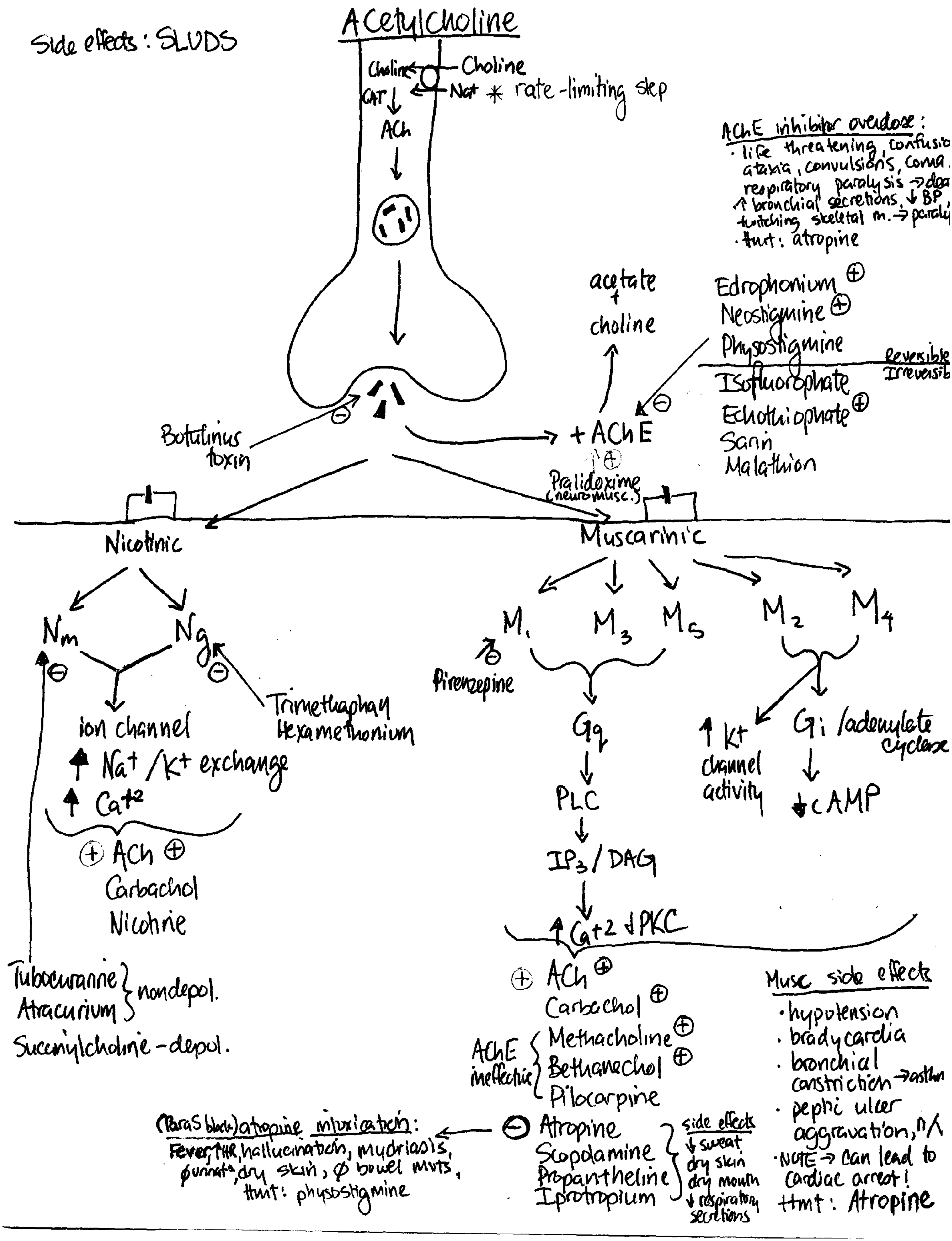

Side effects: SLUDS
Acetylcholine
Choline
Choline
CAT
Na+
* rate-limiting step
ACh
AChE inhibitor overdose:
· life threatening, confusio
ataxia, convulsions, coma
respiratory paralysis → dea
↑ bronchial secretions, ↓ BP
twitching skeletal m. → paraly
· tmt: atropine
acetate
+
choline
Edrophonium ⊕
Neostigmine ⊕
Physostigmine
Reversible
Irreversib
Isofluorophate
Echothiophate ⊕
Sarin
Malathion
Botulinus toxin
+ AChE
Pralidoxime (neuromusc.)
Nicotinic
Muscarinic
Nm
Ng
M1
M3
M5
M2
M4
Trimethaphan
Hexamethonium
Pirenzepine
ion channel
↑ Na+ / K+ exchange
↑ Ca+2
⊕ ACh ⊕
Carbachol
Nicotine
Gq
PLC
IP3 / DAG
↑ Ca+2 + PKC
↑ K+ channel activity
Gi / adenylate cyclase
↓ cAMP
Tubocurarine
Atracurium
nondepol.
Succinylcholine - depol.
⊕ ACh ⊕
Carbachol ⊕
Methacholine ⊕
Bethanechol ⊕
Pilocarpine
AChE ineffective
Musc side effects
· hypotension
· bradycardia
· bronchial constriction → asthm
· peptic ulcer aggravation, n/v
· NOTE → can lead to cardiac arrest!
tmt: Atropine
(Paras block) atropine intoxication:
Fever, ↑HR, hallucination, mydriasis,
ø urinat., dry skin, ø bowel mvts,
tmt: physostigmine
⊖ Atropine
Scopolamine
Propantheline
Ipratropium
side effects
↓ sweat
dry skin
dry mouth
↓ respiratory secretions

ACh

N_m

muscle contraction

N_g

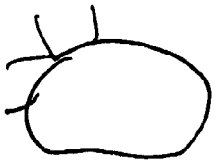
ANS ganglia depol.

Adrenal medulla → catecholamine release

M_1

ANS ganglia depol.

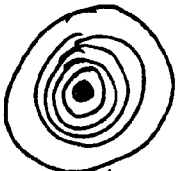
M_2



Heart

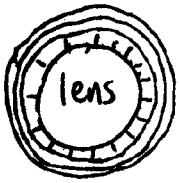
↓ HR (SA)
↓ contractility
↓ AV conduction

M_3

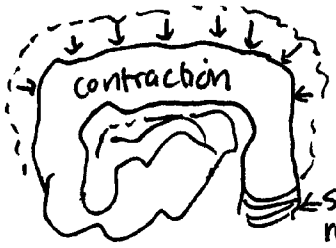


iris circular m. (sphincter) of eye (miosis)

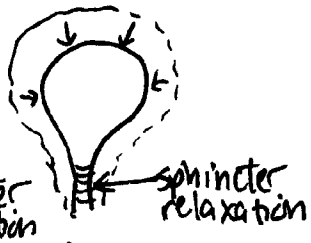
also opens canal of Schlemm to ↑ outflow aqueous humor



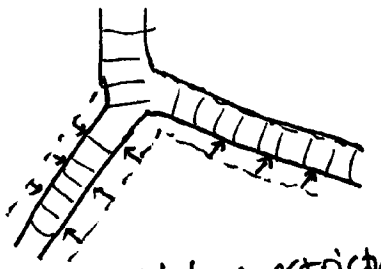
ciliary m. contraction → ↑ accomodation



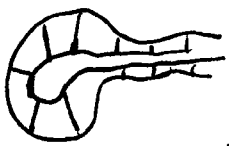
GI ↑ motility



GU micturition



Bronchial constriction

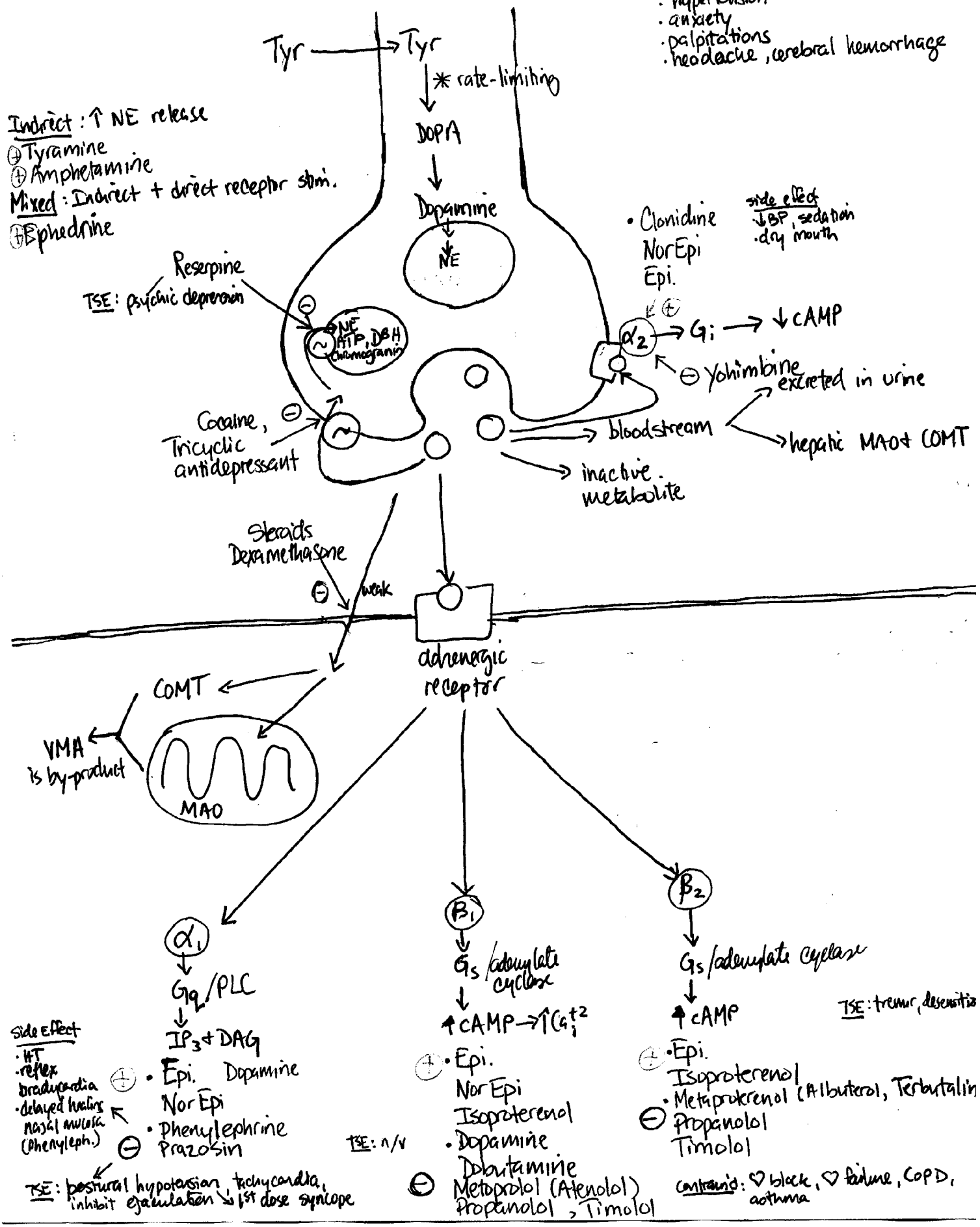


secretory glands
↑ secretion (saliva, bronchial, GI)

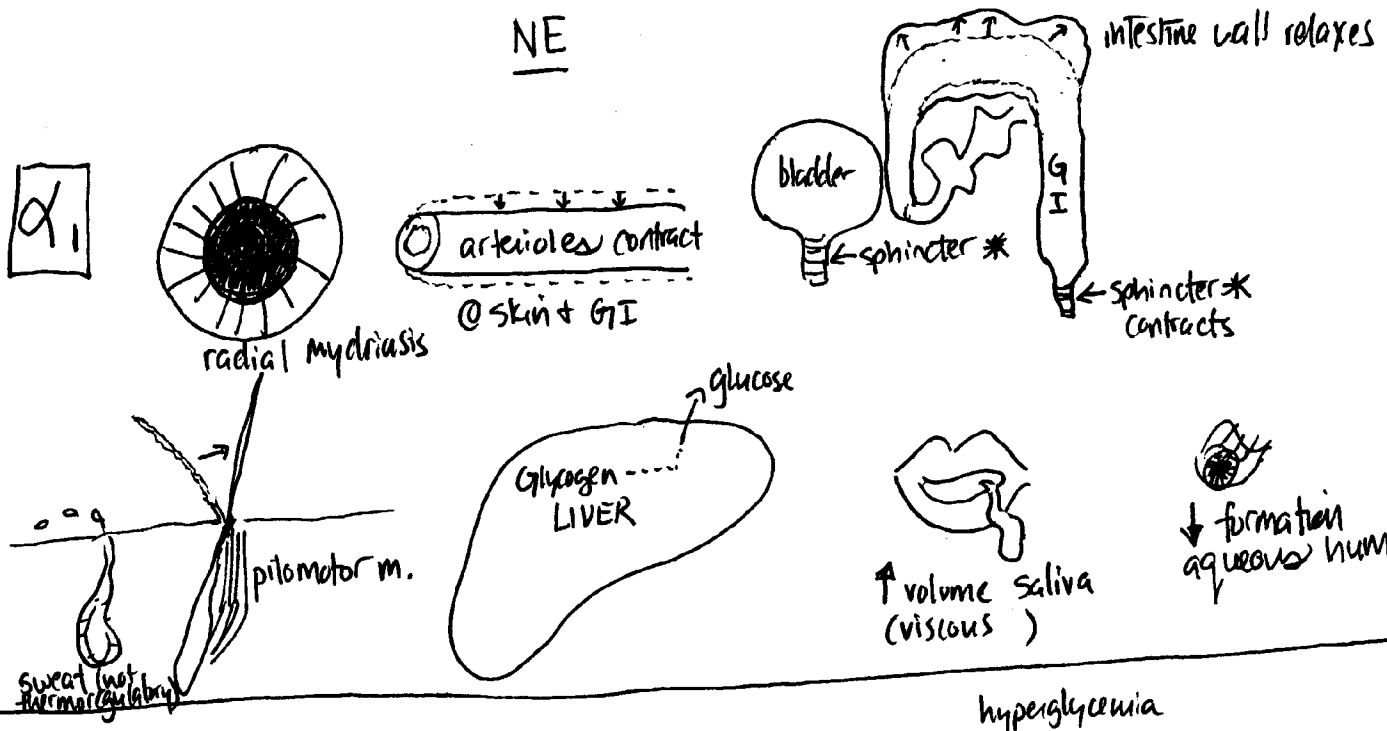
↑ watery saliva

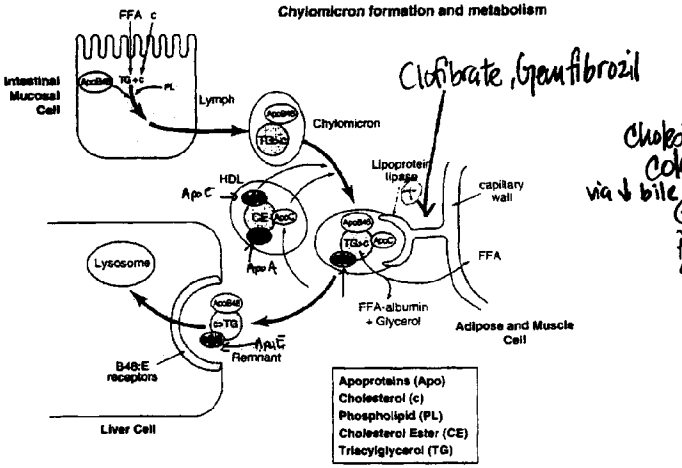
↑ lacrimal secretion

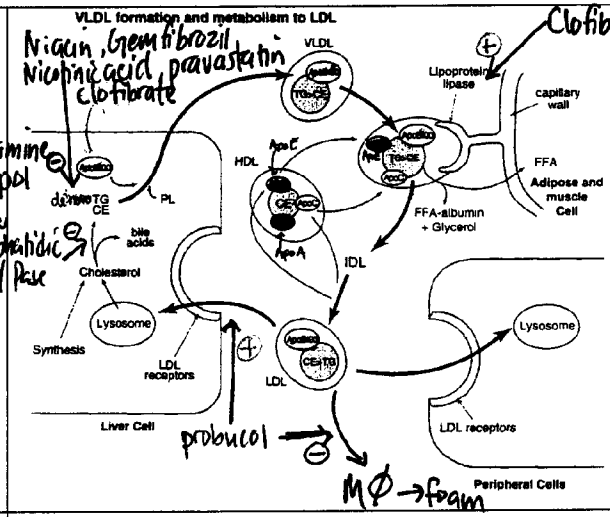
NOREPINEPHRINE

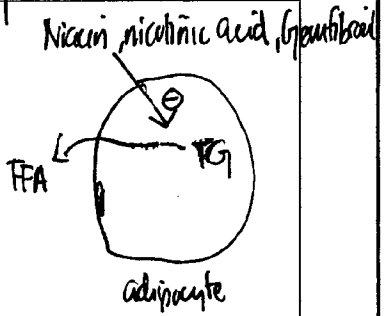


NE

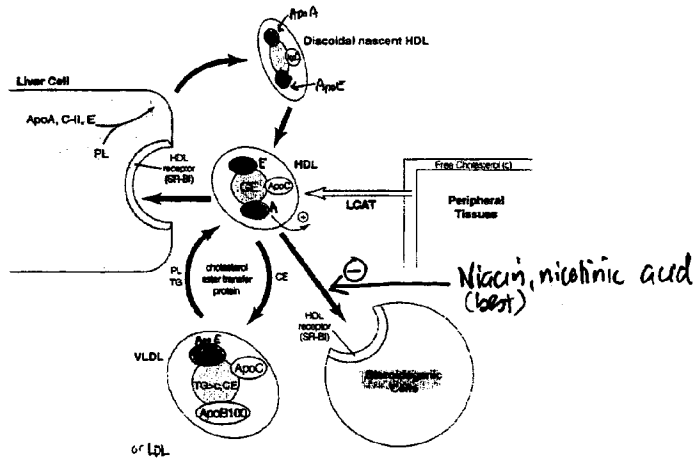

α1
radial mydriasis
arterioles contract
@ skin + GI
intestine wall relaxes
bladder
GI
sphincter *
sphincter * contracts
pilomotor m.
sweat (not thermoregulatory)
glucose
Glycogen
LIVER
↑ volume saliva (viscous)
↓ formation aqueous humor
α2
arterioles dilate
passive b/c ↓ NE
platelets aggregate
hyperglycemia
β
insulin
LIVER
β1
HEART
↑ contraction force
↑ AV conduction
↑ SA rate
↑ CO
renin
JG
Glomerulus
JG cells → ↑ renin
TG
↑ FFA
↑ glycerol
Adipocyte lipolysis
↑ salivary amylase
β2
vasc. smooth m.
dilate
few @ renal, skin + fat
many @ skeletal m.
Bronchiolar smooth muscles relax
GI
GU
Relaxation
↓ motility
uterus relaxes
Glycogen → glucose
skeletal muscle
glucose
glycogenolysis
LIVER







6. HDL Formation and Metabolism



Summary of Serum Lipoproteins

Lipoprotein/ (Synthesis)	Major Core Lipids	Apoproteins	Protein Source/ {Turnover}	Mechanism of lipid delivery
Chylomicron (intestine)	Dietary triacylglycerols	B-48 C-II, E	*de novo* synthesis Serum HDL	Hydrolysis by lipoprotein lipase to remnant
Chylomicron remnant	Dietary cholesterol (esters)	B-48 [C-II]	*de novo* synthesis Serum HDL Transferred to HDL	Taken up by liver via receptor-recognition of B-48 and E
VLDL (liver)	Endogenous triacylglycerols	B-100 C-II, E	*de novo* synthesis Serum HDL	Hydrolysis by serum lipoprotein lipase to LDL and IDL
LDL IDL	Endogenous cholesterol (esters)	B-100, C-II] E	*de novo* synthesis Transferred to HDL	Taken up by liver and other tissue via receptor-recognition of B-100
HDL (liver)	Endogenous cholesterol (esters)	C-II, A E	*de novo* synthesis	Taken up by liver and steroidogenic tissue via receptor.

LIPID ↓ DRUGS 1

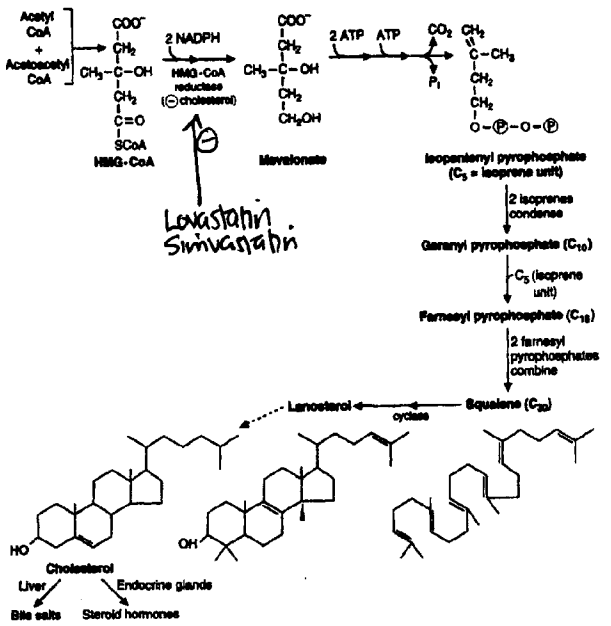
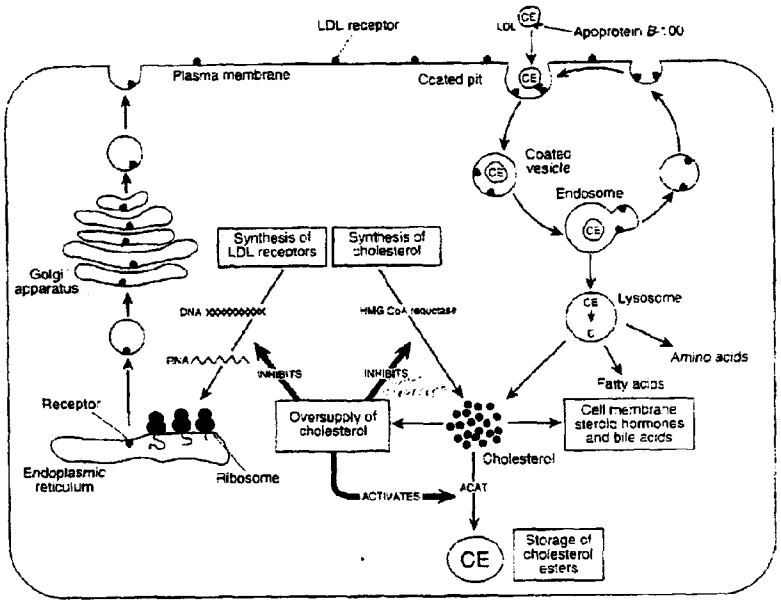
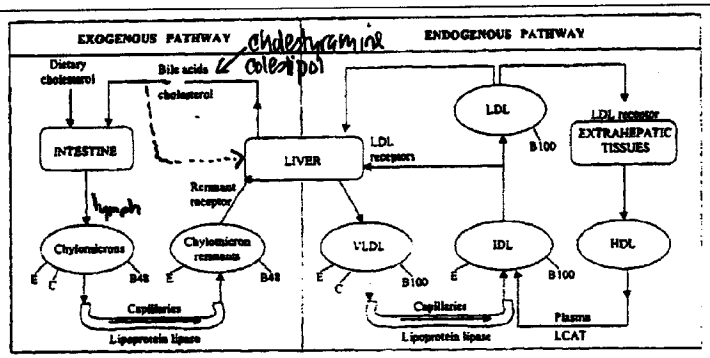


Figure 6-6. Cholesterol biosynthesis. *HMG CoA* = hydroxymethylglutaryl CoA; ⊖ = inhibited by; circled *P* = phosphate group.

8. Regulation of receptor and cholesterol synthesis





LIPID ↓ DRUGS

TSE: ♡ block, supraventricular arrhythmia due to WPW Syndrome, asthma / COPD, mask diabetic hypoglycemia, sleep disorders, w/drawal syndrome

TSE: ↑ ischemia arrhythmias

Dobutamine
Dopamine

Metoprolol, Atenolol
propanolol, carvedilol

Ca^{+2}

Verapamil, Diltiazem

TSE: CHF, SA node disease or AV node disease WPW syndrome, hypotension, peripheral edema, constipation

Ca^{+2} channel

β_1 Adr. rec.

cAMP

Milrinone → Phosphodiesterase

TSE: arrhythmias

Ca^{+2}_{SR} → Ca^{+2}_{in} → Acto-myosin ATPase → muscle cell

Ca^{+2} ATPase

Na^+/K^+ ATPase

K^+

Na^+

Na^+

Ca^{+2} out

Digitalis
Digoxin

↑ K^+

↑ Ca^{+2}

closure

K^+ channel

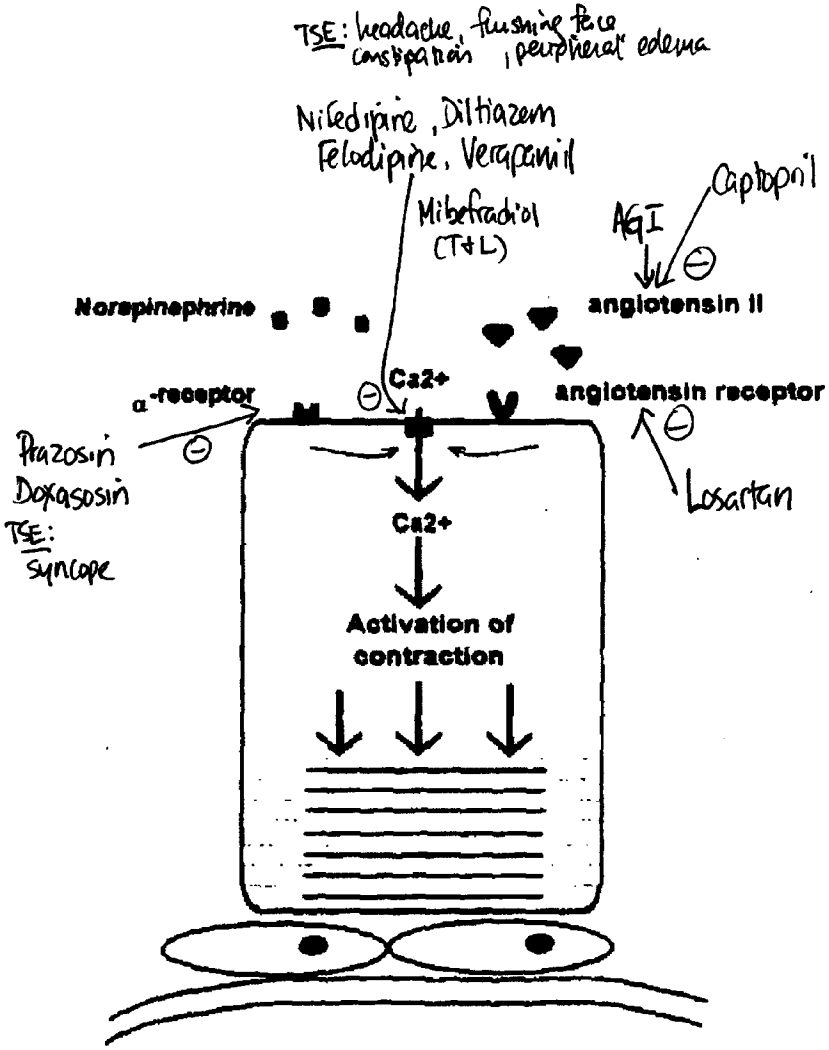
TSE:
- general - malaise, GI symptoms (chemoreceptic Trigger zone)
- ♡ - arrhythmias, bradycardia
- ♡ block, supraventricular + ventricular tachyarrhythmias
- AV junctional tachycardia
- visual Δs + color distortions
- gynecomastia

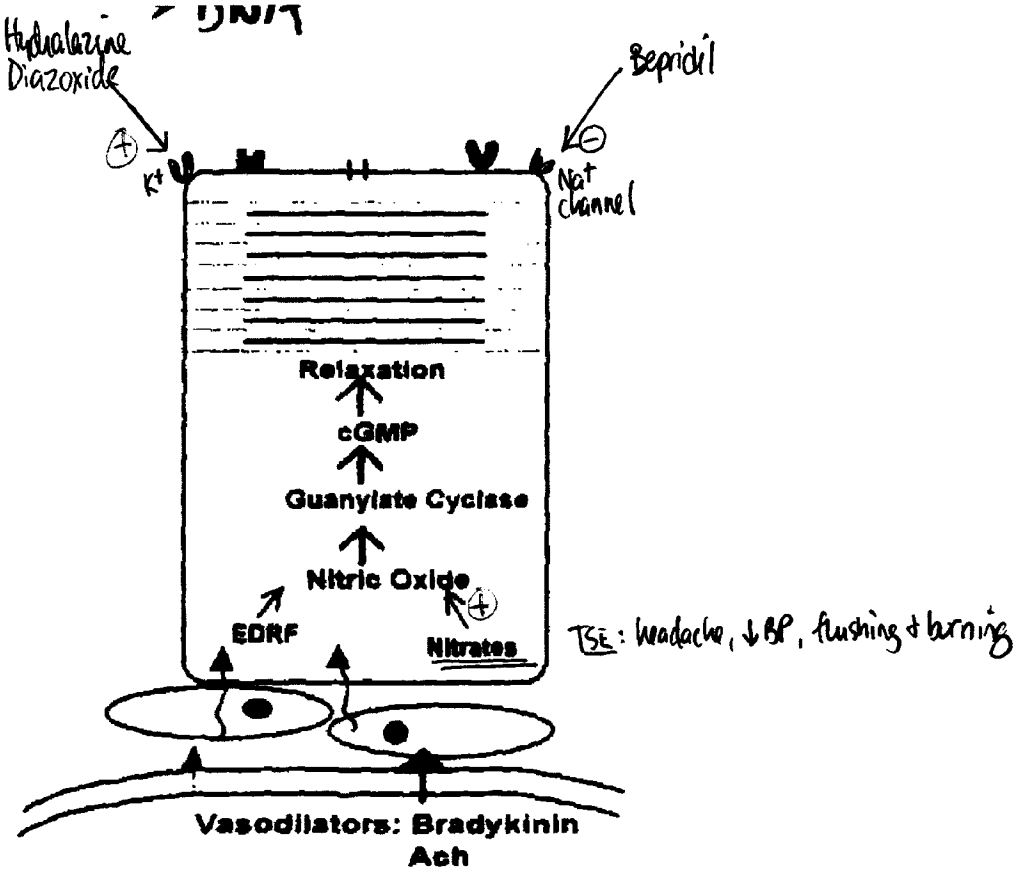
Tmt: immunoassay, slow clearance ($T_{1/2}$ - 1.6d)
correct serum electrolyte abnormalities, antiarrhythmia
digoxin-binding Ab

INOTROPES

Venous - 70% BV, ↓P → preload Organic Nitrates, Nitroprusside, Prazosin, Doxasosin

Arterial - 10% BV, ↑R → afterload Hydralazine, Minoxidil, Diazoxide, Nitroprusside, Nifedipine, Nitrates, Prazosin* Doxasosin*
Captopril, Losartan, Nifedipine, Diltiazem, Felodipine, Verapamil





TSE: headache, ↓BP, flushing & burning

VASODILATORS