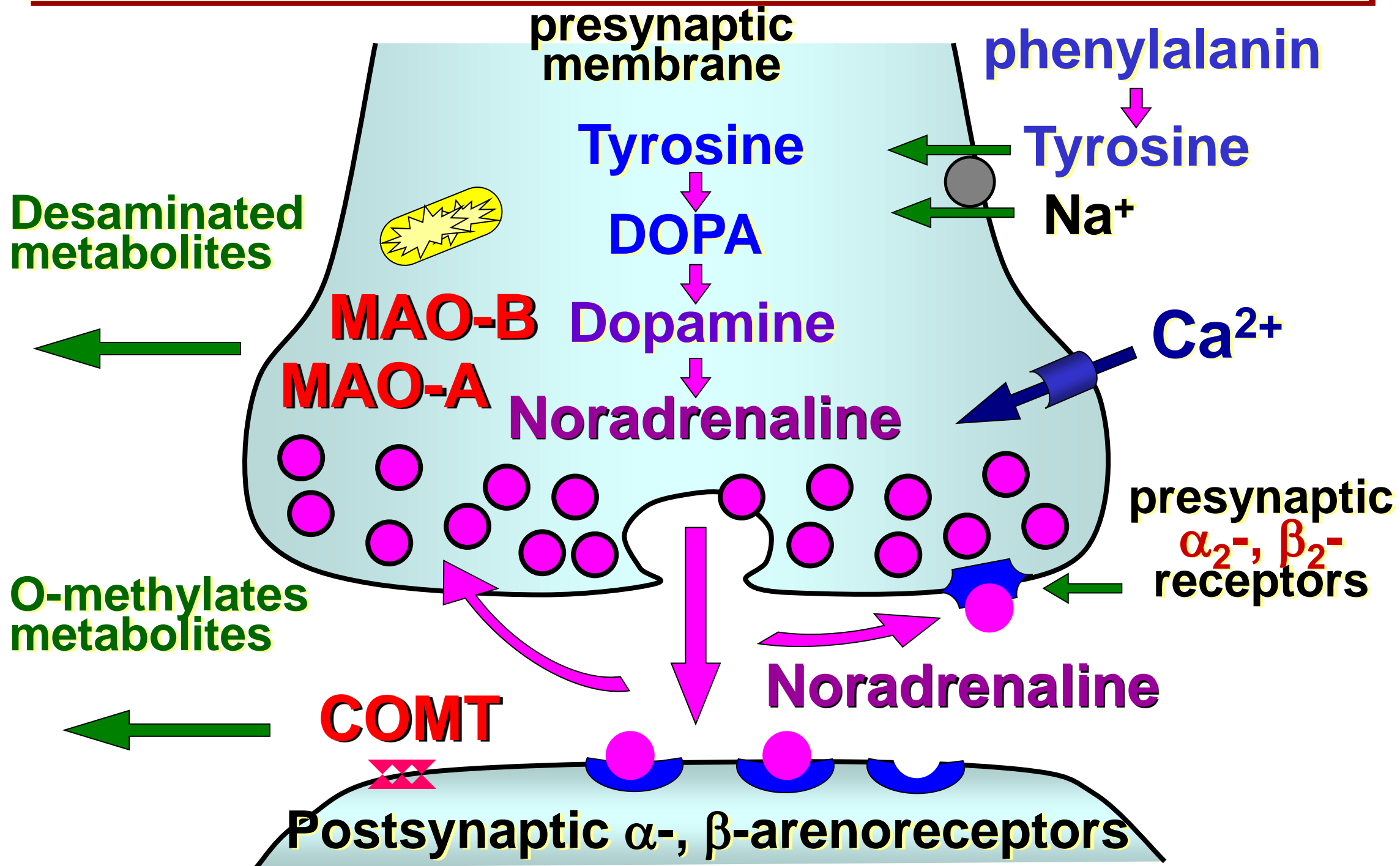


ADRENERGIC

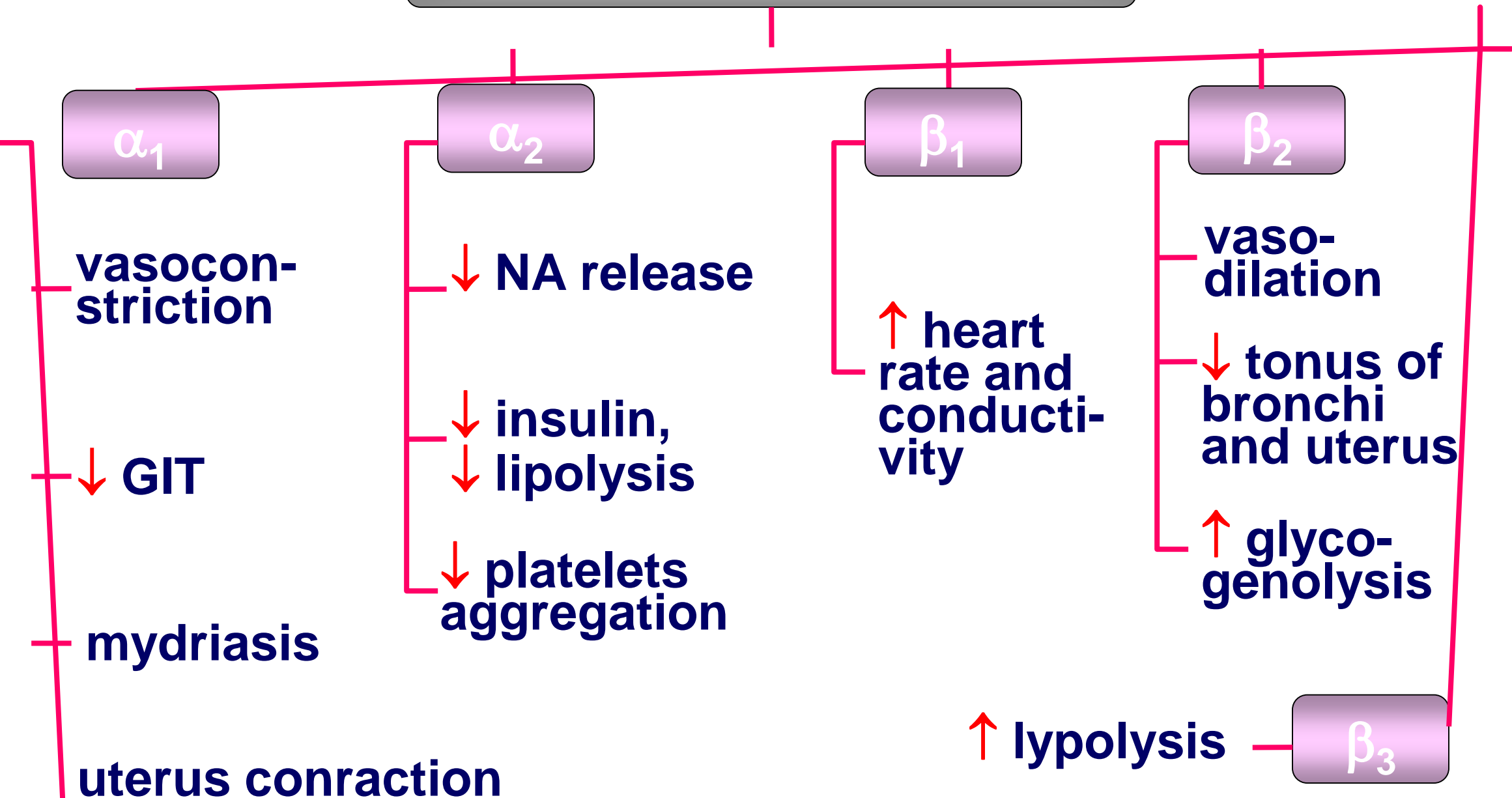
AGENTS

ADRENERGIC JUNCTION



BASIC EFFECTS OF ADRENORECEPTORS

ADRENORECEPTORS



CLASSIFICATION OF ADRENOMIMETICS

⇒ **α -, β - adrenomimetics:**

✓ *direct action:* adrenaline

✓ *indirect action :* ephedrine, dopamine

⇒ **α -adrenomimetics :** noradrenaline, mesaton (phenylephrine), naphthizine (naphazolin) and **central α_2 - (clonidine)**

⇒ **β -adrenomimetics :**

✓ *non-selective ($\beta_1 + \beta_2$):* isadrine (isoproterenol), orciprenalin (metoproterenol)

✓ *selective (β_1):* dobutamine

✓ *selective (β_2):* **short-acting (3-8 hrs) – salbutamol, fenoterol; long-acting (10-12 hrs) – clinbuterol, formoterol**

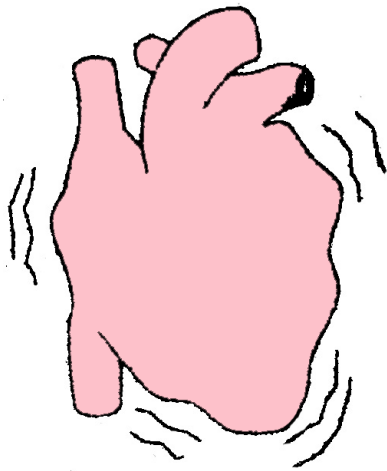
PHARMACODYNAMICS OF ADRENOMIMETICS

Index	adrenaline (α , β)	mesaton (α)	isadrine (β)
Blood vessels tonus: <ul style="list-style-type: none"> • skin (α) • skeletal muscles (β_2, α) • kidneys (D_1, α) • internal organs (α) • systemic peripheral resistance 	<p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">↓ or ↑</p> <p style="text-align: center;">↑</p> <p style="text-align: center;">↓ or ↑</p> <p style="text-align: center;">↓ or ↑</p>	<p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">↑</p> <p style="text-align: center;">↑</p> <p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">↑↑↑↑</p>	<p style="text-align: center;">0</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">↓↓↓</p>
Blood pressure: <ul style="list-style-type: none"> • systolic • diastolic • pulse 	<p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">↓ or ↑</p> <p style="text-align: center;">↑↑↑</p>	<p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">↑↑↑</p> <p style="text-align: center;">0</p>	<p style="text-align: center;">0 or ↓</p> <p style="text-align: center;">↓↓↓</p> <p style="text-align: center;">↑↑↑</p>

ADRENOMIMETICS PHARMACODYNAMICS

heart

«+» **chrono-, inotropic,**
 ↑ **O₂ demand of myocardium**

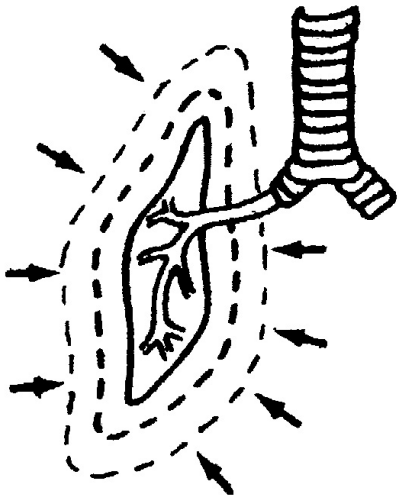


Index	Adrena- line (α, β)	Mesa- ton (α)	Isadrine (β)
• contractility	↑↑↑	0 or ↑	↑↑↑
• heart rate	↓ or ↑	↓↓	↑↑↑
• stroke volume	↑	0, ↓, ↑	↑
• cardiac output	↑	↓	↑↑

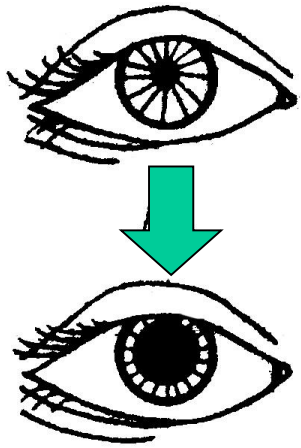
breathing

(β₂, vessels of airways – α₁)

bronchodilation, decongestive



EFFECTS OF ADRENOMIMETICS



eye

mydriasis,

α -agonists – \uparrow fluid outflow, \downarrow intraocular pressure,

β -agonists – \uparrow production

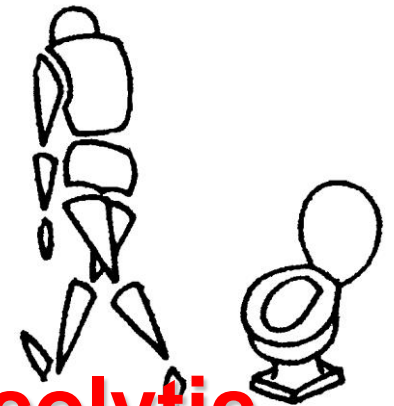
GIT

motorics – decreasing,
sphincters – contraction

urogenital system

uterus (α - и β_2) – relaxation (tocolytic action),

urinary bladder (β_2) - relaxation,
sphincter of urethra and prostate (α) – contraction



exocrine glands **apocrine sweat glands (α) – \uparrow secretion**

EFFECTS OF ADRENOMIMETICS

metabolism

↑ glycogenolysis, ↑ glucose in blood,
 β_3 – adipose tissue \Rightarrow
↑ lipolysis

CNS

Poorly crossing BBB (*catecholamines etc*)
– nervousness (large doses),
Well crossing BBB (*indirect acting –
ephedrine, amphetamine, cocaine etc*) –
psychostimulation, insomnia etc.



ARENOMIMETICS

Adrenaline (epinephrine) – $\alpha=\beta$

- **cardiostimulation** (+ **chrono-**, **inotropic** effect, sharp \uparrow oxygen demand of myocardium). *At I.V. administration bradycardia can develop!*
- **vasoconstriction**, but dilate the vessels that contain β -receptors (skeletal muscles, heart, brain, liver, lungs)
- \uparrow SAP, \downarrow or \uparrow DAP and systemic peripheral resistance
- at adrenoblockers administration **adrenaline** «reversal» \downarrow BP
- **bronchodilation**
- \downarrow **intraocular pressure, mydriasis**

ARENOMIMETICS

Noradrenaline – $\alpha_1 = \alpha_2 > \beta_1 > \beta_2$

- **vasoconstrictor** (\uparrow SAP, \uparrow DAP, \uparrow systemic peripheral resistance)
- **+ inotropic effect**
- **only I.V. administration !**

Mesaton – α

- **vasoconstrictor** (\uparrow SAP, \uparrow DAP)
- **mydriasis**
- **decongestant**
- ***is not inactivated by COMT \Rightarrow longer action !***

Isadrine – $\beta_1 = \beta_2$

- **vasodilator** (\uparrow cardiac output, insignificantly \uparrow SAP + \downarrow DAP, peripheral resistance)
- **+ chrono-, ino-, dromotropic effects**
- **bronchodilator, \downarrow GIT tonus, \uparrow CNS**

INDICATIONS FOR ADRENOMIMETICS

- **cardiac arrest** – *adrenaline*
- **acute hypotension (shock, collapse)** – *noradrenaline, dopamine, mesaton*
- **cardiogenic shock** – *isadrine, dobutamine*
- **anaphylactic shock** – *adrenaline*
- **hypoglycemia** – *adrenaline*
- **decreasing of regional blood flow (local anesthesia)** – *adrenaline, mesaton*
- **asthma - β -salbutamol)**
- **risk of miscarriage** – *fenoterol, hexoprenaline*
- **rhinitis** – *naphthizine, halazoline*
- **ophthalmology (glaucoma, diagnost)**
mesaton, adrenaline u òp.



ADVERSE EFFECTS OF ADRENOMIMETICS

- ✓ **↑ BP (stroke, pulmonary edema)**
- ✓ **arrhythmia, myocardial infarction**
- ✓ **insomnia, tremor (ephedrine etc)**
- ✓ **development of necrosis at S.C. administration (noradrenaline)**
- ✓ **dryness in mouth (β -adrenomimetics)**
- ✓ **dryness of nasal mucosa (α -adrenomimetics)**
- ✓ **conjunctiva irritation, mydriasis**
- ✓ **tachyphylaxia (ephedrine etc)**
- ✓ **tolerance**
- ✓ **dependence (ephedrine, amphetamine)**



ADRENOBLOCKERS

Sympatholytics	$\alpha 1 + \alpha 2$ -adrenolytics	$\alpha 1$ -adrenolytics	$\beta 1 + \beta 2$ – adrenolytics	$\beta 1$ -adrenolytics
Reserpine, octadine	Phentolamine, nicergoline	Prazosin, terazosin	Propranolol, pindolol	Atenolol, metoprolol
Decrease peripheral vascular resistance, lower BP	Decrease peripheral vascular resistance, lower BP, facilitation of urination, reflex tachycardia, nasal congestion		Diminish cardiac output, rate, and oxygen consumption; inhibit cardiac excitability and conductivity	

ADRENOBLOCKERS

Sympatholytics	$\alpha 1 + \alpha 2$ -adrenolytics	$\alpha 1$ -adrenolytics	$\beta 1 + \beta 2$ – adrenolytics	$\beta 1$ -adrenolytics
Hypertension	Hypertension, pheochromocytoma, spasm of blood vessels, benign prostate hyperplasia		Hypertension, angina pectoris, arrhythmia, hyperthyroidism, glaucoma, migraine	
Diarrhea, ulcer of stomach, collapse bradycardia	Orthostatic hypotension, redness of skin, tachycardia		Bronchoconstriction, atrioventricular block, spasm of vessels, hypoglycemia	

PROPERTIES OF BETA-BLOCKERS

Agents	ISA*	MSA**	Lipid solubility	Bioavail ability	Elimination Half-Life
<i>I. Nonselective β- ($\beta_1 + \beta_2$) adrenergic agonists</i>					
Propranolol	No	Yes	High	≈ 30	3-6 hours
Nadolol	No	No	Low	≈ 33	14-24 hr
Timolol	No	No	Moderate	≈ 50	4-5 hours
Pindolol	Yes	Yes	Moderate	≈ 90	3-4 hours
Labetalol	No	Yes	Moderate	≈ 30	5 hours
Sotalol	No	No	Low	≈ 90	12 hours

Footnote: * - **Intrinsic sympathomimetic activity** (partial agonists)

** - **Membrane-stabilizing activity** (local anesthetic action)

PROPERTIES OF BETA-BLOCKERS

Agents	ISA*	MSA**	Lipid solubility	Bioavail ability	Elimination Half-Life
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II. Selective β_1 adrenergic agonists

Metoprolol	No	Yes	Moderate	≈ 50	3-4 hours
Acebutolol	Yes	Yes	Low	≈ 50	3-4 hours
Atenolol	No	No	Low	≈ 40	6-9 hours
Esmolol	No	No	Low	...	10 minutes
Sotalol	No	No	Low	≈ 90	12 hours

Footnote: * - **Intrinsic sympathomimetic activity** (partial agonists)
** - **Membrane-stabilizing activity** (local anesthetic action)