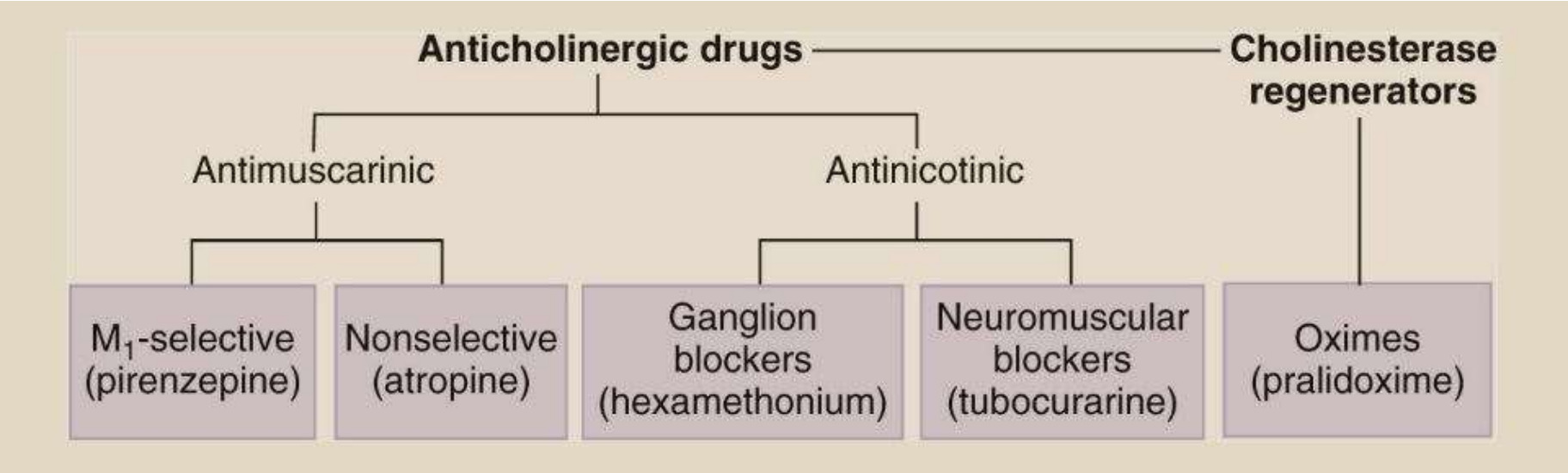
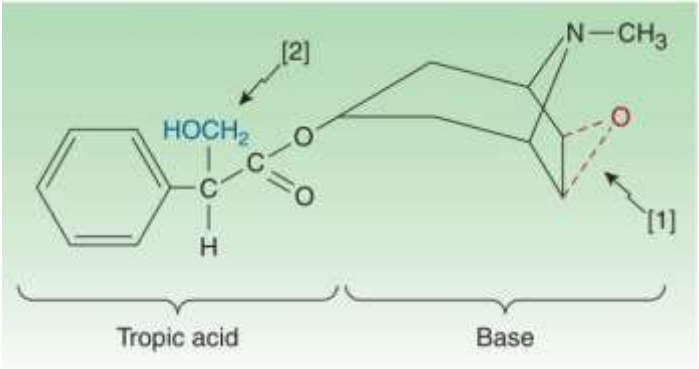
Anticholinergics

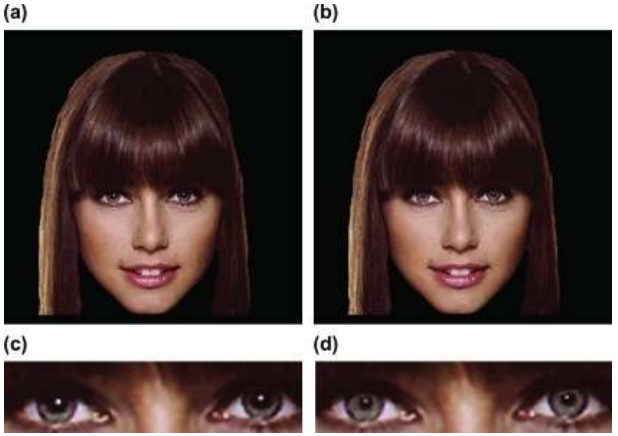
(cholinoceptor blockers and cholinesterase regenerators)



Atropine



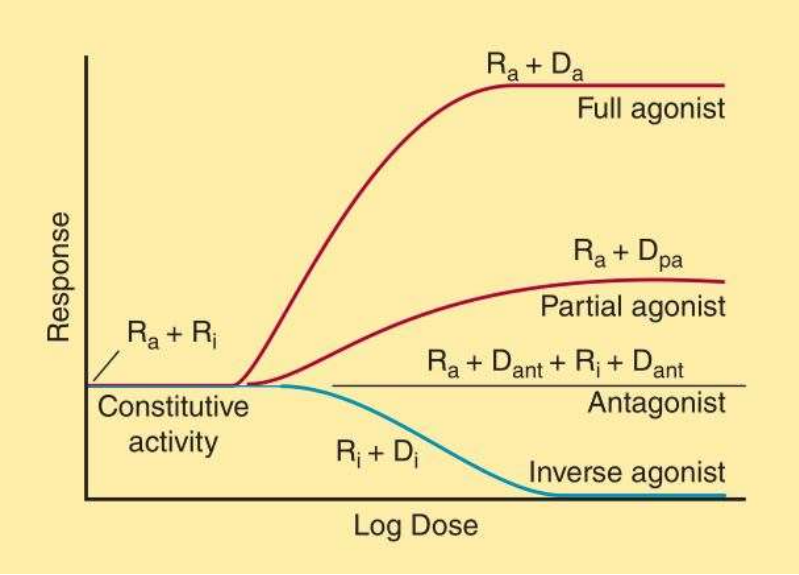
- *Atropa belladonna, Datura stramonium*



Demos KE, Kelley WM, Ryan SL, Davis FC, Whalen PJ. **Human amygdala sensitivity to the pupil size of others**. *Cereb Cortex*. **2008** Dec;18(12):2729-34. doi: 10.1093/cercor/bhn034. Epub 2008 Mar 27. PubMed PMID: 18372291; PubMed Central PMCID: PMC2583162. “the right amygdala and left amygdala/substantia innominate were sensitive to the pupil size of others, exhibiting increased activity for faces with relatively large pupils.”

Atropine

- surmountable blockade of M receptors
  - non-selective for subtypes
  - L isomer more potent
  - inverse agonist

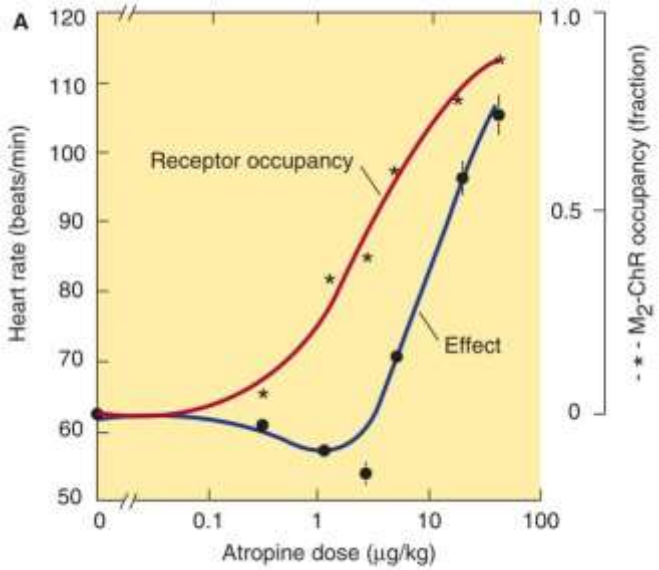


Antimuscarinic effects

- CNS
  - normal dose
    - minimal stimulant / longer-lasting sedative
    - see scopolamine – drowsiness / amnesia
      - used in motion sickness
  - high dose
    - excitement, agitation, hallucinations, coma
  - Parkinson's disease
    - benztropin / biperiden / trihexyphenidyl
- Eye
  - mydriasis / cycloplegia / dry eyes

Antimuscarinic effects

- CV
  - tachycardia
    - see paradox bradycardia
  - ↓ PR interval
  - inhibited vasodilation
    - mostly non-innervated M receptors
- respiratory system
  - bronchodilation
  - secretion↓
- gastrointestinal tract
  - dry mouth
  - gastric secretion is blocked less effectively
  - smooth muscle relaxation



Antimuscarinic effects

- genitourinary tract
  - relax ureters and bladder wall
  - urinary retention
- sweat glands
  - atropine fever

primarily in infants

Therapeutic use of antimuscarinic agents

- CNS
  - Parkinson's disease - benztropine
  - motion sickness – scopolamine
- eye
  - measurement of refractive error / ophthalmoscopy

Drug	Duration of Effect (days)	Usual Concentration (%)
Atropine	7–10	0.5–1
Scopolamine	3–7	0.25
Homatropine	1–3	2–5
Cyclopentolate	1	0.5–2
Tropicamide	0.25	0.5–1

Therapeutic use of antimuscarinic agents

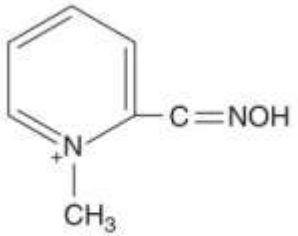
- respiratory disorders
  - premedication in anesthesiology
  - COPD / asthma
    - ipratropium / tiotropium
- cardiovascular disorders
  - myocardial infarction
  - hyperactive carotid sinus reflex
- gastrointestinal disorders
  - peptic ulcer – pirenzepine / telenzepine
  - mild hypermotility
    - diarrhea (see diphenoxylate + atropine)
    - IBS

Therapeutic use of antimuscarinic agents

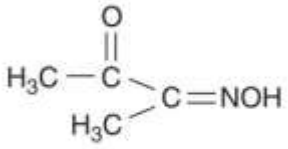
- urinary disorders
  - urinary urgency / after urologic surgery
  - overactive bladder
  - incontinence
    - M_3: oxybutynin / trospium / darifenacin / solifenacin / tolterodine / fesoterodine
- cholinergic poisoning
  - organophosphates
- hyperhidrosis ?

Organophosphate poisoning

- antagonize muscarinic effects - atropine
  - nicotinic agonists will cause blockade – no antag.
  - repeat
- cholinesterase regenerators
  - pralidoxime (PAM), diacetylmonoxime (DAM), obidoxime



Pralidoxime



Diacetylmonoxime

Organophosphate poisoning

- atropine dose
  - repeat as needed – huge amounts
- cholinesterase regenerators
  - ASAP – see aging
    - 1-2 g iv. infusion 30 min
    - multiple doses
  - PAM do not cross BBB
  - not recommended in carbamate intoxication
- pretreatment
  - pyridostigmine + atropine

Adverse effects of antimuscarinic agents

- depends on the purpose
- atropine poisoning
  - “dry as a bone, blind as a bat, red as a beet, mad as a hatter.”
  - hyperthermia – infants, children
  - symptomatic treatment – but see physostigmine

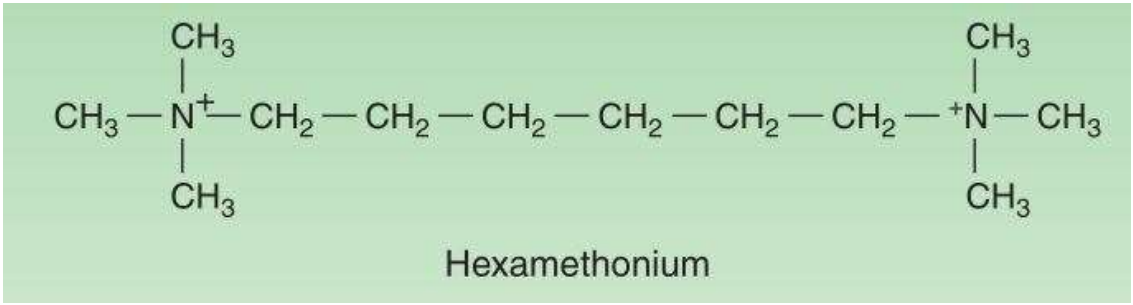
- other drugs with antimuscarinic effects
  - TCA, antipsychotics, antihistamines, meperidine = pethidine

Contraindications of antimuscarinic agents

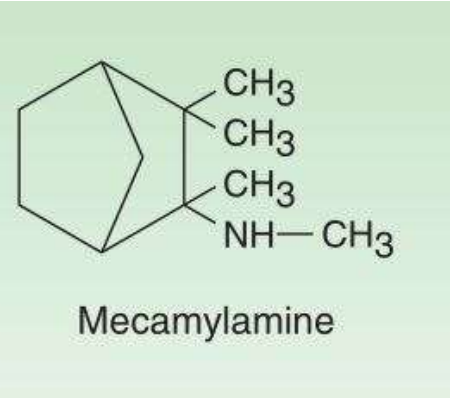
- relative
  - e.g. organophosphate poisoning must be treated
- glaucoma (primarily closed angle)
- prostatic hyperplasia
- gastric ulcer
  - slow gastric emptying → may ↑ symptoms
  - but see selective M_1 blockers

Ganglion blockers

- first drugs for hypertension – now obsolete
- lack of selectivity → limited use
  - hexamethonium, mecamylamine, trimethaphan



Hexamethonium



Mecamylamine

- adverse effects
  - cycloplegia, orthostatic hypotension, moderate tachycardia, impaired sexual function