of noradrenaline release

- NE release involves Ca^{2+} influx
- α_2R activation → inhibit Adenylat cyclase → cAMP ↓ → Ca^{2+} influx ↓

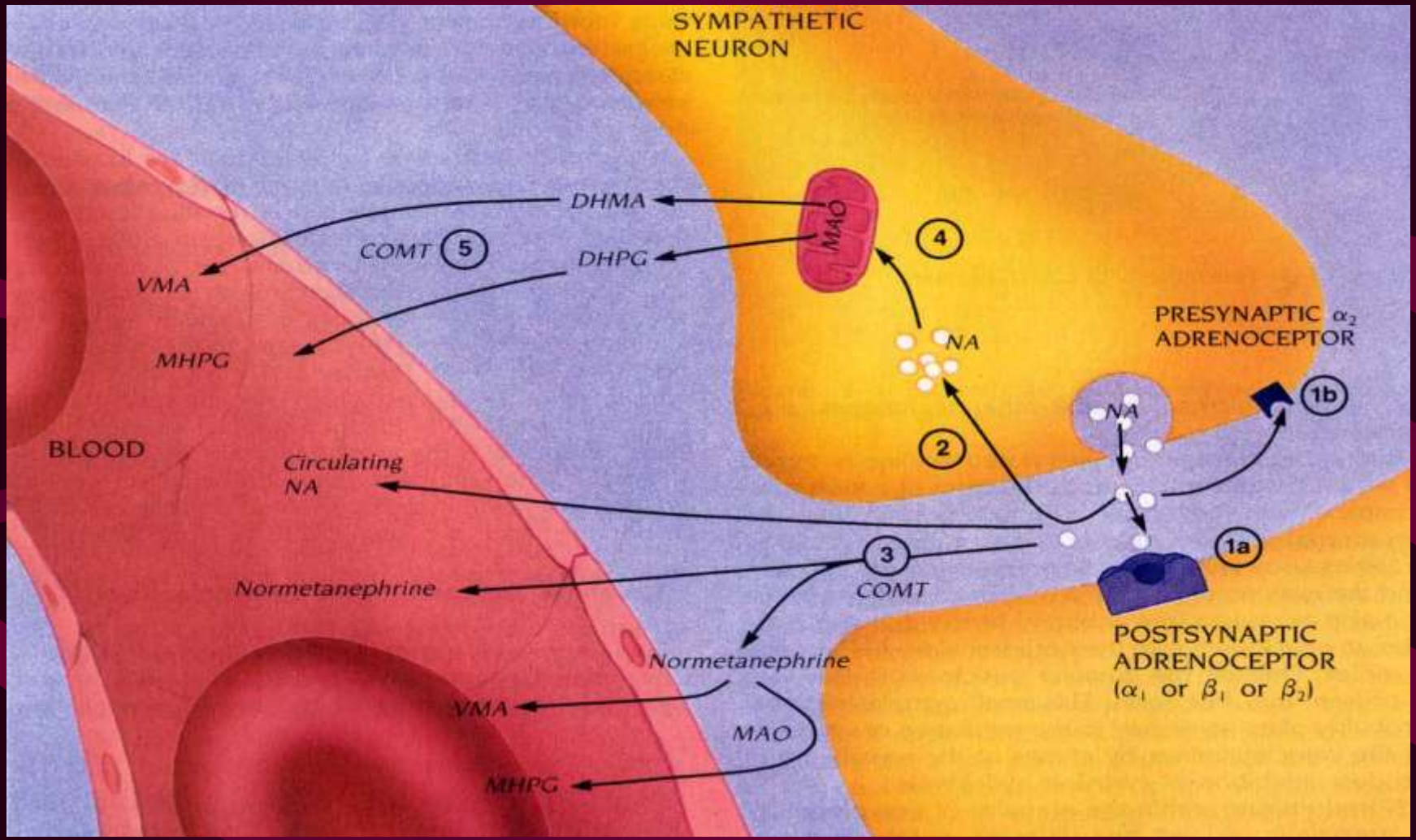
Uptake 1 inhibitors:
Antidepressants,
Cocaine,
Amphetamine

Uptake 2 inhibitor:
normetanephrine

Metabolism of noradrenaline



Degradation of catecholamines



βAdr-R Subtypes

- β1 → Heart

  (increase HR and contractility)

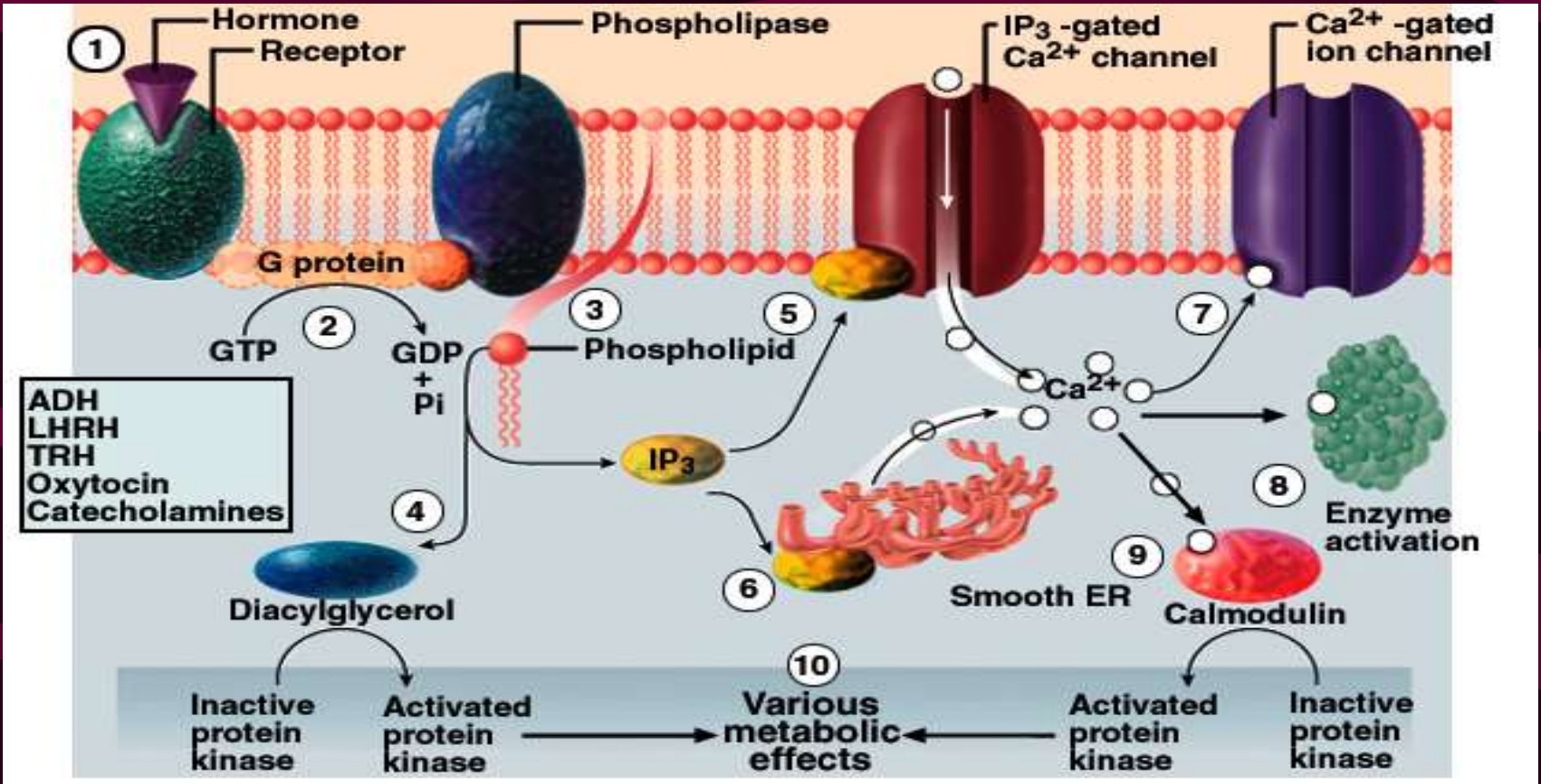
- β2 → Smooth Muscle

  (relaxation of smooth muscle in lung, uterus, blood vessels)

- β3 → Adipose Tissue

  (stimulation of lipolysis)

MEKANISME SINYAL TRANSDUKSI RESEPTOR α-1 ADRENERGIK



NOR ADRE
EPINEPRNE
DOPAMIN

+ reseptor

G-protein → adenyllate siklase → ATP → cAMP

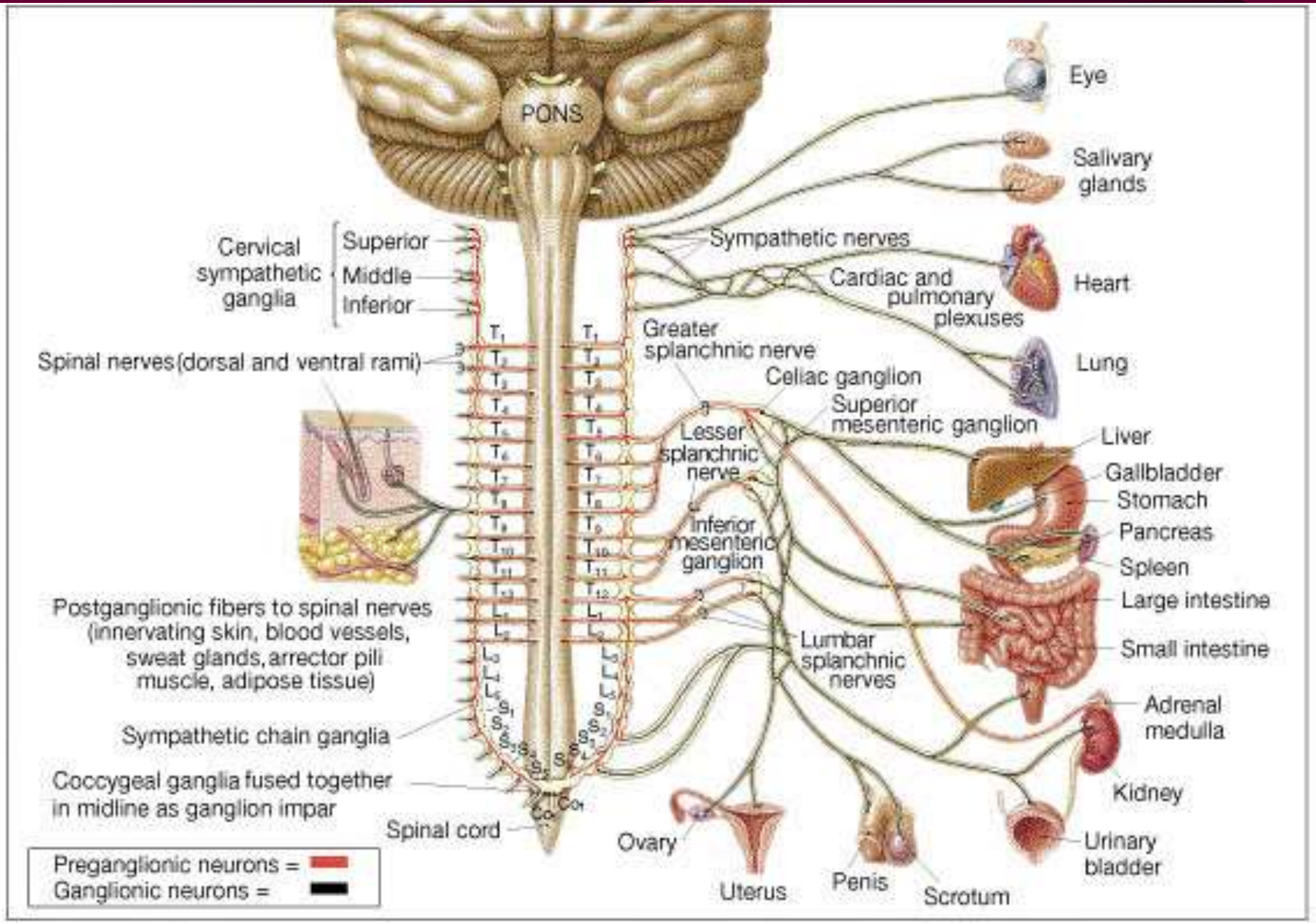
G-protein →Pospolipase → pospolipid → IP3, DAG

Ca++

RESUME MEK. SINYAL TRANSDUKSI RESEPTOR β dan α

α_1	G_q coupled	↑ phospholipase C →↑ IP_3, DAG, Ca^{2+}
α_2	G_i coupled	↓ adenylyl cyclase → ↓ cAMP
$\beta_1\beta_2 D_1$	G_s coupled	↑ adenylyl cyclase → ↑ cAMP

DISTRIBUSI RESEPTOR SIMPATIS



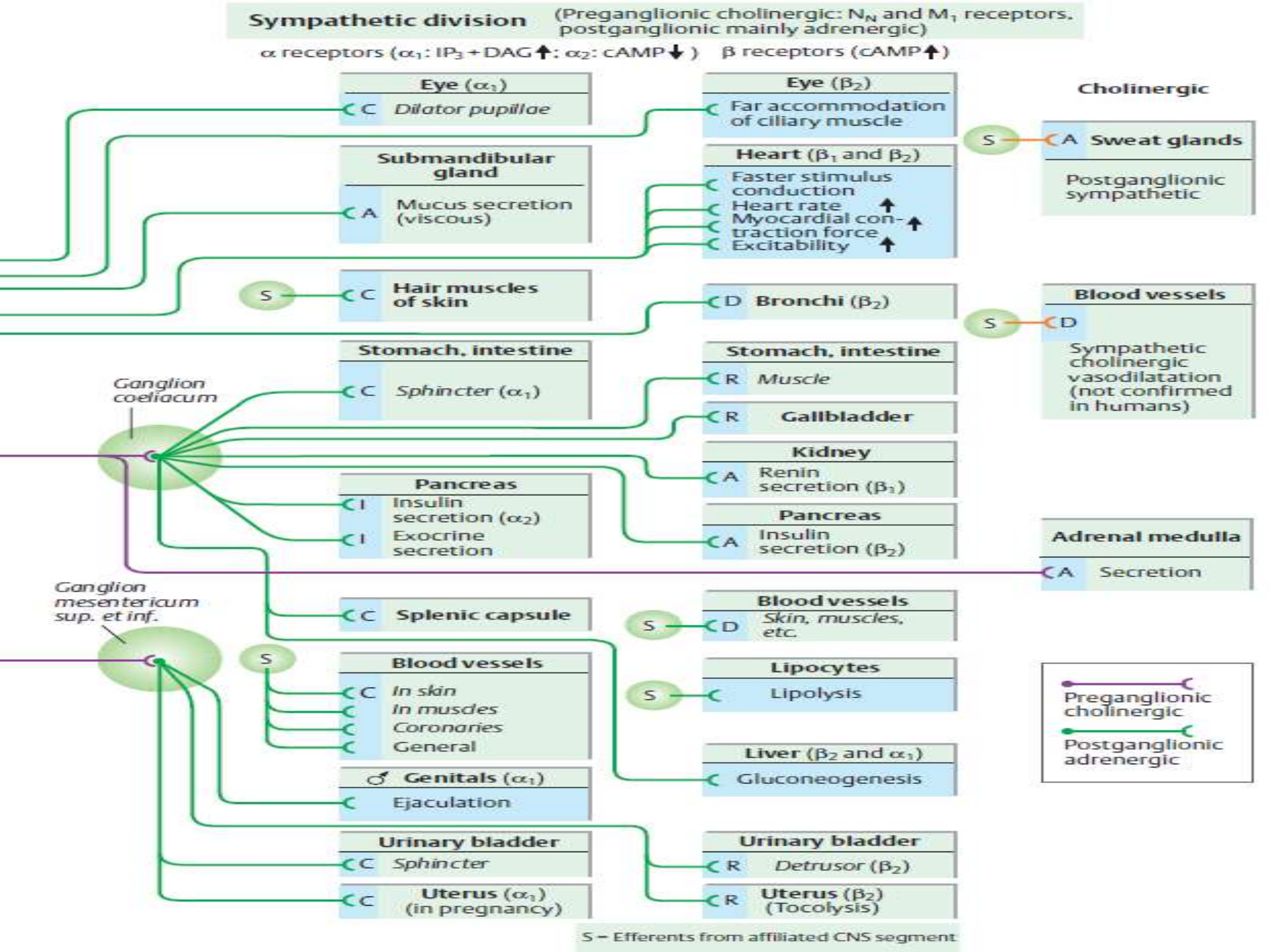

Sympathetic division
(Preganglionic cholinergic: N_N and M_1 receptors, postganglionic mainly adrenergic)
α receptors (α_1: IP_3 + DAG ↑; α_2: cAMP ↓) β receptors (cAMP ↑)
Eye (α_1)
C Dilator pupillae
Submandibular gland
A Mucus secretion (viscous)
S
C Hair muscles of skin
Ganglion coeliacum
Stomach, intestine
C Sphincter (α_1)
Pancreas
I Insulin secretion (α_2)
I Exocrine secretion
Ganglion mesentericum sup. et inf.
C Splenic capsule
S
Blood vessels
C In skin
In muscles
Coronaries
General
♂ Genitals (α_1)
Ejaculation
Urinary bladder
C Sphincter
C Uterus (α_1) (in pregnancy)
Eye (β_2)
Far accommodation of ciliary muscle
Heart (β_1 and β_2)
Faster stimulus conduction
Heart rate ↑
Myocardial contraction force ↑
Excitability ↑
D Bronchi (β_2)
Stomach, intestine
R Muscle
R Gallbladder
Kidney
A Renin secretion (β_1)
Pancreas
A Insulin secretion (β_2)
S
D Blood vessels Skin, muscles, etc.
S
Lipocytes
Lipolysis
Liver (β_2 and α_1)
Gluconeogenesis
Urinary bladder
R Detrusor (β_2)
R Uterus (β_2) (Tocolysis)
Cholinergic
S
A Sweat glands
Postganglionic sympathetic
Blood vessels
S
D Sympathetic cholinergic vasodilatation (not confirmed in humans)
Adrenal medulla
A Secretion
Preganglionic cholinergic
Postganglionic adrenergic
S = Efferents from affiliated CNS segment

Table 13.2 Location and pharmacological responses mediated by adrenergic receptors.

Type of receptor	Location	Response	Cellular mechanism	Selective antagonists
α_1	smooth muscle		activation of PLC	doxazosin
	blood vessels	vasoconstriction	$\uparrow IP_3$ $\uparrow$ DAG	prazosin
	bronchi	constriction	$\uparrow Ca^{2+}$ entry	terazosin
	bladder	contraction	$\uparrow [Ca^{2+}]_i$	
	intestine	relaxation		
	uterus	contraction		
	iris (radial muscle)	contraction		
	cardiac muscle	contraction		
	liver/skeletal muscle	glycogenolysis		
α_2	platelets	aggregation	inhibition of AC	yohimbine
	pancreatic β-cells	↓insulin secretion	↓cAMP	rauwolscine
	blood vessels	vasoconstriction	$\downarrow [Ca^{2+}]_i$	
	sympathetic nerve endings	↓NA release		
β_1	heart	↑rate	activation of AC	atenolol
		↑force of contraction	↑cAMP	bisoprolol
		↑excitability	$\uparrow [Ca^{2+}]_i$	metoprolol
	sympathetic nerve endings	↑NA release		nebivolol
	renal juxtamedullary cells	↑renin secretion		
	salivary glands	↑amylase secretion		
β_2	smooth muscle		activation of AC	butoxamine
	blood vessels	vasodilatation	↑cAMP	α—methylpropanol
	bronchi	dilatation	PKA activation	
	bladder	relaxation	MLCK inactivation	
	uterus	relaxation		
	heart	↑rate	activation of AC	
		↑force of contraction	↑cAMP	
	sympathetic nerve endings	↑NA release	$\uparrow [Ca^{2+}]_i$	
	pancreatic β-cells	↑insulin secretion		
	liver	glycogenolysis	↑phosphorylase	
	skeletal muscle	tremor		
		hypokalaemia	$\uparrow Na^+/K^+$ ATPase	
β_3	fat	thermogenesis	activation of AC	bupranolol
	subcutaneous tissues	lipolysis	↑cAMP	cyanopindolol
	? skeletal muscle	glucose uptake	$\uparrow [Ca^{2+}]_i$	

PLC, phospholipase C; IP_3, inositol trisphosphate; DAG, diacylglycerol; AC, adenylate cyclase; cAMP, cyclic adenosine monophosphate; NA, noradrenaline; PKA, protein kinase A; MLCK, myosin light chain kinase; $[Ca^{2+}]_i$, intracellular calcium ions.

Table 13.3 Adrenergic receptors that are involved in different sympathetic responses.

Organ or tissue	Response	Receptor
Heart		
	↑rate	β_1 (? β_2)
	↑force of contraction	β_1 (? β_2) α_1
	↑automaticity	β_1 (? β_2)
Vascular smooth muscle		
skin	vasoconstriction	α_1 (? α_2)
skeletal muscle	vasoconstriction	α_1 (? α_2)
	vasodilatation	β_2
splanchnic area	vasoconstriction	α_1 (? α_2)
	vasodilatation	$\beta_2 D_1$
renal vessels	vasoconstriction	α_1 (? α_2)
	vasodilatation	$\beta_2 D_1$
Non-vascular smooth muscle		
bronchi	constriction	α_1
	dilatation	β_2
intestine	contraction	α_1
	relaxation	$\alpha_1 \beta_2$
uterus	contraction	α_1
	relaxation	β_2
Other effects		
renin secretion	increased	β_1
	decreased	α_1
glycogenolysis	increased	$\alpha_1 \beta_2$
lipolysis	increased	β_3
insulin secretion	increased	β_2
	decreased	α_2

Distribusi Adrenoreseptor

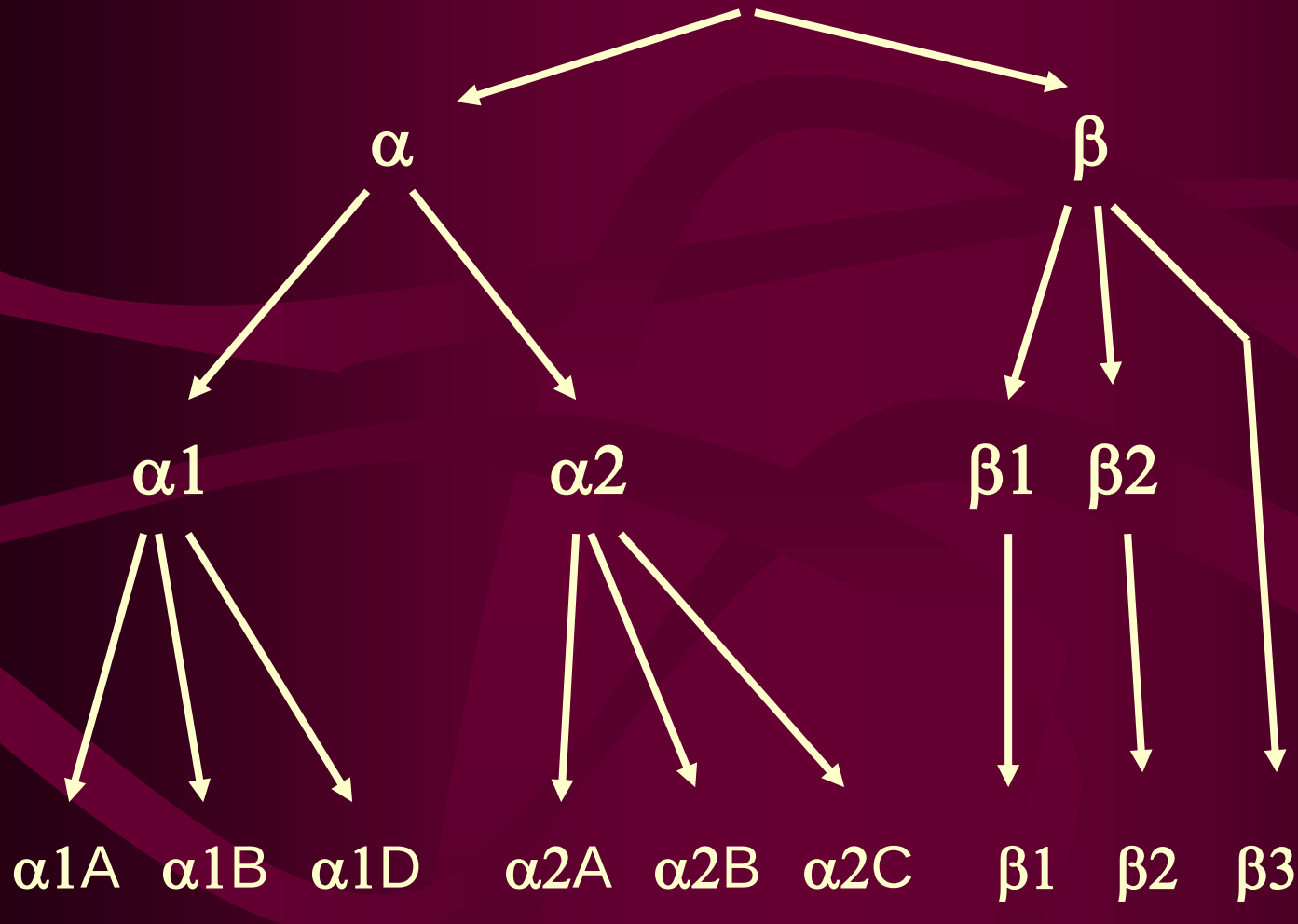
Type	Tissue	Actions
α_1	Most vascular smooth muscle (innervated)	Contraction
	Pupillary dilator muscle	Contraction (dilates pupil)
	Pilomotor smooth muscle	Erects hair
	Prostate	Contraction
	Heart	Increases force of contraction
α_2	Postsynaptic CNS adrenoceptors	Probably multiple
	Platelets	Aggregation
	Adrenergic and cholinergic nerve terminals	Inhibition of transmitter release
	Some vascular smooth muscle	Contraction
	Fat cells	Inhibition of lipolysis
β_1	Heart	Increases force and rate of contraction
β_2	Respiratory, uterine, and vascular smooth muscle	Promotes smooth muscle relaxation
	Skeletal muscle	Promotes potassium uptake
	Human liver	Activates glycogenolysis
β_3	Fat cells	Activates lipolysis
D_1	Smooth muscle	Dilates renal blood vessels
D_2	Nerve endings	Modulates transmitter release

Receptor	Response
α_1	
Eye: radial (dilator) muscle	Contraction: mydriasis
Arterioles (skin, viscera)	Contraction: ↑ TPR, ↑ diastolic pressure, ↑ afterload
Veins	Contraction: ↑ venous return, ↑ preload
Bladder trigone and sphincter and prostatic urethra	Contraction: urinary retention
Male sex organs	Vas deferens: ejaculation
Liver	↑ glycogenolysis
Kidney	↓ renin release
α_2	
Prejunctional nerve terminals	↓ transmitter release and NE synthesis
Platelets	Aggregation
Pancreas	↓ insulin secretion
β_1	
Heart SA node	↑ HR (positive chronotropy)
AV node	↑ conduction velocity (positive dromotropy)
Atrial and ventricular muscle	↑ force of contraction (positive inotropy), conduction velocity, CO and oxygen consumption
His-Purkinje	↑ automaticity and conduction velocity
Kidney	↑ renin release
β_2 (mostly not innervated)	
Blood vessels (all)	Vasodilation: ↓ TPR: ↓ diastolic pressure, ↓ afterload
Uterus	Relaxation
Bronchioles	Dilation
Skeletal muscle	↑ glycogenolysis: contractility (tremor)
Liver	↑ glycogenolysis
Pancreas	↑ insulin secretion
D_1 (peripheral)	
Renal, mesenteric, coronary vasculature	Vasodilation: in kidney ↑ RBF, ↑ GFR, ↑ Na^+ secretion

Classification of adrenoceptors

- 1896 Oliver and Schafer-adrenal extracts increase BP
- 1913 Dale-
  - adrenaline alone produced both vasodilation or vasoconstriction
  - In combination with ergot derivative (α1 antagonist), adrenaline produced a decrease in BP (β2-mediated)
- 1948 Ahlquist- postulated α and β based on agonist potency:
  - Alpha: A>NA>>isoprenaline=isoproterenol
  - Beta: Iso>A>NA

Adrenergic Receptor Family



Alquist

Classic Pharmacology

Molecular Pharmacolgy

RESEPTOR UNTUK NEROTRANSMITER ADRENERGIK

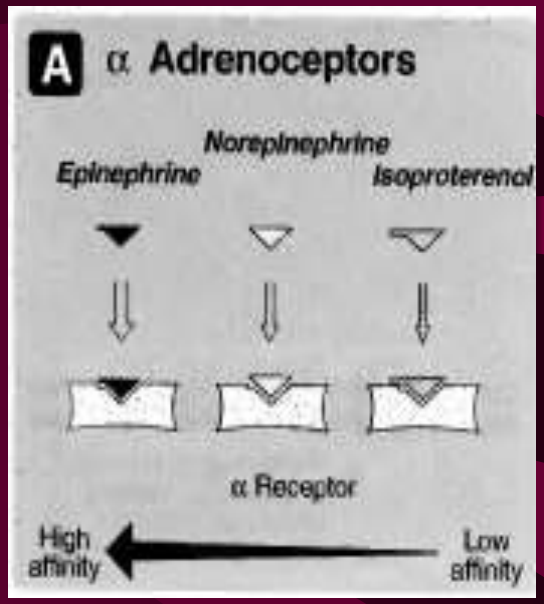
BERDASARKAN JENIS ;

alpha adrenergik reseptor

alpha 1, alpha 2 dan alpha 3

beta adrenergik reseptor

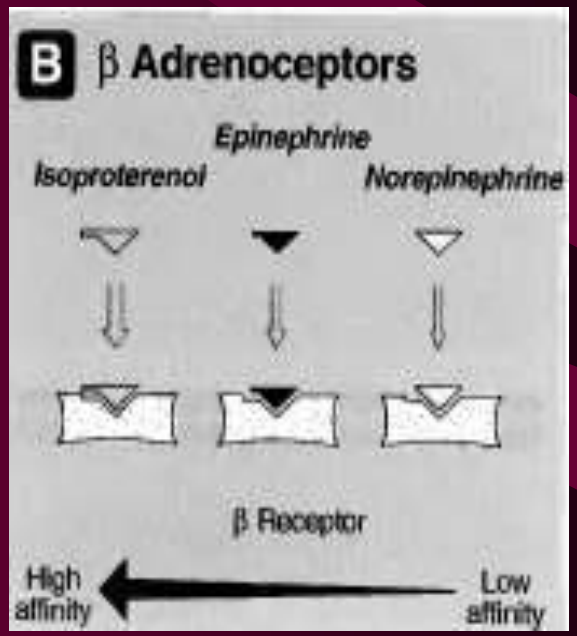
beta 1, beta 2 dan beta 3



MENGAPA DISEBUT SEBAGAI ALPHA ATAU BETA

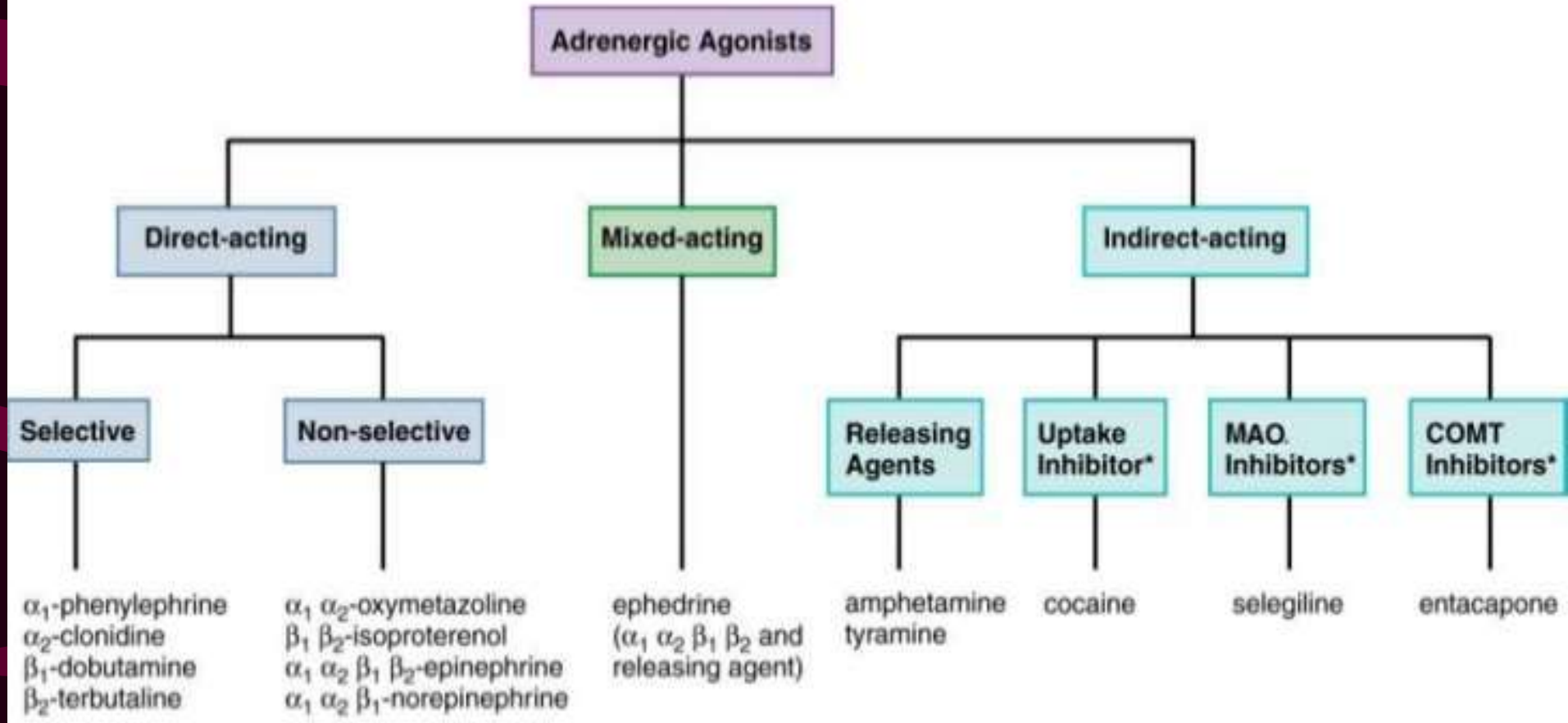
Reseptor yang berespon pada saraf simpatis dengan urutan potensi (kekuatan efek) dimana NE > EPI >D> isoproterenol dinamakan sebagai ***alpha*** receptors.

Sedang reseptor yang berespon dengan urutan potensi dimana isoproterenol > EPI > NE >D dinamakan sebagai ***beta*** receptors.



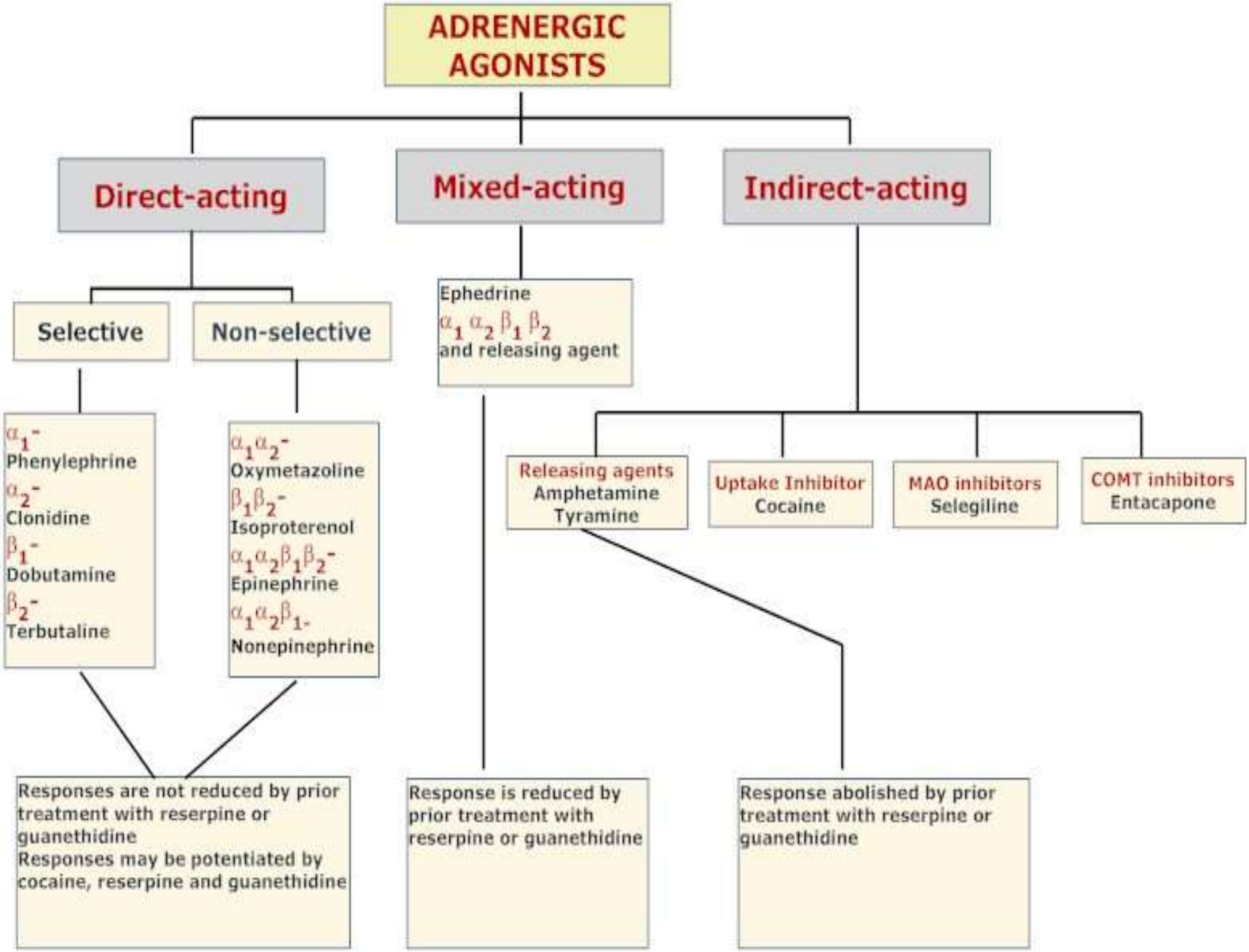
Relative Selectivity of Adrenoceptor Agonists.

	Relative Receptor Affinities
Alpha agonists	
Phenylephrine, methoxamine	$\alpha_1 > \alpha_2 >>>>> \beta$
Clonidine, methylnorepinephrine	$\alpha_2 > \alpha_1 >>>>> \beta$
Mixed alpha and beta agonists	
Norepinephrine	$\alpha_1 = \alpha_2$; $\beta_1 >> \beta_2$
Epinephrine	$\alpha_1 = \alpha_2$; $\beta_1 = \beta_2$
Beta agonists	
Dobutamine[1]	$\beta_1 > \beta_2 >>>> \alpha$
Isoproterenol	$\beta_1 = \beta_2 >>>> \alpha$
Terbutaline, metaproterenol, albuterol, ritodrine	$\beta_2 >>> \beta_1 >>>> \alpha$
Dopamine agonists	
Dopamine	$D_1 = D_2 >>> \beta >>> \alpha$
Fenoldopam	$D_1 >>> D_2$



"selective" ≈ 50-100 fold

Goodman & Gilman (2011). Pharmacological Basis of Therapeutics. p. 278.


ADRENERGIC AGONISTS
Direct-acting
Mixed-acting
Indirect-acting
Selective
Non-selective
Ephedrine
α_1 α_2 β_1 β_2
and releasing agent
α_1-
Phenylephrine
α_2-
Clonidine
β_1-
Dobutamine
β_2-
Terbutaline
$\alpha_1\alpha_2$-
Oxymetazoline
$\beta_1\beta_2$-
Isoproterenol
$\alpha_1\alpha_2\beta_1\beta_2$-
Epinephrine
$\alpha_1\alpha_2\beta_1$-
Nonepinephrine
Releasing agents
Amphetamine
Tyramine
Uptake Inhibitor
Cocaine
MAO inhibitors
Selegiline
COMT inhibitors
Entacapone
Responses are not reduced by prior treatment with reserpine or guanethidine
Responses may be potentiated by cocaine, reserpine and guanethidine
Response is reduced by prior treatment with reserpine or guanethidine
Response abolished by prior treatment with reserpine or guanethidine

OBAT-OBAT YANG BEKERJA PADA SISTEM ADRENERGIK

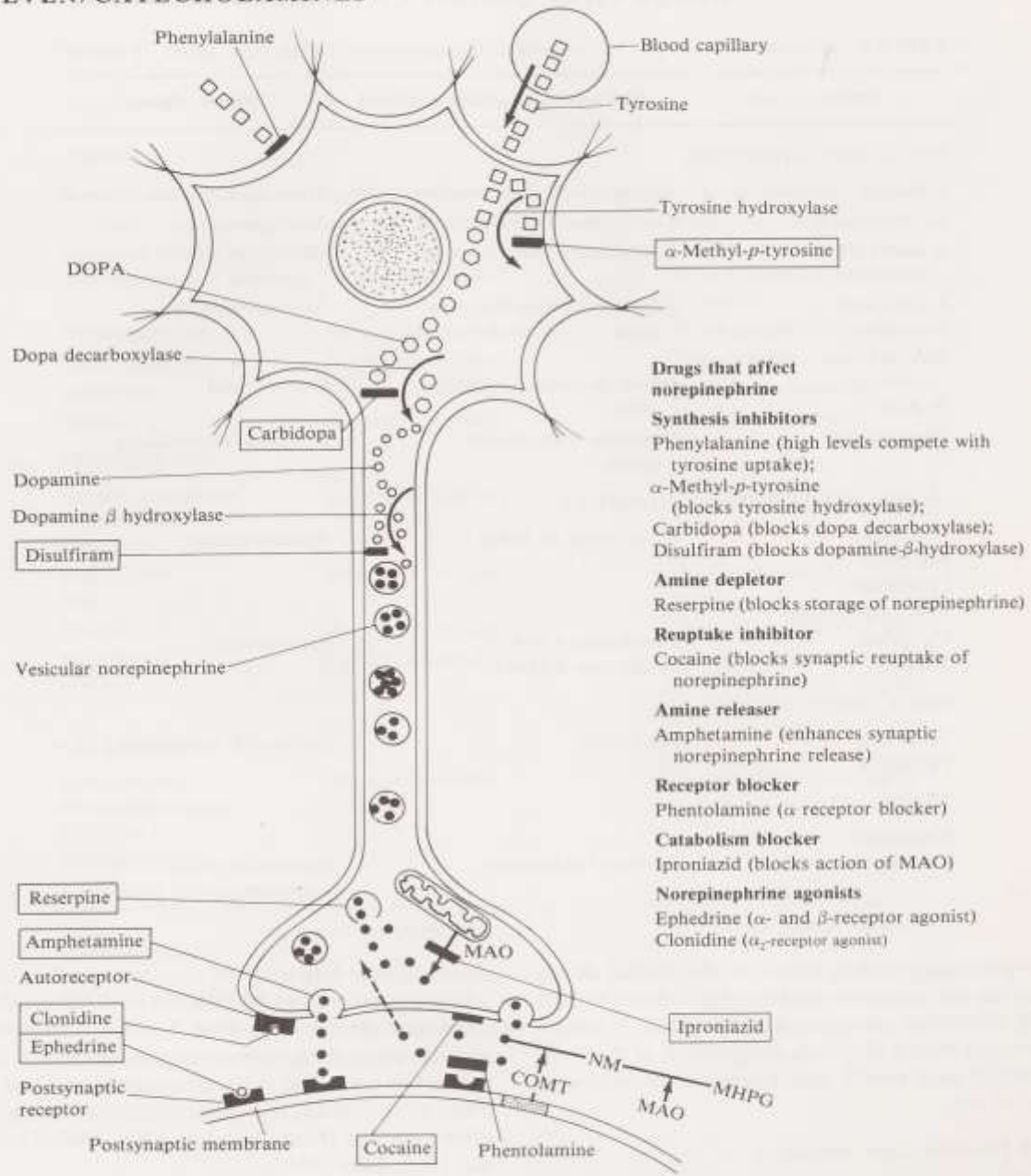
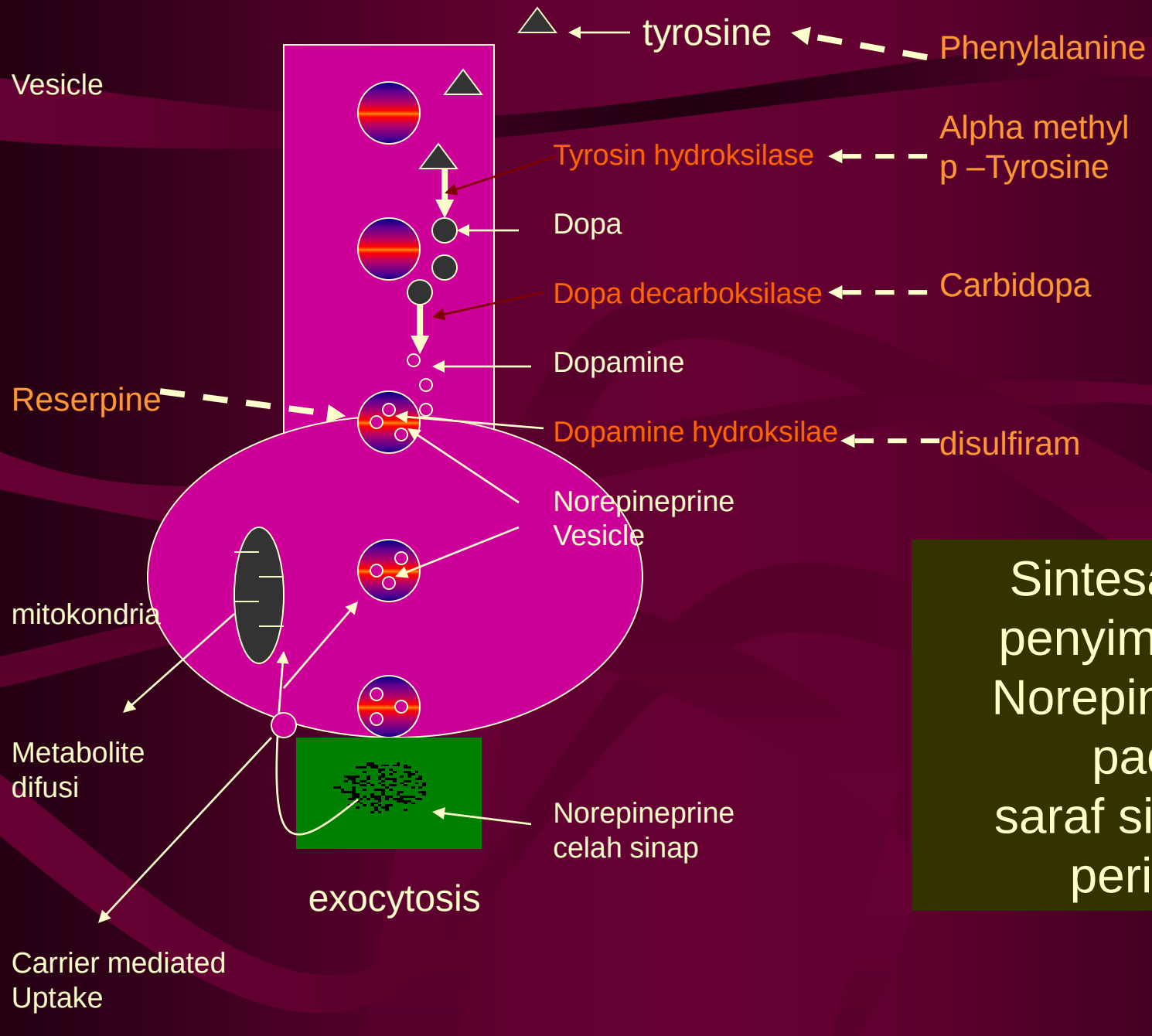
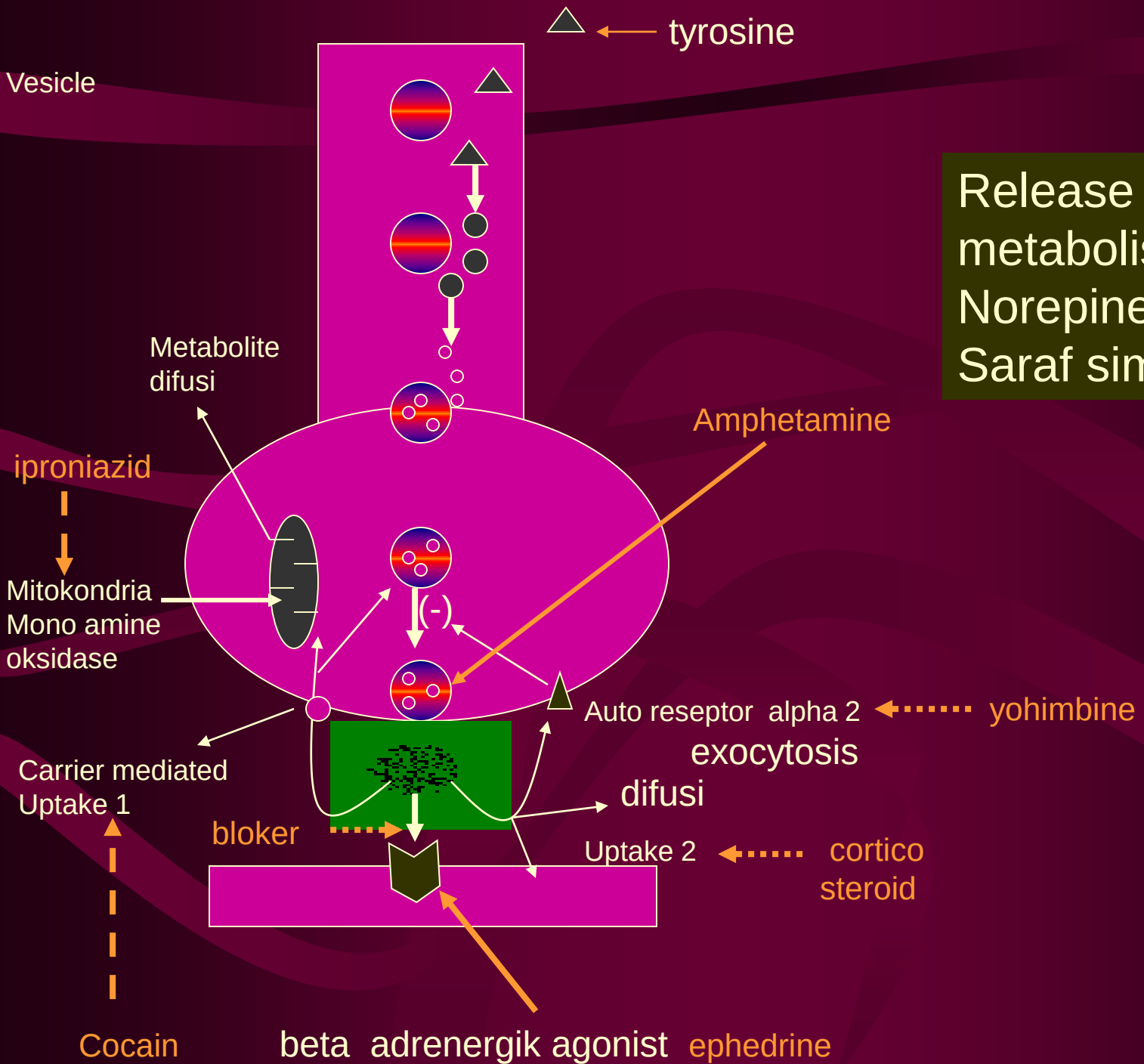


FIGURE 19 NORADRENERGIC SYNAPSES IN THE CNS. NE synthesis, storage, and release is shown in the neuron; and NA receptors are shown on the presynaptic as well as on the postsynaptic membrane. Some noradrenergic drugs are listed on the right, and their sites of action are shown in the figure.



Sintesa dan penyimpanan Norepineprine pada saraf simpatis periper

Release , uptake dan metabolisme Norepineprine pada Saraf simpatis periper



APLIKASI KLINIS OBAT SIMPATOMIMETIK

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Direct-acting catecholamines				
Epinephrine	$\alpha_1, \alpha_2, \beta_1, \beta_2, \beta_3$ agonist	Anaphylaxis • hemostatic • cardiac arrest	Parenteral and topical only • does not enter CNS • Duration: short	Hypertension, arrhythmia, stroke, myocardial infarction, pulmonary edema
Norepinephrine	$\alpha_1, \alpha_2, \beta_1, \beta_3$ agonist	Shock	Like epinephrine •IV only	Vasospasm, tissue necrosis, excessive blood pressure increase, arrhythmias, infarction
Dopamine	$D_1, \alpha_1, \alpha_2, \beta_1, \beta_3$ agonist	Shock, especially with renal shutdown • sometimes used in heart failure	Like epinephrine • IV only	Cardiovascular disturbance, arrhythmias
Isoproterenol: $\beta_1, \beta_2, \beta_3$ agonist; primary use is by nebulizer (in acute asthma) and IV (in AV block)				
Dobutamine: β_1 agonist; primary use is in acute heart failure to increase cardiac output				
Noncatecholamine α-selective				
Phenylephrine	α_1, α_2 agonist	Decongestant, mydriatic, neurogenic hypotension	Oral, topical, and parenteral • Duration: 15–60 min	Hypertension, stroke, myocardial infarction

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Noncatecholamines β_2-selective				
Albuterol, metaproterenol, terbutaline	β_2 agonist	Prompt onset for acute bronchospasm	Inhalant via aerosol canister • Duration: 2–6 h	Tachycardia, tremor
Salmeterol, formoterol, indacaterol, vilanterol, olodaterol: β_2 agonists; slow onset, long action. Not useful in acute bronchospasm, used only with corticosteroids for prophylaxis of asthma or with antimuscarinics for COPD.				
Indirect-acting phenylisopropylamines				
Amphetamine, methamphetamine	Displaces stored catecholamines from nerve endings	Anorexiant, ADHD, narcolepsy	Oral and parenteral • Duration: ≥4–6 h	High addiction liability. Paranoia, aggression; insomnia; hypertension; seizures
Ephedrine: displacer like amphetamine plus some direct activity; oral activity; duration 4–6 h. Sometimes used for narcolepsy, idiopathic postural hypotension, enuresis. Lower addiction liability than amphetamines				
Cocaine				
Cocaine	Blocks norepinephrine reuptake (NET) and dopamine reuptake (DAT)	Local anesthetic with intrinsic hemostatic action	Parenteral only (topical nasal, IV, local injection) Duration: 2 h	Very high addiction liability. Hypertension, arrhythmias, seizures
Tyramine				
Tyramine	Displaces stored catecholamines	No clinical use but found in fermented foods	Not a phenylisopropylamine and normally very high first-pass effect, but is absorbed in patients taking MAO inhibitors	Hypertension, arrhythmias, stroke, myocardial infarction

ADHD, attention deficit hyperactivity disorder; COPD, chronic obstructive pulmonary disease; CNS, central nervous system; DAT, dopamine transporter; MAO, monoamine oxidase; NET, norepinephrine transporter.

POTENSI OBAT PADA RESEPTOR ADRENERGIK

Potency	*AGONIST*	*ANTAGONIST*
++++(+)	DEXMEDETOMIDINE	ATIPAMEZOLE
++++	CLONIDINE	YOHIMBINE
+++	NOREPINEPRINE	PENTHOLAMINE
++	EPINEPRINE	PHENOXYBENZAMINE
++	DOPAMINE	TOLAZOLINE
+	ISOPROTERENOL	LABETALOL

EFEK AGONIS ADRENERGIK

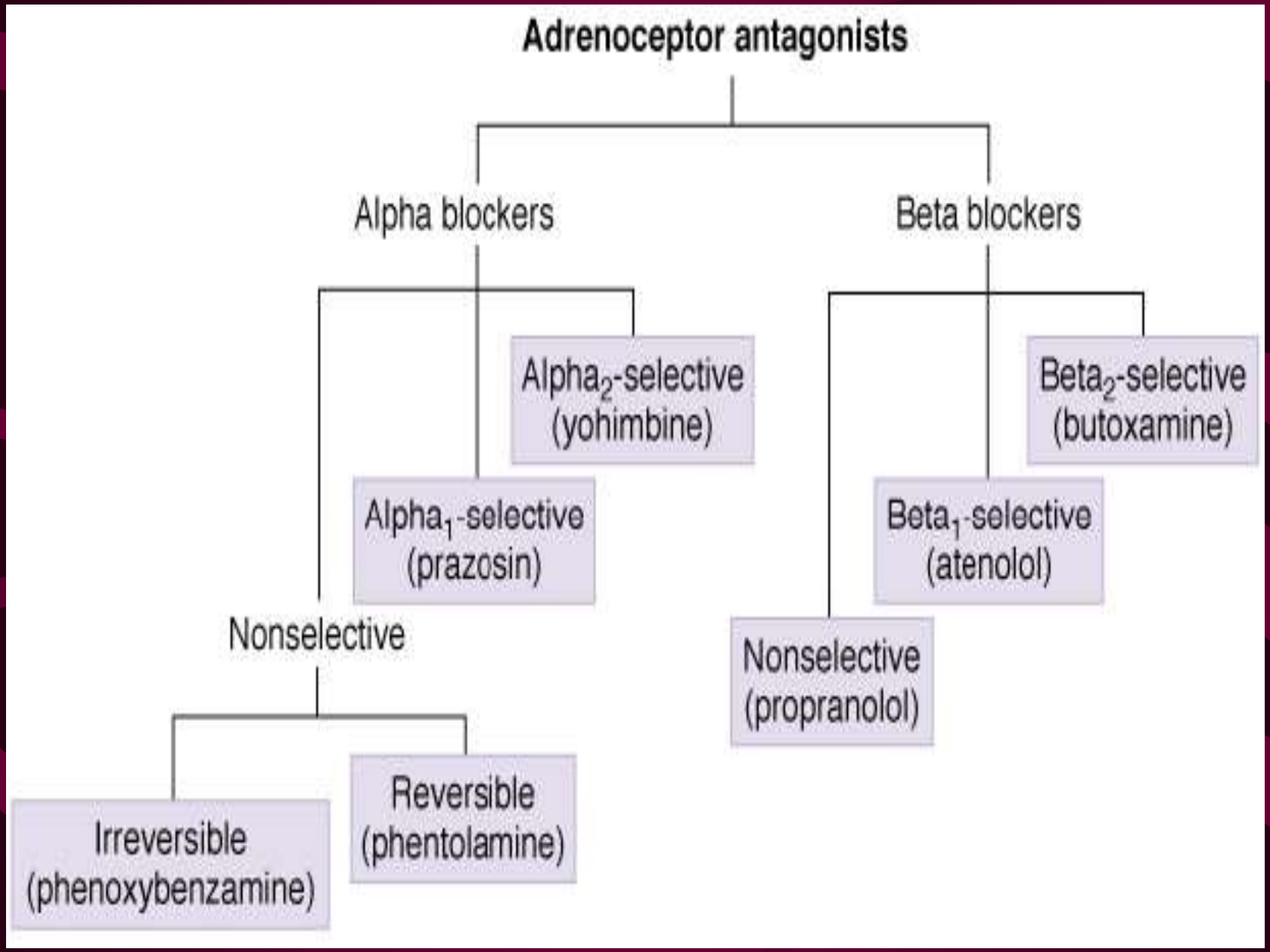
ORGAN	EFEK	RESEPTOR
Mata	Midriasis (kontraksi otot& spinkter radial)	$\alpha 1$
Bronkhus	bronkodilatasi	$\beta 2$
Jantung	Takikardi, aritmia	$\beta 1$
Ginjal	Sekresi renin	$\beta 1$
Genitourinari	Kontraksi spinkter uri (Retensi urine)	$\alpha 1$
	Relaksasi otot polos (Impotensi)	$\alpha 1$
	Relaksasi uterus	$\beta 2$
Pembuluh drh	Vasokonstriksi	$\alpha 1$
	vasodilatasi	$\alpha 2$, $\beta 2$

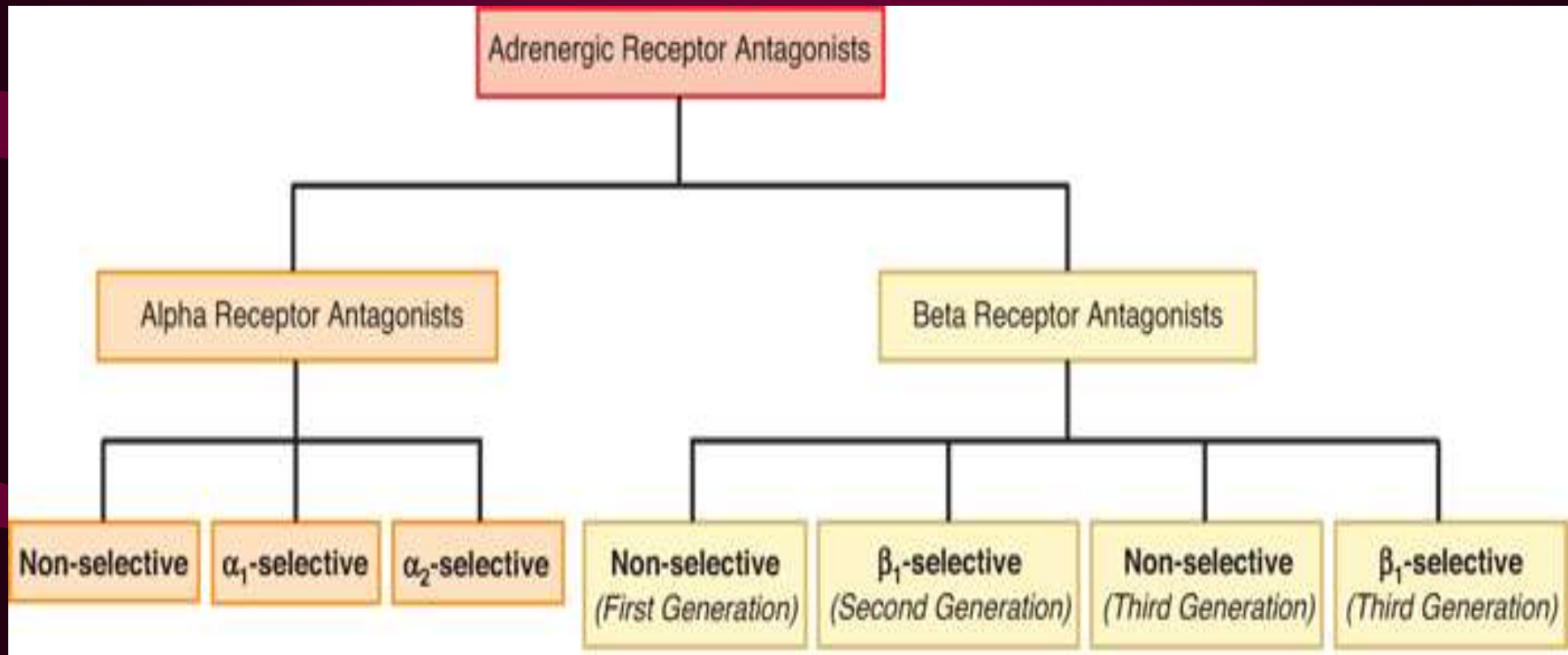
APLIKASI KLINIS AGONIS ADRENERGIK

ORGAN	APLIKASI	OBAT-MEKANISME
Mata	Glaukoma	Fenilefrin, Efedrin,Clonidin -α agonis (me$\uparrow$ outflow / me $\downarrow$ sekresi ??)
	Pemeriksaan mata	Fenilefrin (midriasis)
	Subkonjungtiva Bleed	
Hidung	Dekongestan	Efedrin, Pseudoefedrin, Fenilefrin-α1 agonis
Bronkus	Asma	Salbutamol-β2 agonis
GIT	Diare	Klonidin - α2 agonis
Jantung	Syok, Cardiac Arrest, CHF	Epinefrin, Isoproterenol, Dobutamin
	Hipertensi	Klonidin - α2 agonis
GUT	Inkontinensia Uri	Efedrin, Pseudoefedrin
	Persalinan prematur	β2 agonis

ANTAGONIS ADRENERGIK

• ALPHA	Prazosin	$\alpha 1 >>>> \alpha 2$
	Phenoxybenzamine (irreversible)	$\alpha 1 > \alpha 2$
	Yohimbine	$\alpha 2 >> \alpha 1$
• BETA	Metoprolol	$\beta 1 >>> \beta 2$
	Propranolol	$\beta 1 = \beta 2$
	Timolol	
	Butoxamine	$\beta 2 >>> \beta 1$


Adrenoceptor antagonists
Alpha blockers
Beta blockers
Alpha2-selective (yohimbine)
Beta2-selective (butoxamine)
Alpha1-selective (prazosin)
Beta1-selective (atenolol)
Nonselective
Nonselective (propranolol)
Irreversible (phenoxybenzamine)
Reversible (phentolamine)



Source: L. L. Brunton, B. A. Chabner, B. C. Knollmann: Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 12ed.
www.accesspharmacy.com

EFEK ANTAGONIS ADRENERGIK

ORGAN	EFEK	RESEPTOR
Mata	Miosis Sekresi humor aqueus ↓	α1 β
Bronkhus	Bronkokonstriksi	β2
GIT	Relaksasi otot spinkter Release ACh ↑ (peristaltik ↑) Peristaltik ↑	α1 α2 β2
Genitourinari Prostat	Kontraksi otot polos GUT,uterus	β2 α1
Jantung	Kontraksi ↓ , HR↓	β1
Pembuluh drh	Vasodilatasi (organ/kulit) Vasokonstriksi (skeletal muscle)	α1 β2

APLIKASI KLINIS ADRENOCEPTOR BLOCKERR

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Nonselective α blockers				
Phentolamine	Competitive pharmacologic antagonism at α receptors	Pheochromocytoma, antidote to overdose of α agonists	Oral, IV • short half-life Duration: 2–4 h	Orthostatic hypotension • reflex tachycardia
Phenoxybenzamine	Irreversible (covalent) binding to α receptors	Pheochromocytoma, carcinoid, mastocytosis, Raynaud's phenomenon	Oral, short half-life but long duration of action (24–48 h)	Orthostatic hypotension, reflex tachycardia • gastrointestinal irritation
Alpha$_1$-selective blockers				
Prazosin	Competitive antagonism at α_1 receptors	Hypertension, benign prostatic hyperplasia	Oral Duration: 8 h	Orthostatic hypotension (especially first dose), but little reflex tachycardia
Doxazosin, terazosin: like prazosin; longer duration of action (12–24 h)				
Tamsulosin, silodosin: like prazosin, approved only (and may be partially selective) for benign prostatic hyperplasia				
Alpha$_2$-selective blockers				
Yohimbine	Competitive antagonism at α_2 receptors	Obsolete use for erectile dysfunction • research use	Oral, parenteral	Tachycardia • gastrointestinal upset

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Nonselective β blockers				
Propranolol	Competitive block of β receptors, local anesthetic effect	Angina, arrhythmias (treatment and prophylaxis), hypertension, thyrotoxicosis, tremor, stage fright, migraine	Oral and IV Duration: 4–6 h • Ready entry into CNS	Excessive β blockade: bronchospasm (can be fatal in asthmatics), atrioventricular block, heart failure • CNS sedation, lethargy, sleep disturbances
Timolol, betaxolol, others: lack local anesthetic action; useful in glaucoma *Pindolol:* partial agonist action; possibly safer in asthma *Nadolol:* like propranolol but longer action (up to 24 h) and less CNS effect				
Beta$_1$-selective blockers				
Atenolol	Competitive block of β_1 receptors	Hypertension, angina, arrhythmias	Oral Duration: 6–9 h	Like propranolol with somewhat less danger of bronchospasm
Esmolol: IV agent for perioperative and thyroid storm arrhythmias, hypertensive emergency *Metoprolol:* like atenolol, oral, shown to reduce mortality in heart failure; probably an inverse agonist *Nebivolol:* oral β_1-selective blocker with additional nitric oxide-dependent vasodilating action				
Beta$_2$-selective blockers				
Butoxamine	Competitive block of β_2 receptors	None • research use only	—	Bronchospasm
Alpha + beta blockers				
Labetalol	Four isomers; 2 bind and block both α and β receptors	Hypertension, hypertensive emergencies (IV)	Oral and IV Duration: 5 h	Like atenolol
Carvedilol: like labetalol, 2 isomers; shown to reduce mortality in heart failure				

APLIKASI KLINIS ANTAGONIS ADRENERGIK

ORGAN	APLIKASI	OBAT-MEKANISME
Mata	Glaukoma	Timolol - β bloker
Jantung & pemb drh	CHF Hipertensi	Propanolol Prasozin (α1 bloker) Propanolol,Timolol, Metoprolol (β bloker)
GUT	Benign Prostat Hypertrophy	Prasozin (α1 bloker)

Terima kasih.....