Congestive Heart Failure

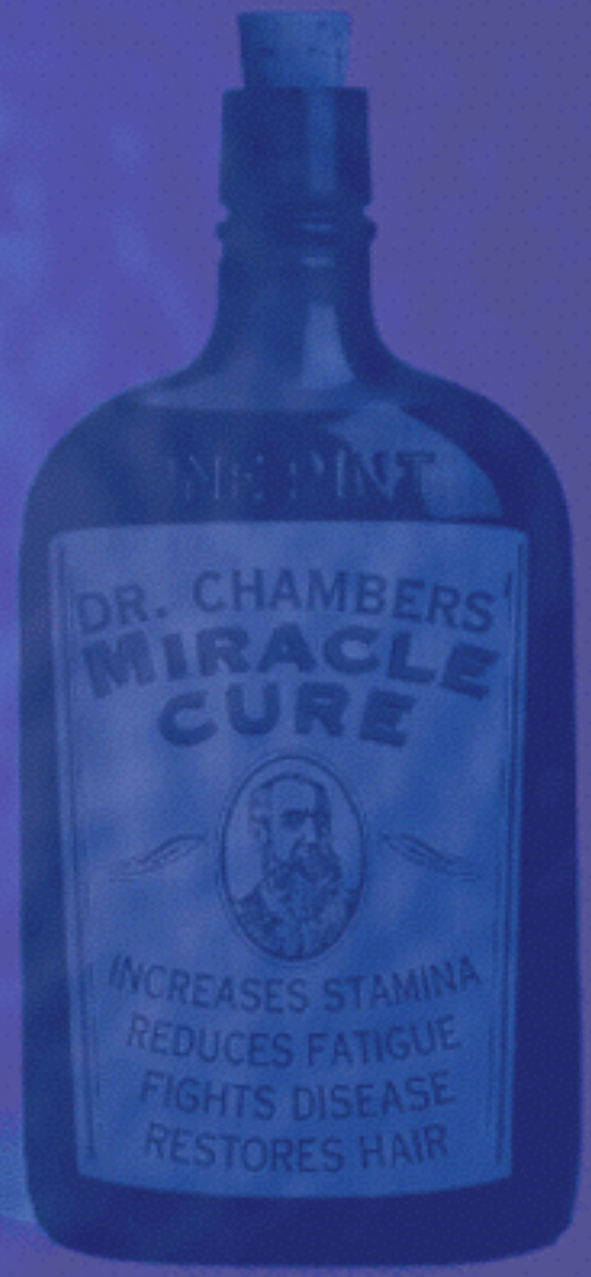
more interesting stuff…

by the end of this lecture

- you should be able to formulate a prioritised treatment plan for an animal with congestive heart failure

congestive heart failure

- rest
- low salt diet
- diuretics
- vasodilators
- long acting inotropes
- (antiarrhythmics)



7 yr old Doberman

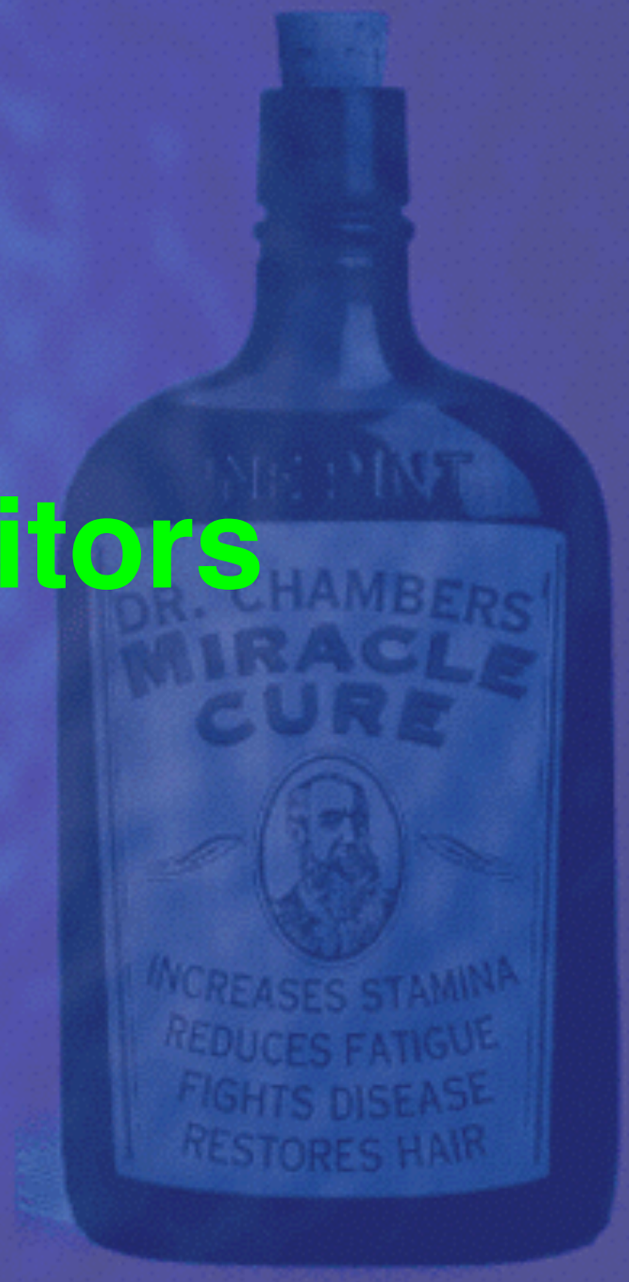
- cough
- lethargy / exercise intolerance
- anorexia
- ascites
- sudden onset 1 week ago

examination

- soft systolic murmur
- heart rate 148
- harsh lung sounds

positive inotropes

- sympathomimetics
- cardiac glycosides
- phosphodiesterase inhibitors

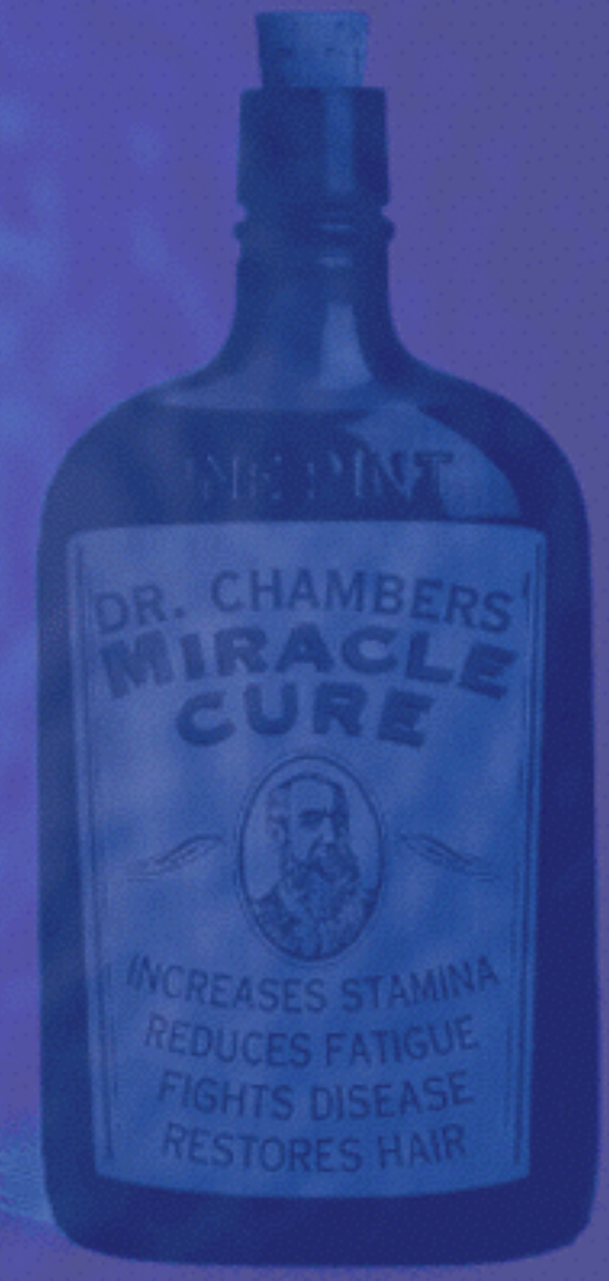


cardiac glycosides

- = digitalis

cardiac glycosides

- **digoxin**
  - digitoxin
  - oubain
  - lanatoside C
  - strophanthin
  - squill
  - convallotoxin
  - some toads' skin



chemistry

- steroid nucleus
- lactone group
- 3 sugars

effects

- positive inotropic
- negative chronotropic

β ADRENOCEPTOR AGONISTS

CALCIUM CHANNEL BLOCKERS

LOCAL ANAESTHETICS

DIGITALIS

β1 adrenoceptor

adenyl cyclase

L type Ca channel (dihydropyridine receptor)

Ca++

Na channel

Na+

sodium pump

Na / Ca exchanger

out

in

ATP

5'AMP

cAMP

Ca++

Na+

Ca++ Na+

Na+ K+

PDI

sarcoplasmic reticulum

Ca++

ryanodine receptor

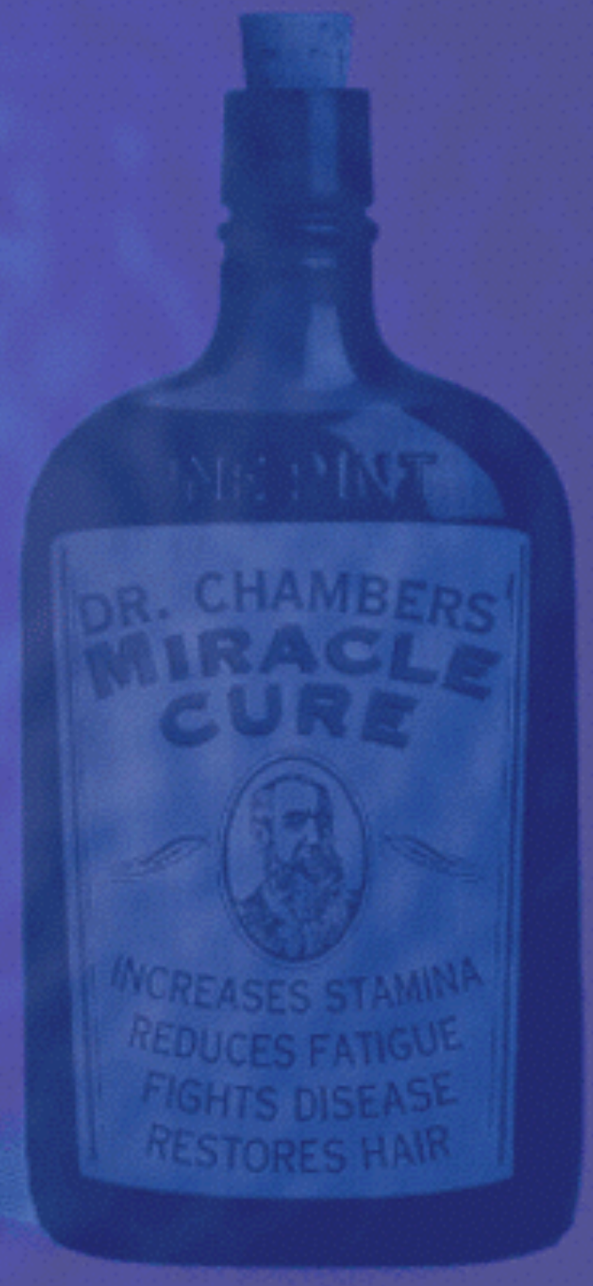
+

[Ca++]

myofibrils

negative chronotropy

- vagal stimulation
- potentiation of ACh
- SA & AV node



indications

- **congestive heart failure**
  - –especially DCM
- **supraventricular tachycardias**
  - –atrial fibrillation

side effects

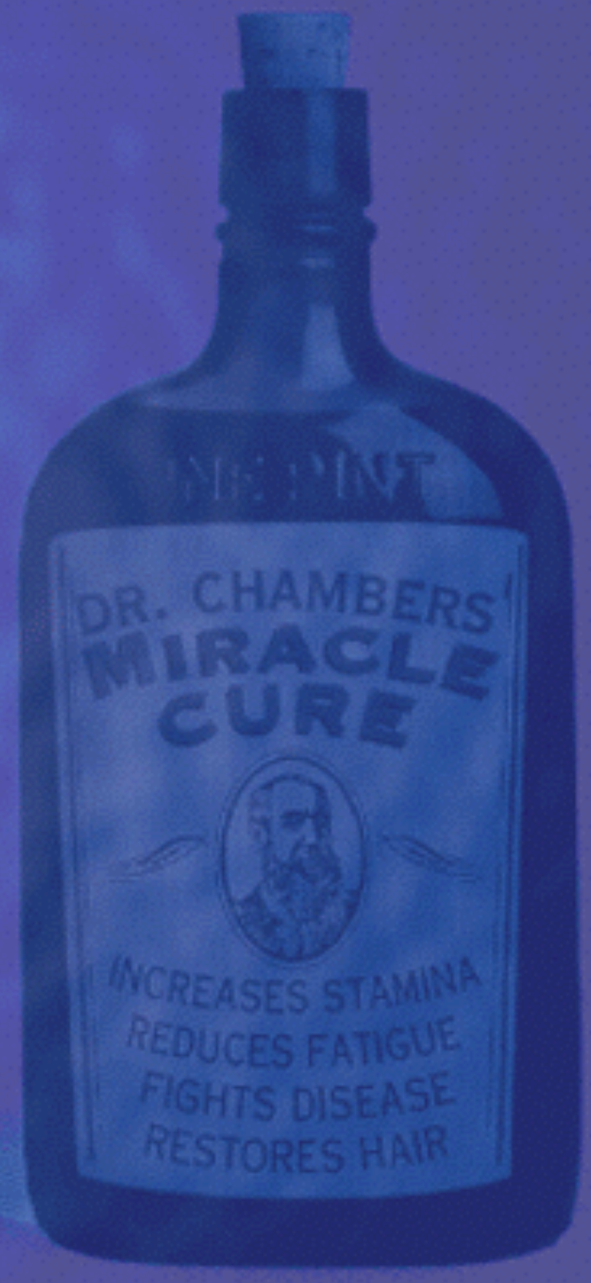
- **cardiac**
  - –ventricular tachyarrhythmias
  - –heart block
- **generalised**
  - –nausea / anorexia
  - –vomiting

contra-indications

- ventricular tachycardias
- pericardial disease

toxicity

- **mild**
  - –reduce dose / withdraw drug
- **ventricular tachyarrhythmias**
  - –lignocaine, phenytoin
  - –Ca blockers
- **accidental overdose**
  - –cholestyramine
  - –digoxin antibodies



pharmacokinetics

- **half life**
  - –dog 24 - 36h
  - –cat 33 - 58h
- **elimination**
  - –85% renal

clinical use

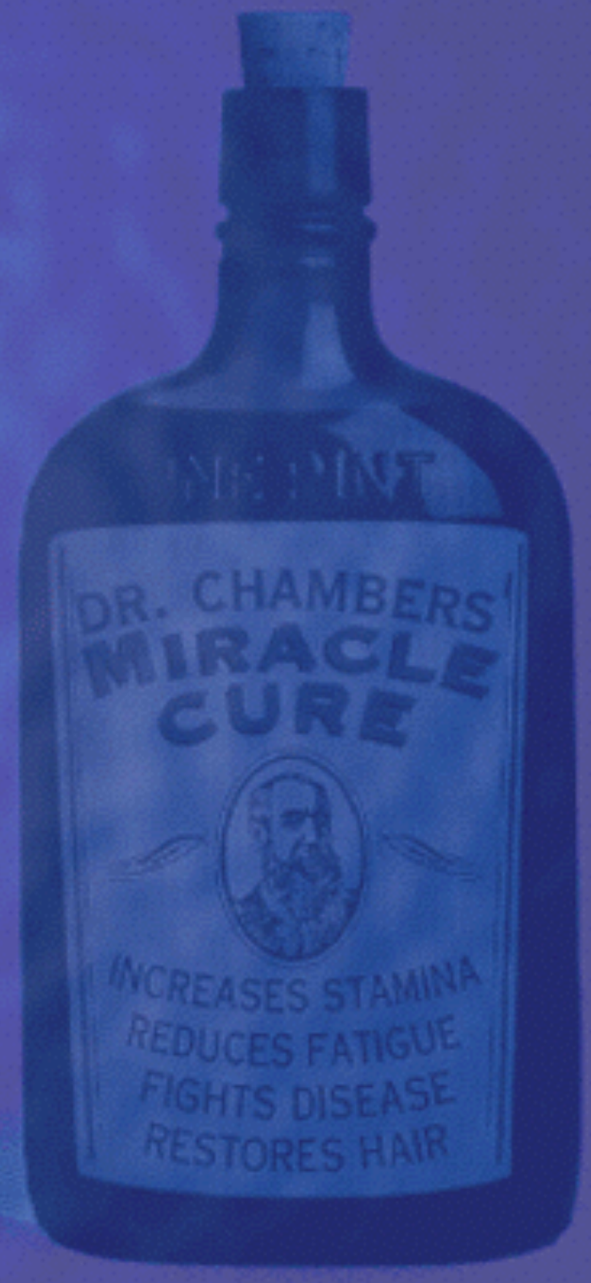
- **loading dose then maintenance dose**
  - –not recommended
- **small dose and work up**

monitoring

- nausea / vomiting
- plasma levels

interactions

- **do not use with**
  - –quinidine
  - –verapamil
- **care with**
  - –diuretics
  - –altered K^+ concentrations

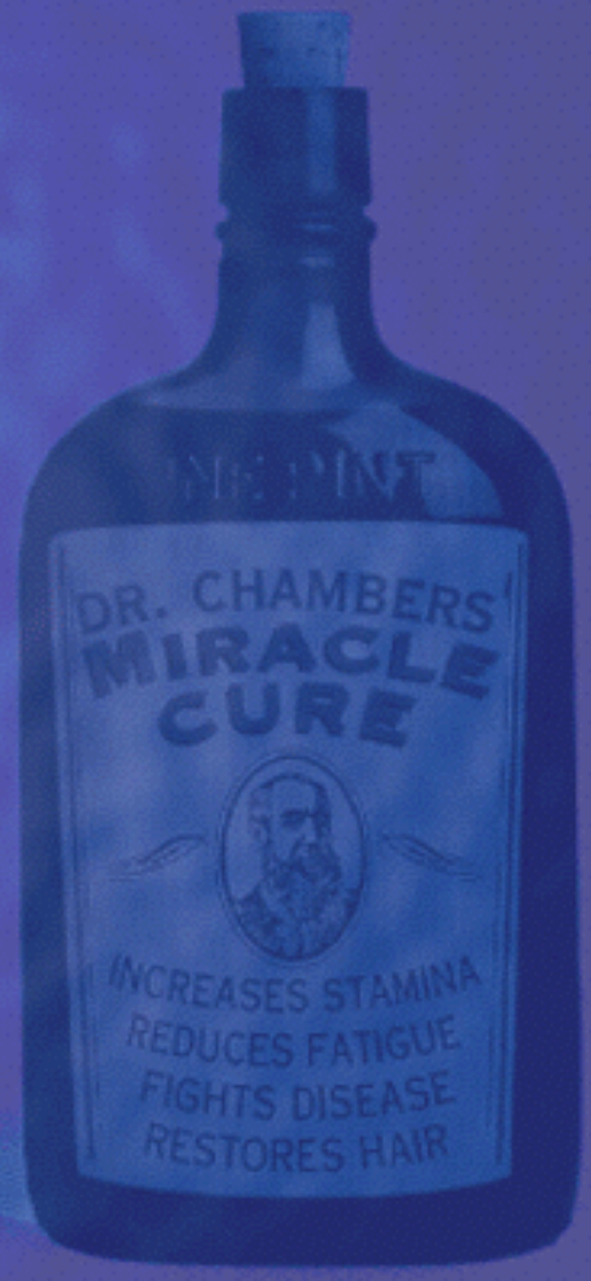


positive inotropes

- sympathomimetics
- cardiac glycosides
- phosphodiesterase inhibitors

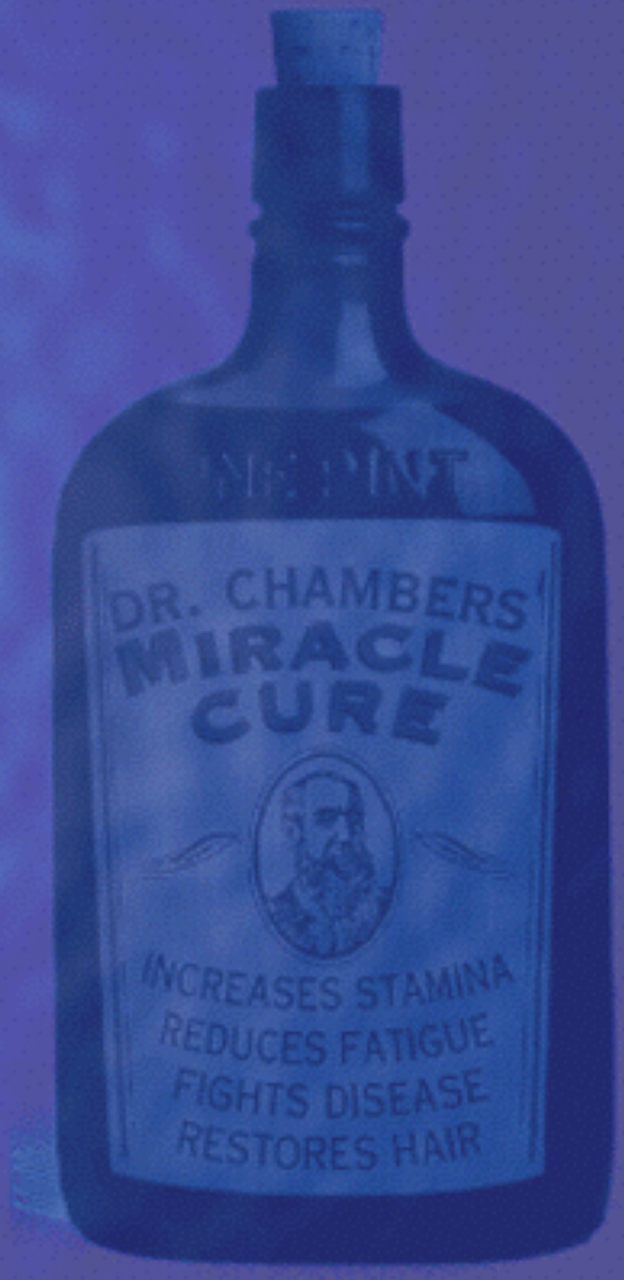
phosphodiesterase inhibitors

- **methylxanthines**
  - –caffeine
  - –theophylline
    - aminophylline
    - etamiphylline
  - –theobromine
- **synthetic**



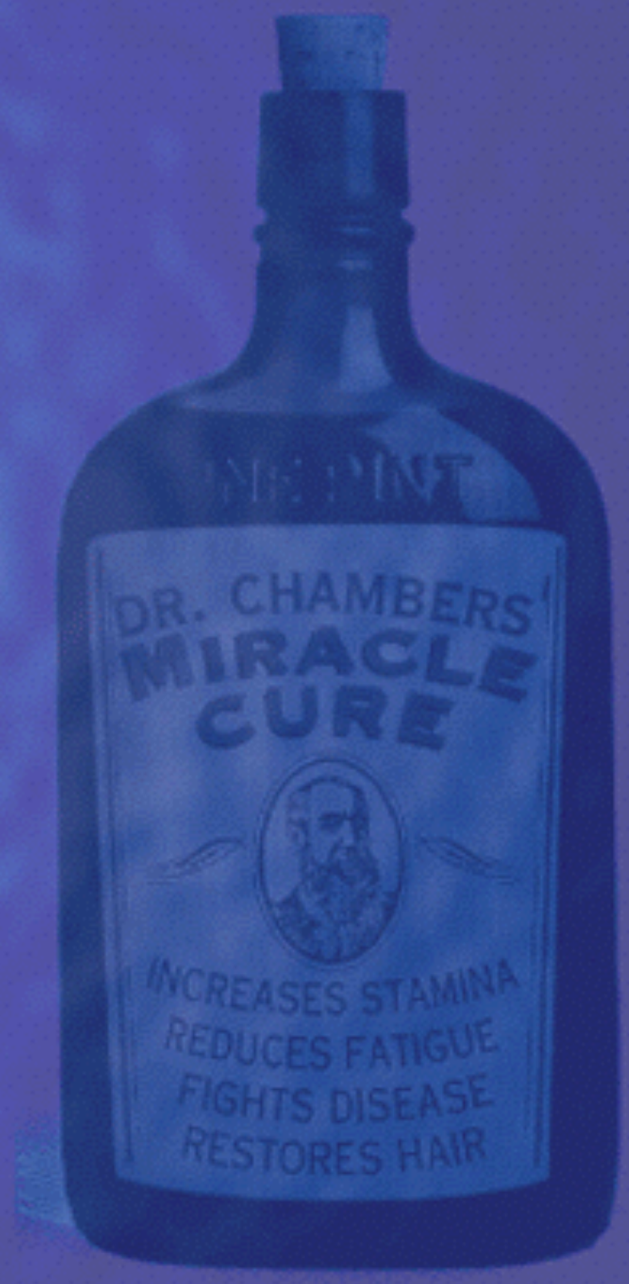
phosphodiesterase inhibitors

- **methylxanthines**
- **synthetic**
  - –milrinone
  - –oxpentifylline
  - –sildenafil
  - –pimobendan



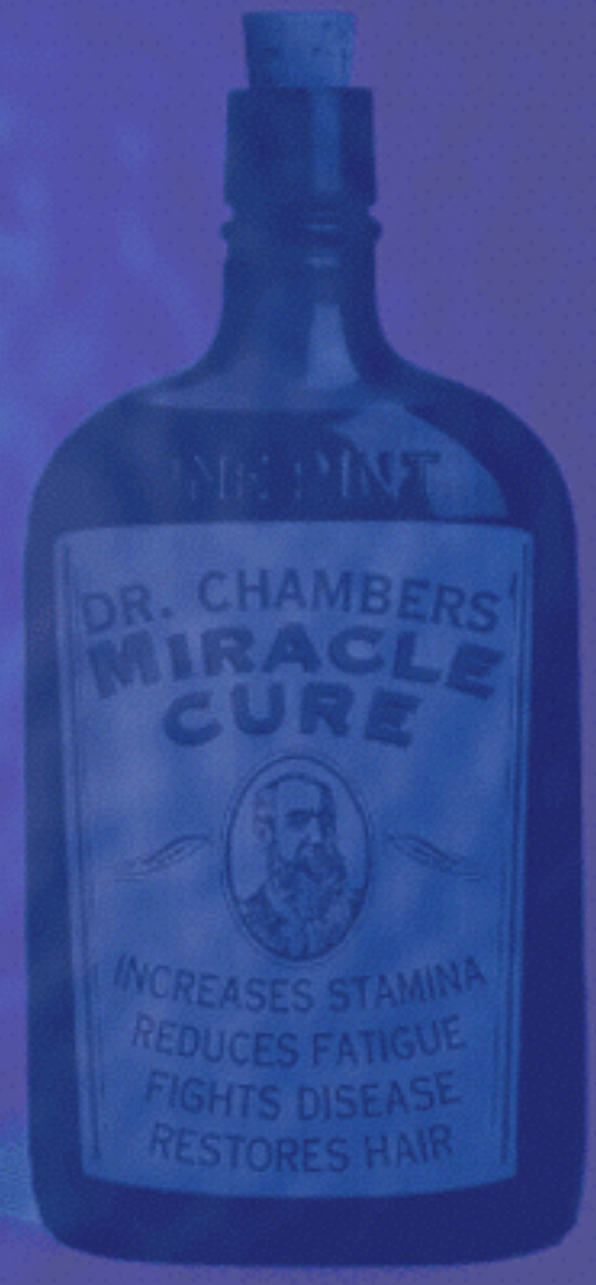
phosphodiesterase

- **PDE 3**
  - –milrinone
  - –pimobendan?
- **PDE 4**
  - –oxpentifylline
- **PDE 5**
  - –sildenafil
- **all & A2**
  - –theophylline



PDI effects

- positive inotropy
- vasodilatation
- bronchodilatation
- CNS stimulation
- diuresis



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CALCIUM CHANNEL BLOCKERS

LOCAL ANAESTHETICS

DIGITALIS

β_1 adrenoceptor

adenyl cyclase

L type Ca channel (dihydropyridine receptor)

Ca^{++}

Na channel

Na^+

Na / Ca exchanger

sodium pump

out

in

Ca^{++}

Na^+

Ca^{++} Na^+

Na^+ K^+

5'AMP

ATP

phosphodiesterase

cAMP

PDI

+

$[Ca^{++}]$

sarcoplasmic reticulum

Ca^{++}

ryanodine receptor

myofibrils

effects

- **pimobendan**
  - –PDE inhibition
  - –“calcium sensitisation”

indications

- mild - moderate CHF

side effects

- sudden death in people
- none obvious in dogs

overdose

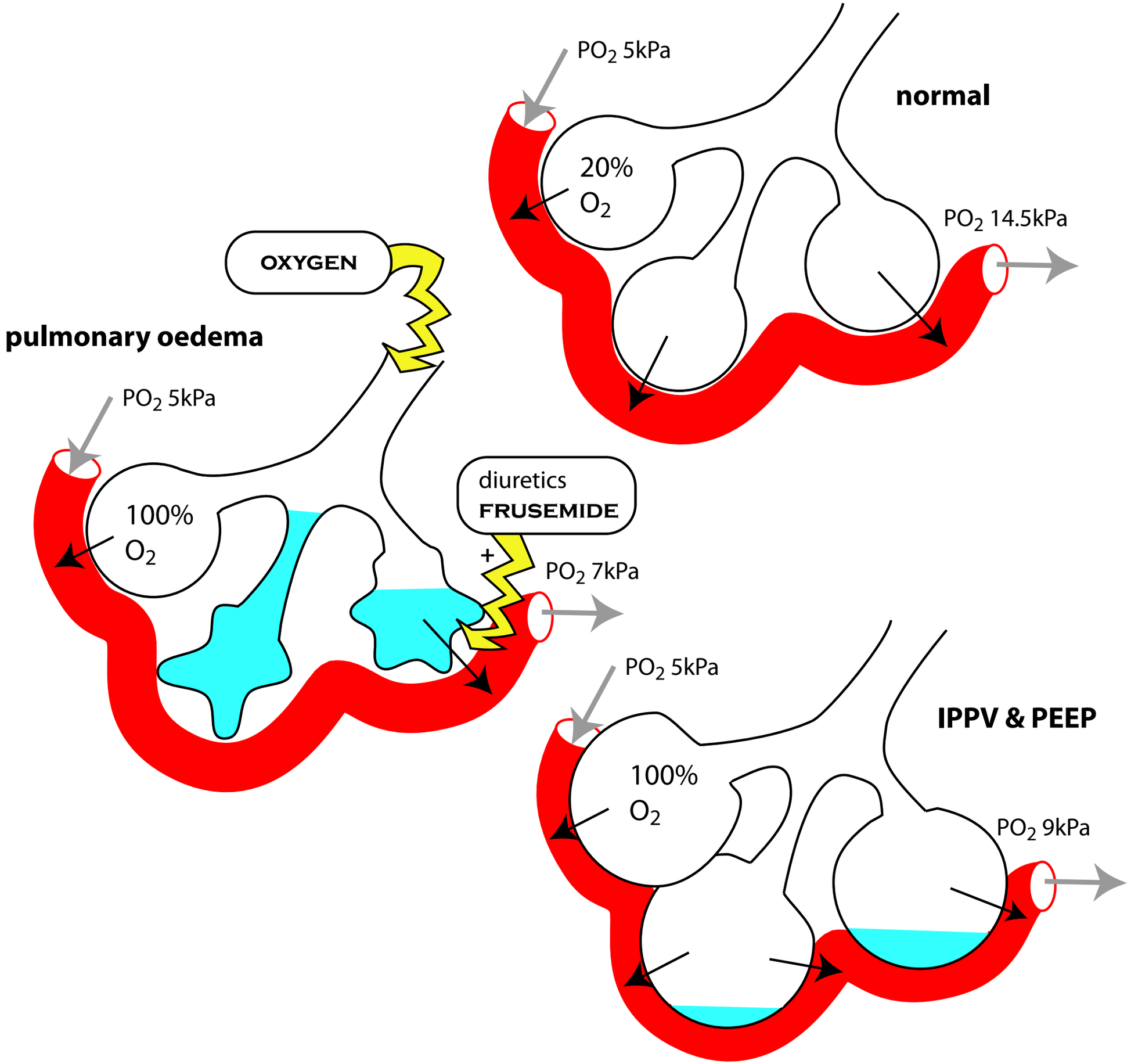
- tachyarrhythmias
- convulsions

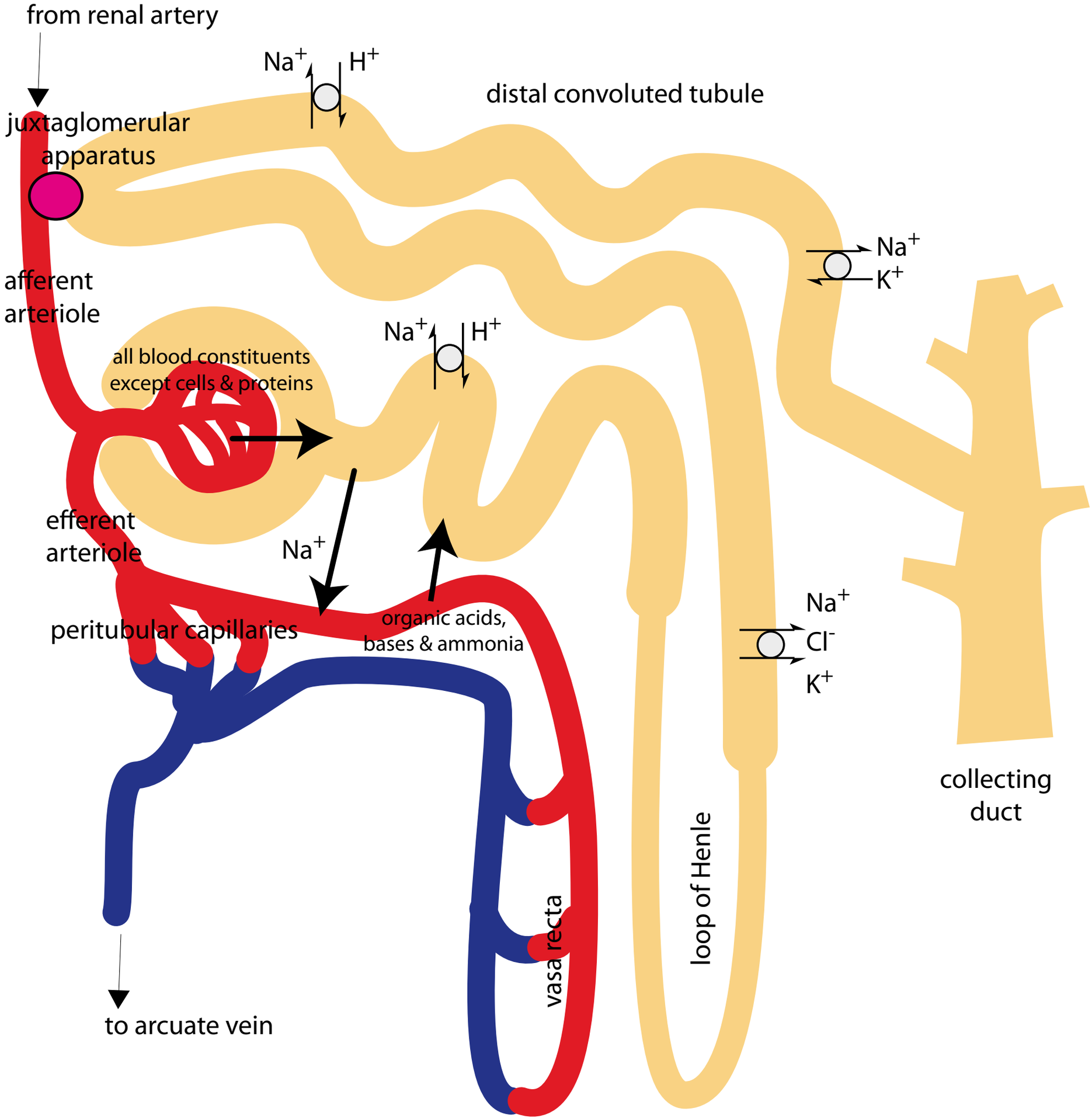
diuretics

- act on the kidney to increase urine flow
- most block reabsorption of ions from tubules
- water kept in tubules by osmotic pressure

diuretics & CHF

- reduce pulmonary oedema
- reduce preload


normal
PO_2 5kPa
20%
O_2
PO_2 14.5kPa
OXYGEN
pulmonary oedema
PO_2 5kPa
100%
O_2
diuretics
FRUSEMIDE
+
PO_2 7kPa
PO_2 5kPa
IPPV & PEEP
100%
O_2
PO_2 9kPa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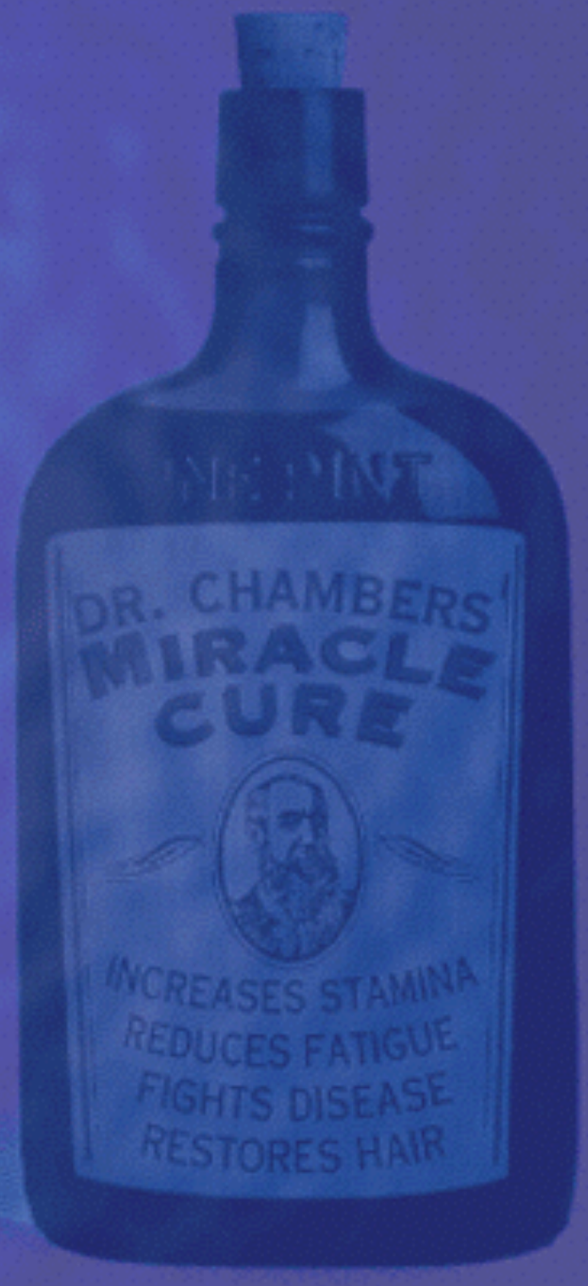
juxtaglomerular apparatus
afferent arteriole
Na^+
H^+
distal convoluted tubule
Na^+
K^+
Na^+
H^+
all blood constituents except cells & proteins
efferent arteriole
Na^+
peritubular capillaries
organic acids, bases & ammonia
Na^+
Cl^-
K^+
collecting duct
loop of Henle
vasa recta
to arcuate vein

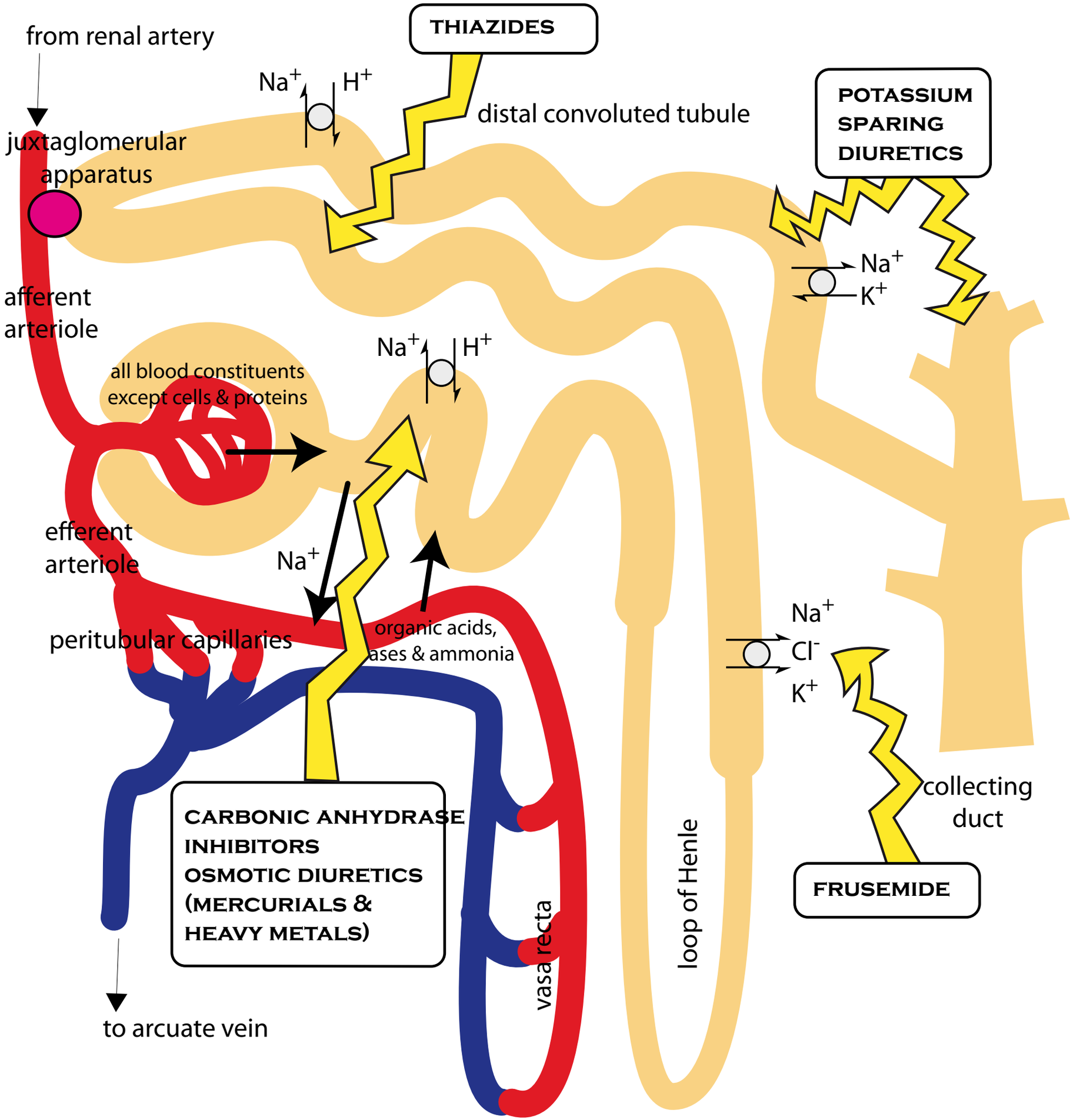
groups of drugs

- loop diuretics
- thiazides
- osmotic diuretics
- potassium sparing diuretics
- carbonic anhydrase inhibitors
- (mercurials)

common drugs

- frusemide
- (hydrochlorthiazide)
- (mannitol)

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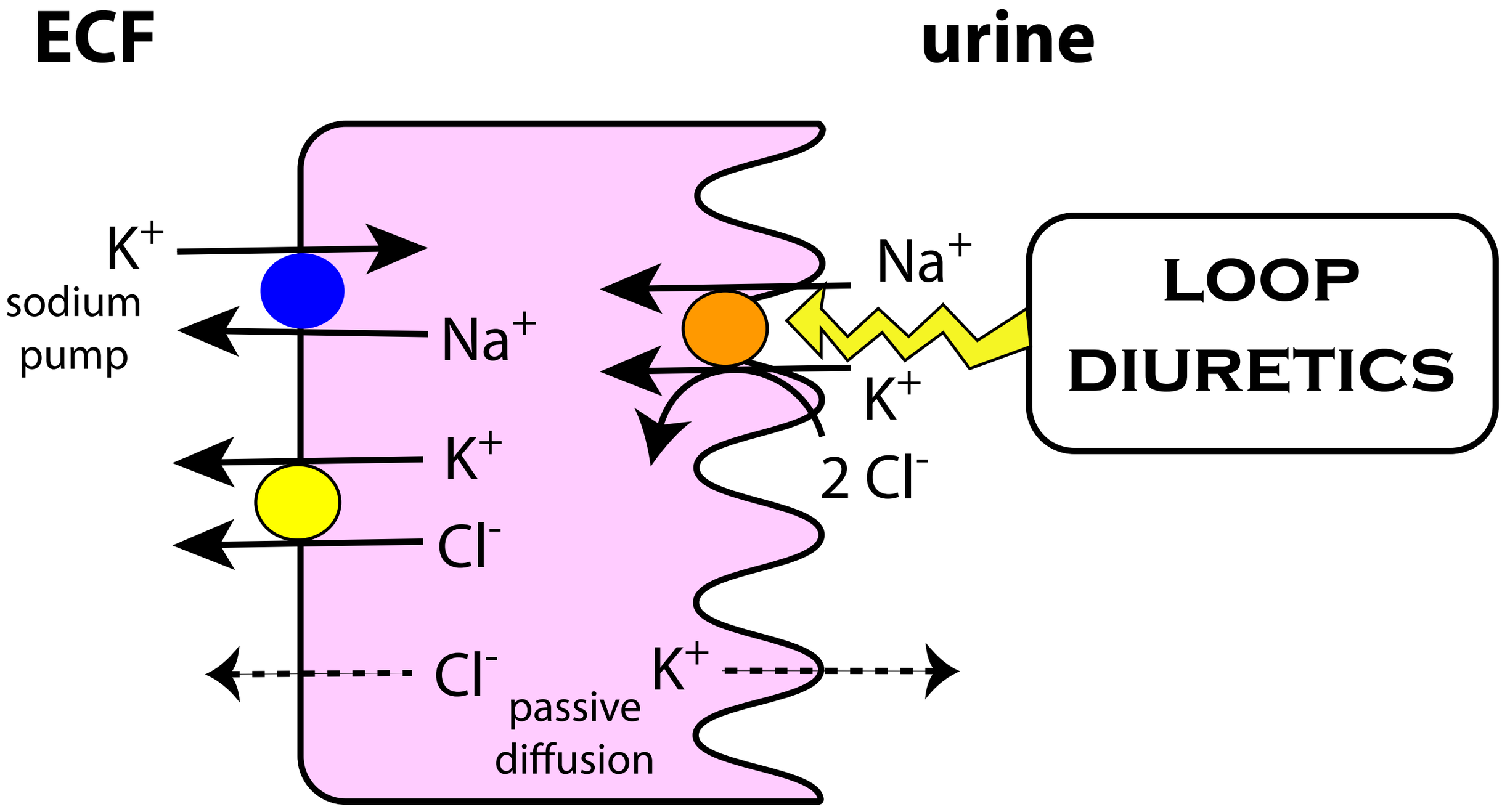
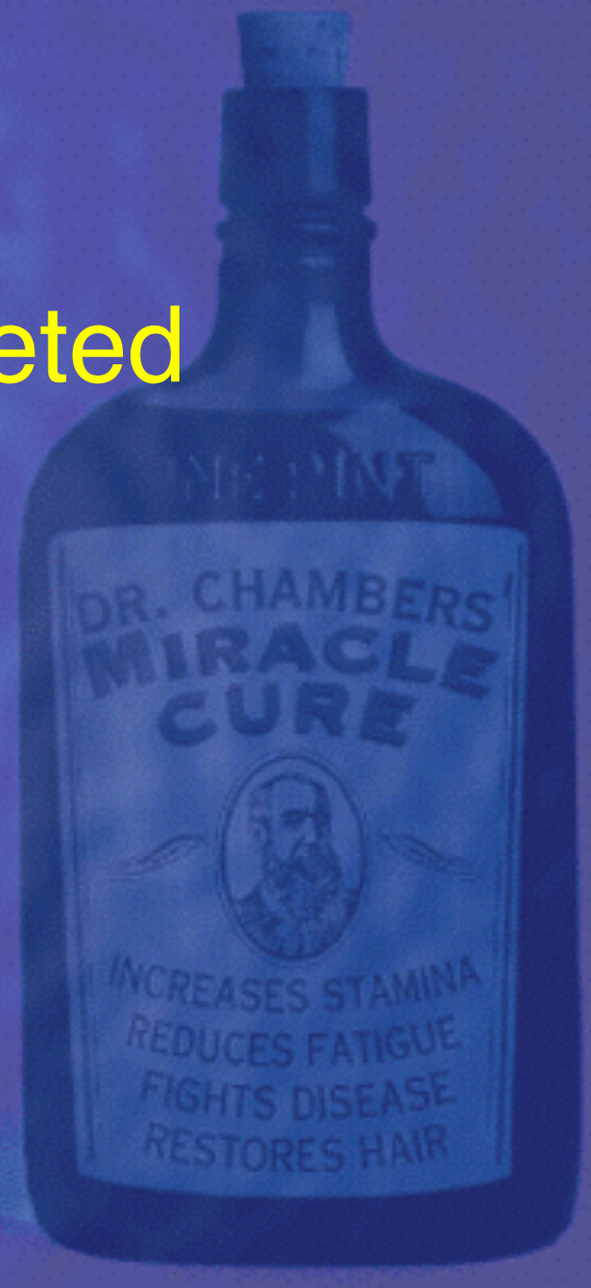
FRUSEMIDE

loop of Henle



frusemide

- **potent**
  - –up to 20% of filtered Na^+ excreted
- **cheap**
- **very widely used**



frusemide indications

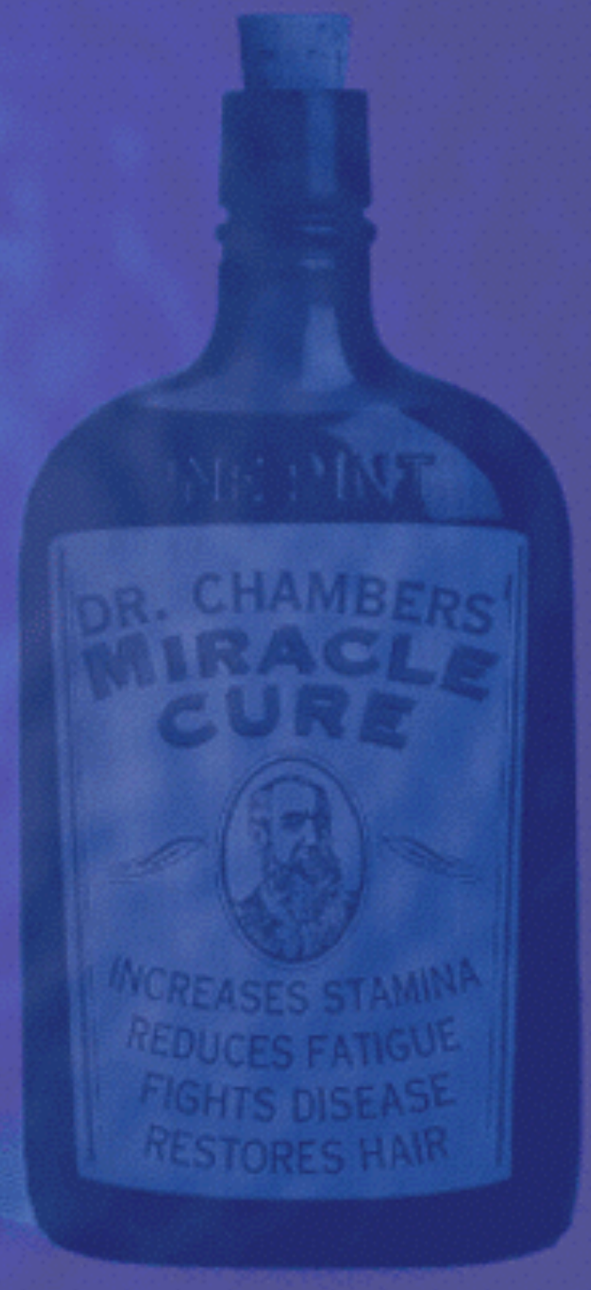
- reduce oedema
- reduce cardiac preload
- (acute renal failure)

minor indications

- hyperkalaemia
- hypercalcaemia
- uraemia
- epistaxis
- hypertension

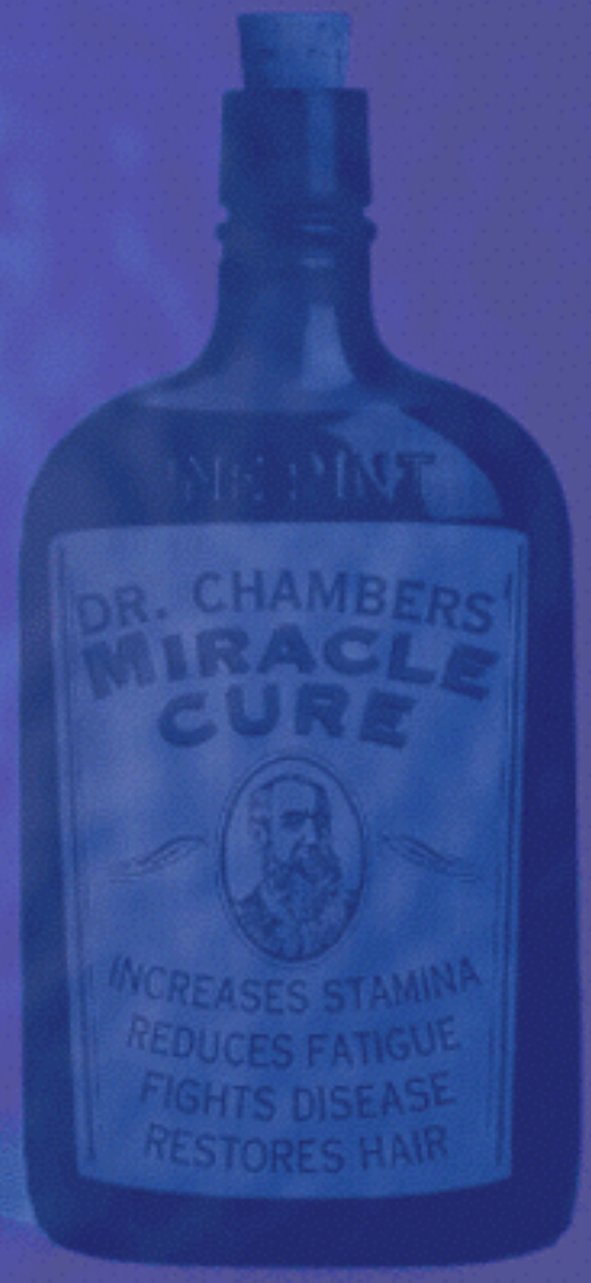
abuse

- speeding up / slowing racehorses



pharmacokinetics

- **iv**
  - –onset minutes
  - –peak 30 mins
  - –duration 2 hours
- **po**
  - –onset 30 - 60 mins
  - –peak 2 hours
  - –duration 4 - 6 hours

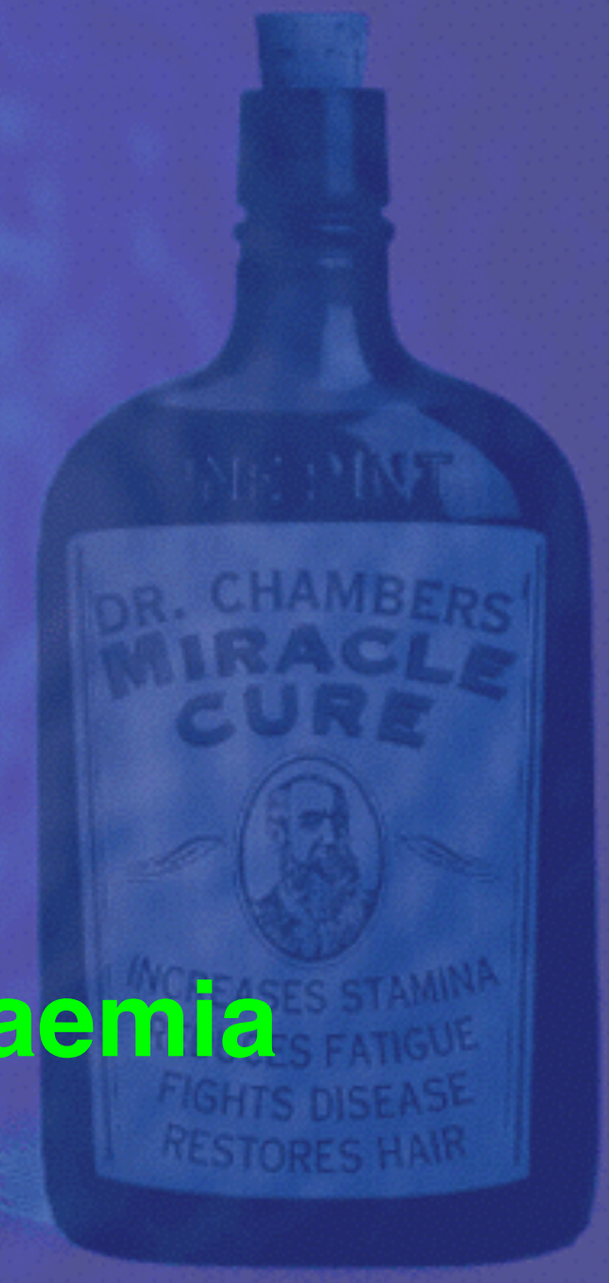


pharmacokinetics

- **metabolism**
  - –negligible
- **elimination**
  - –secreted into PCT by anion pump
  - –passes out in urine
    - horses which eat their bedding may take it in again

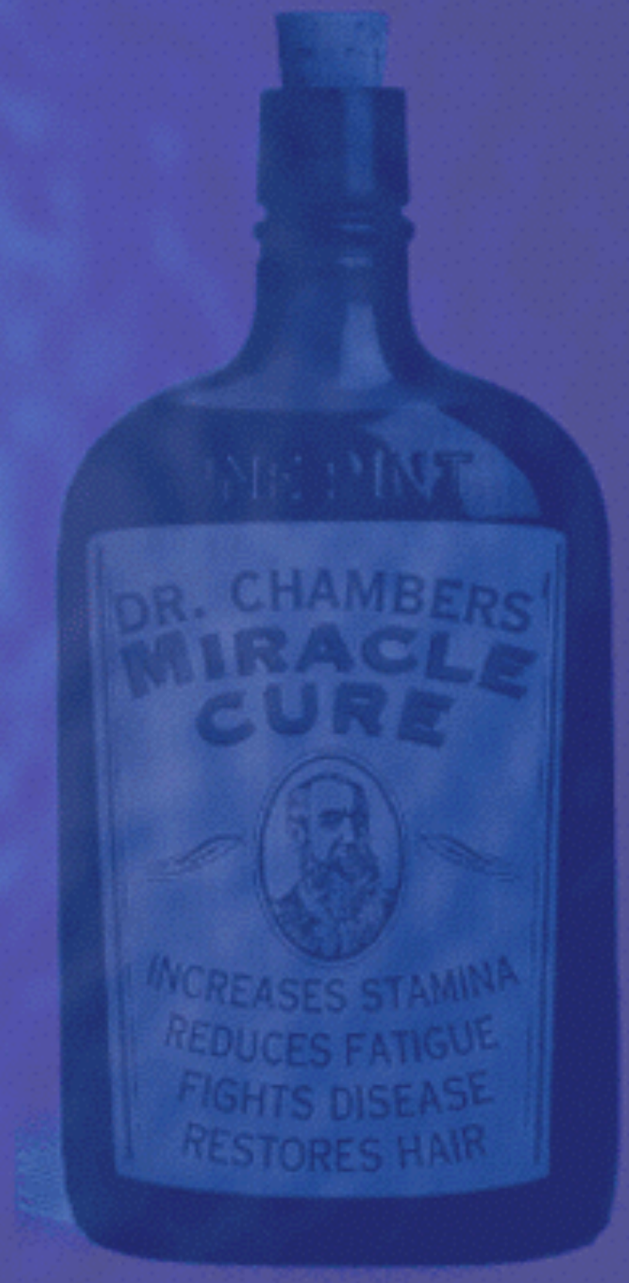
side effects

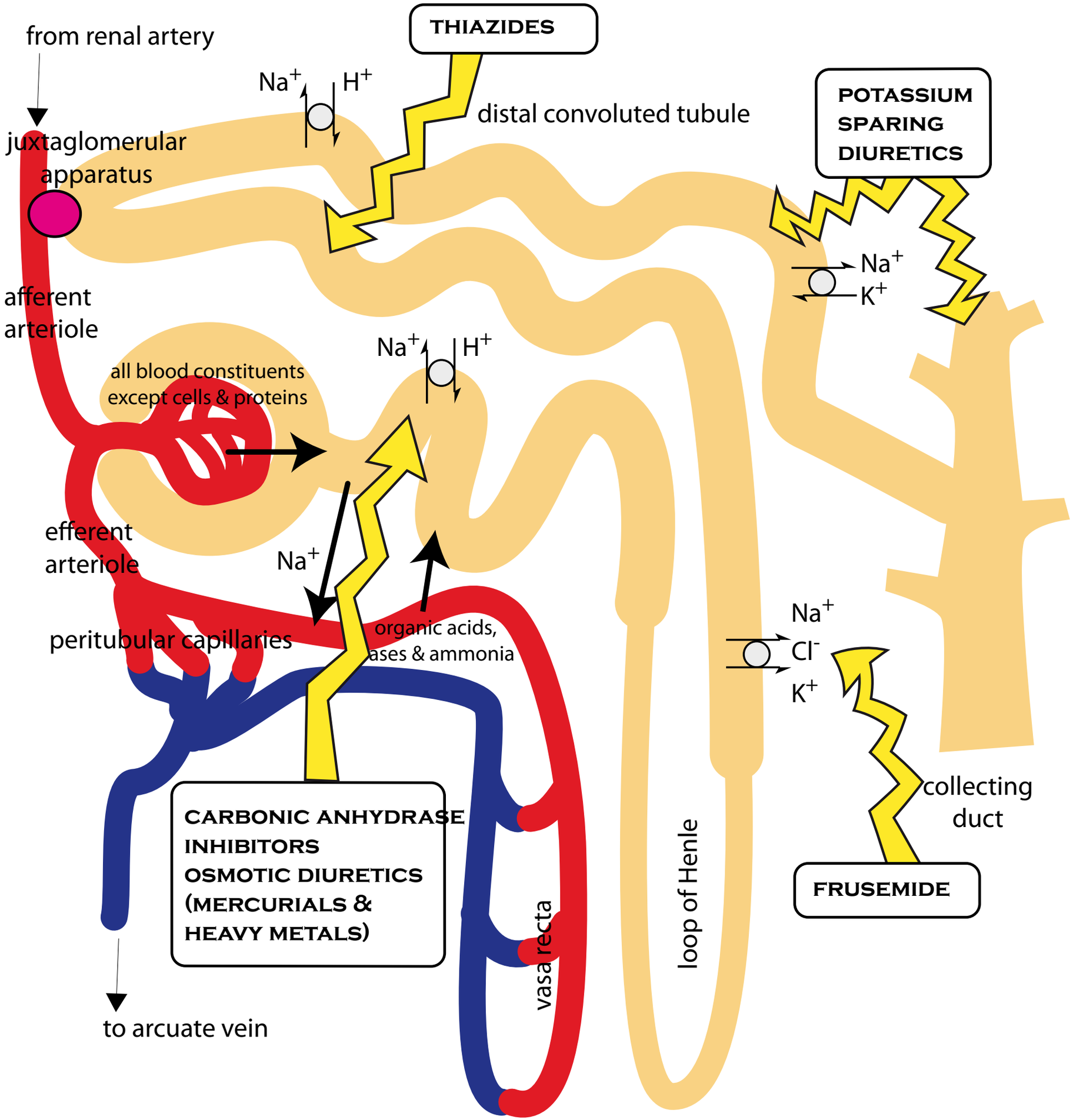
- **hypovolaemia**
  - –reduced glomerular filtration
  - –reduced excretion of other drugs
  - –collapse
  - –direct vasodilatation?
- **hypokalaemia**
- **metabolic alkalosis**
- **hypocalcaemia / hypomagnesaemia**
- **tolerance**



side effects

- **hypovolaemia**
- **hypokalaemia**
  - –digoxin!!!
- **metabolic alkalosis**
- **hypocalcaemia / hypomagnesaemia**
- **tolerance**

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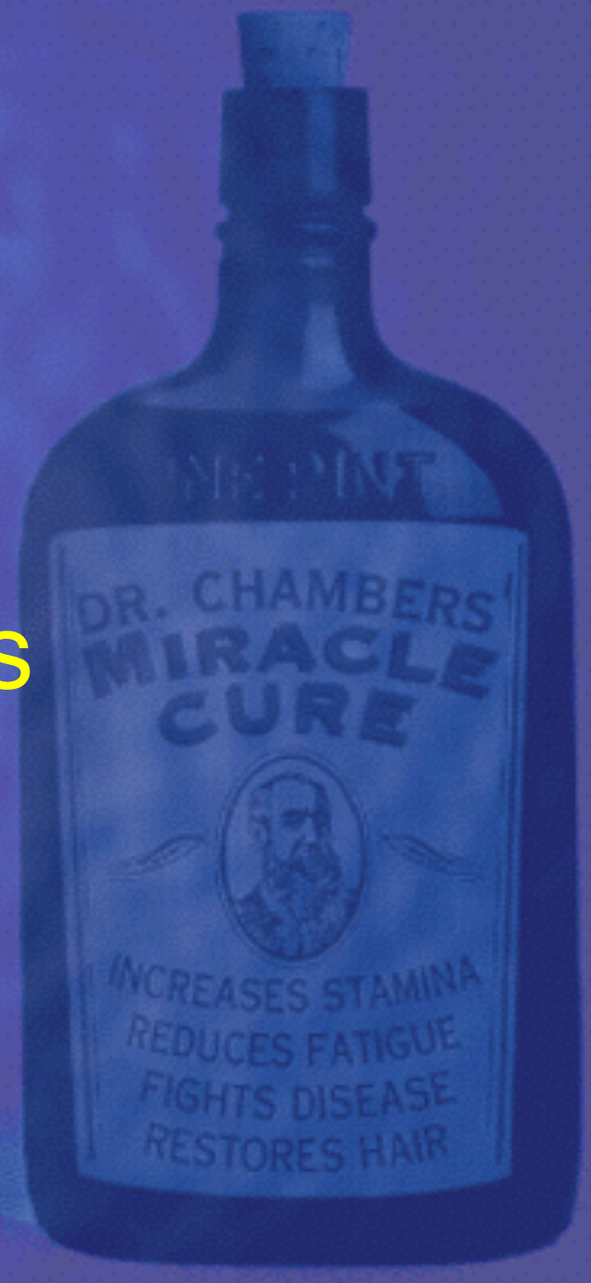
juxtaglomerular apparatus
afferent arteriole
efferent arteriole
peritubular capillaries
to arcuate vein
all blood constituents except cells & proteins
THIAZIDES
Na+
H+
distal convoluted tubule
POTASSIUM SPARING DIURETICS
Na+
K+
Na+
H+
Na+
organic acids, ases & ammonia
CARBONIC ANHYDRASE INHIBITORS
OSMOTIC DIURETICS
(MERCURIALS & HEAVY METALS)
vasa recta
loop of Henle
Na+
Cl-
K+
collecting duct
FRUSEMIDE

side effects

- hypovolaemia
- hypokalaemia
- metabolic alkalosis
- hypocalcaemia / hypomagnesaemia
- tolerance

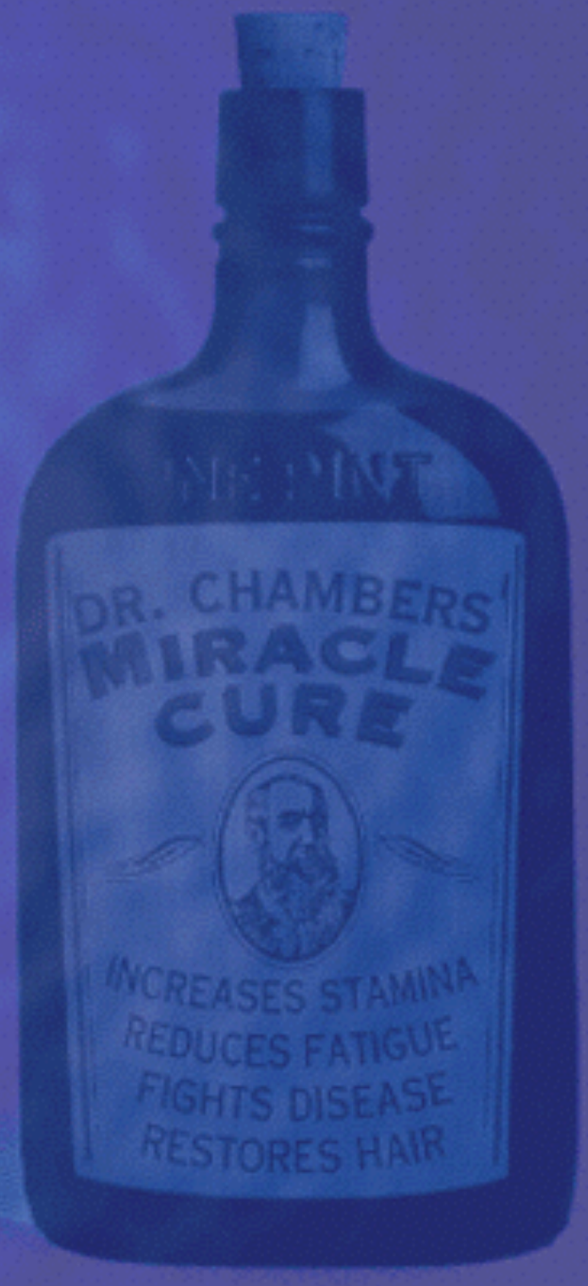
interactions

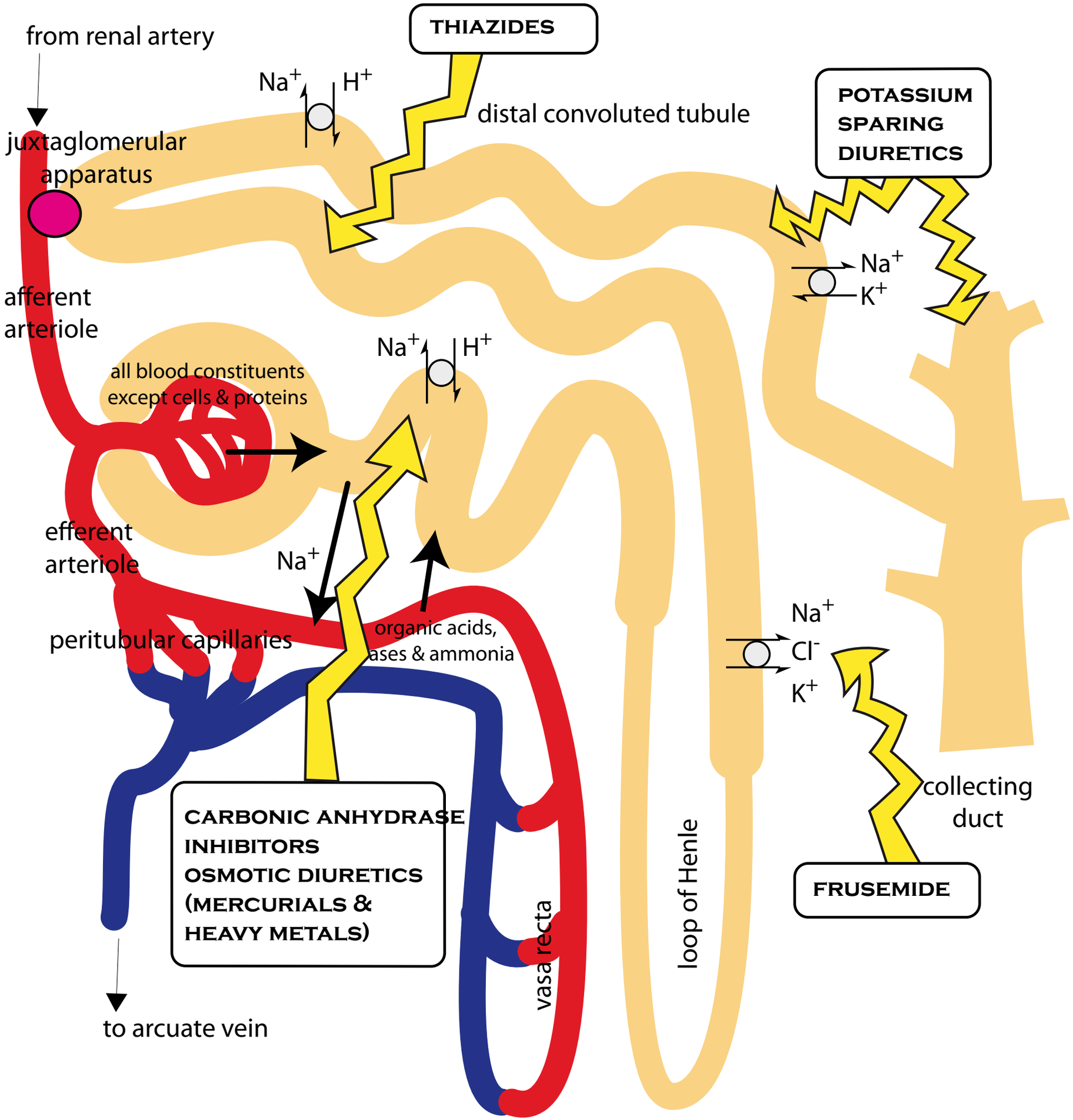
- **increased PCT toxicity**
  - –aminoglycosides
  - –out of date tetracyclines
  - –some obsolete cephalosporins
- **potentiates digoxin**
- **ACE inhibitors?**



common drugs

- frusemide
- (hydrochlorthiazide)
- (mannitol)

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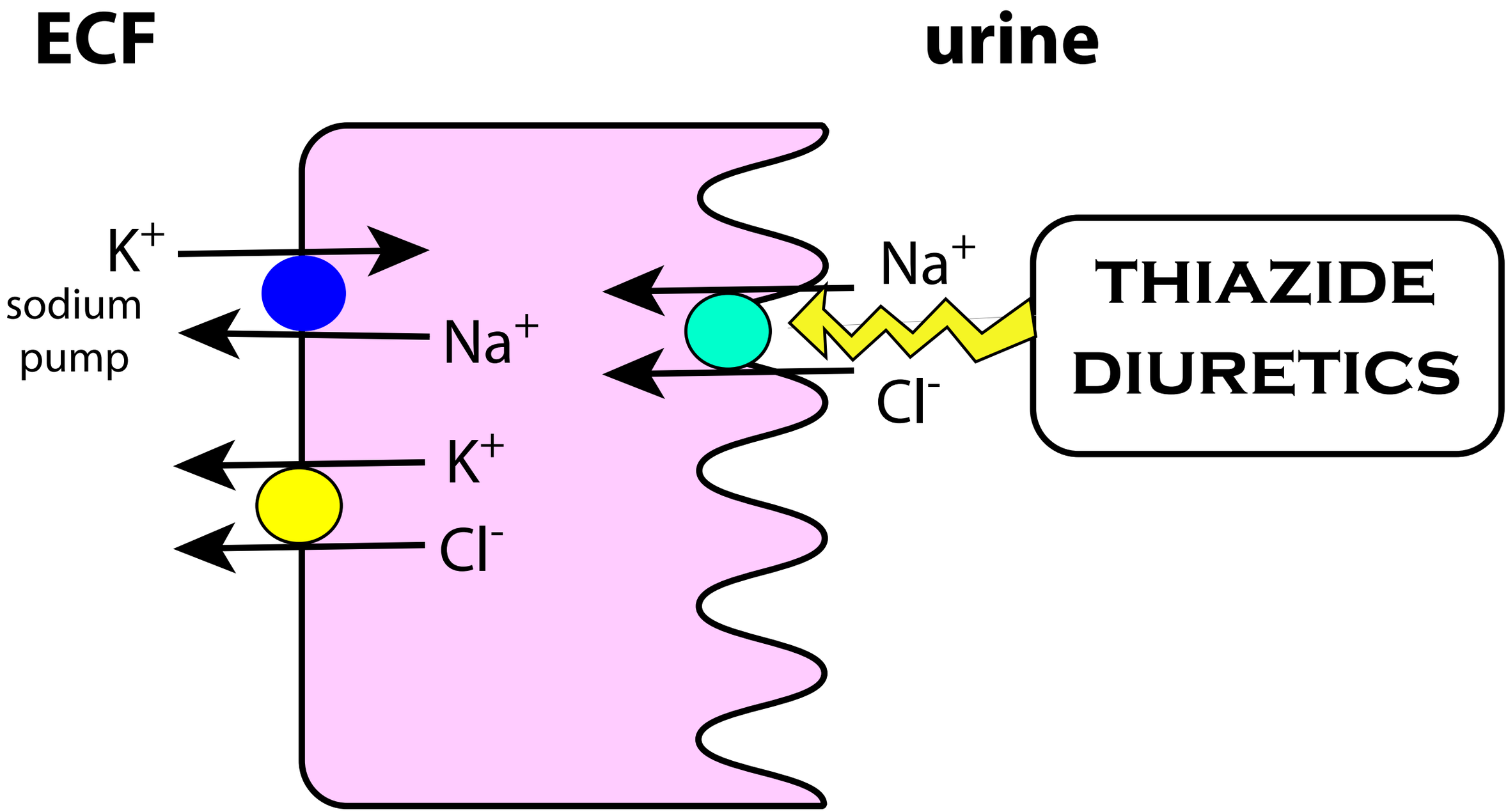
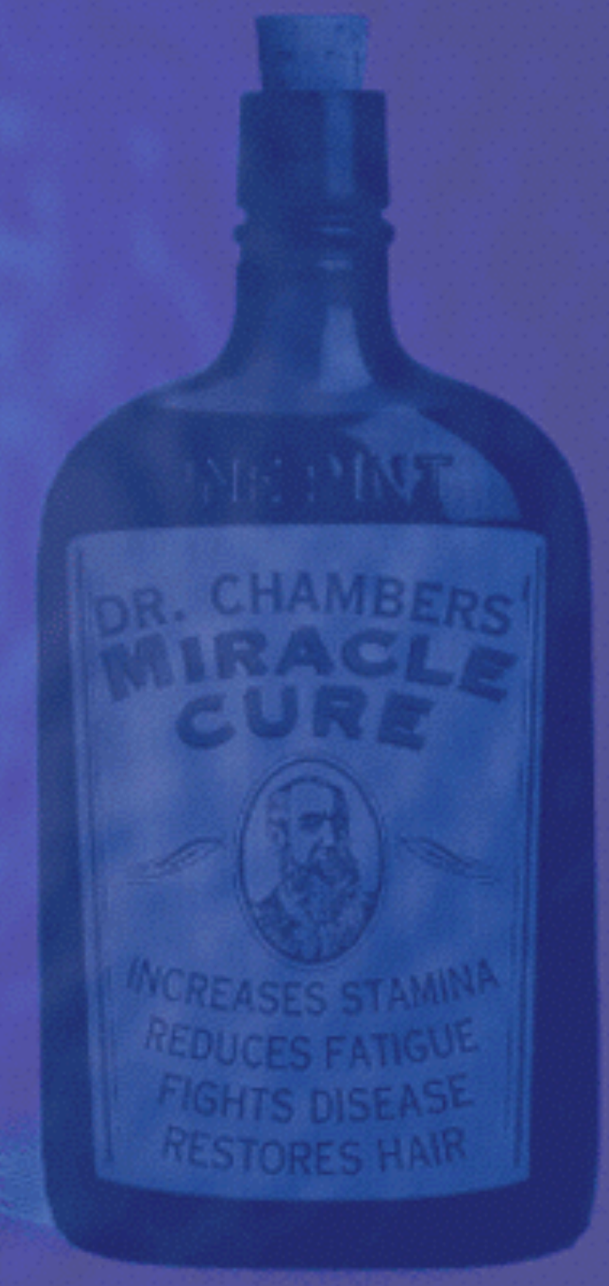
early DCT



thiazides

- **many drugs available**
  - –hydrochlorthiazide
  - –bendrofluazide, etc
- **moderately potent**
- **cheap**



thiazide side effects

- **hypokalaemia**
  –digoxin!!
- **metabolic alkalosis**
- **increased plasma uric acid**
- **hyperglycaemia**

kinetics

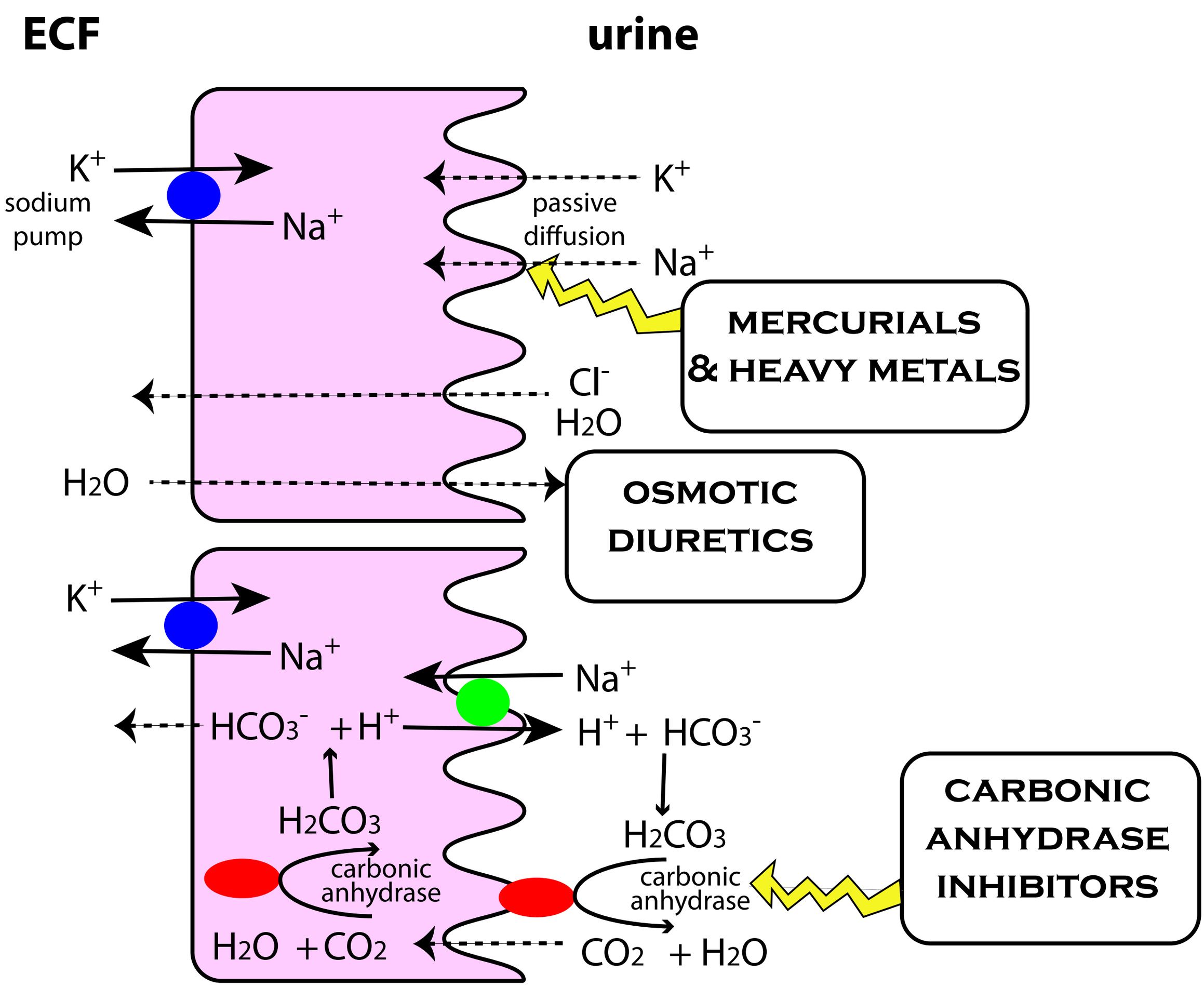
- always given po
- onset 1 - 2 hours
- peak effect 4 - 6 h
- duration 8 - 12 h

indications

- mild / moderate heart failure
- (diabetes insipidus)

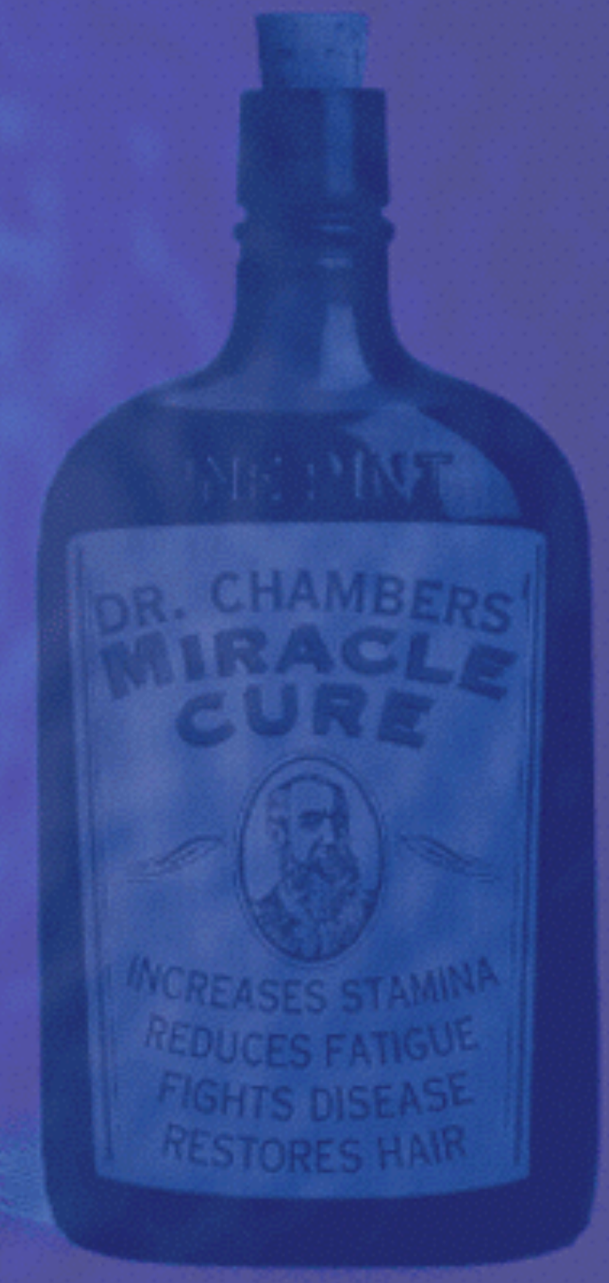
osmotic diuretics

- mannitol
- glycerol
- glucose


ECF
urine
K+
sodium
pump
Na+
K+
passive
diffusion
Na+
MERCURIALS
& HEAVY METALS
Cl-
H2O
H2O
OSMOTIC
DIURETICS
K+
Na+
Na+
HCO3- +H+
H+ + HCO3-
H2CO3
carbonic
anhydrase
H2CO3
carbonic
anhydrase
CARBONIC
ANHYDRASE
INHIBITORS
H2O +CO2
CO2 + H2O

mannitol

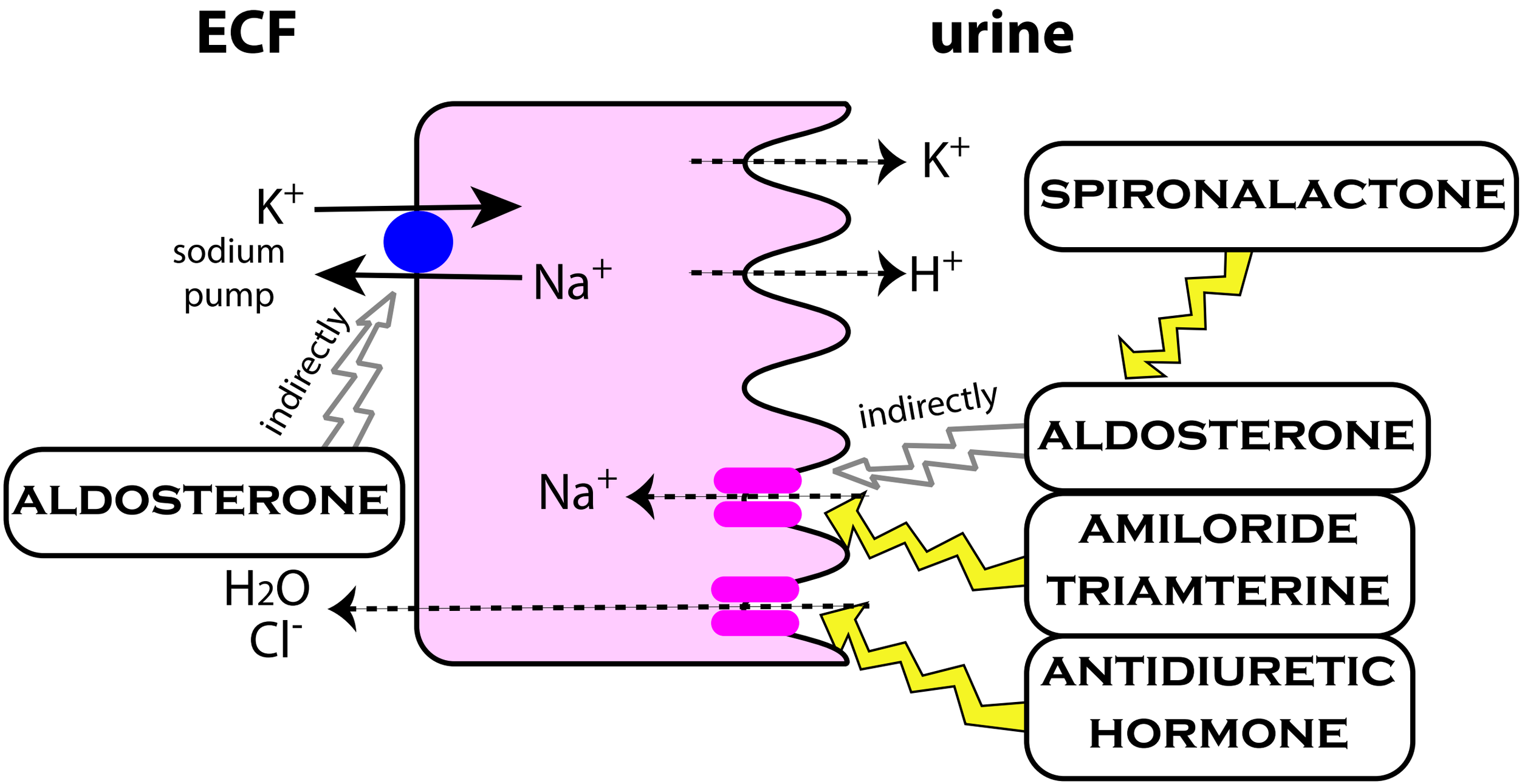
- **indications**
  - –glaucoma
  - –cerebral oedema
  - –acute renal failure
- **contraindications**
  - –heart disease
- **caution**
  - –**must** be given iv



K^+ sparing diuretics

- amiloride
- triamterene
- spironalactone

late DCT

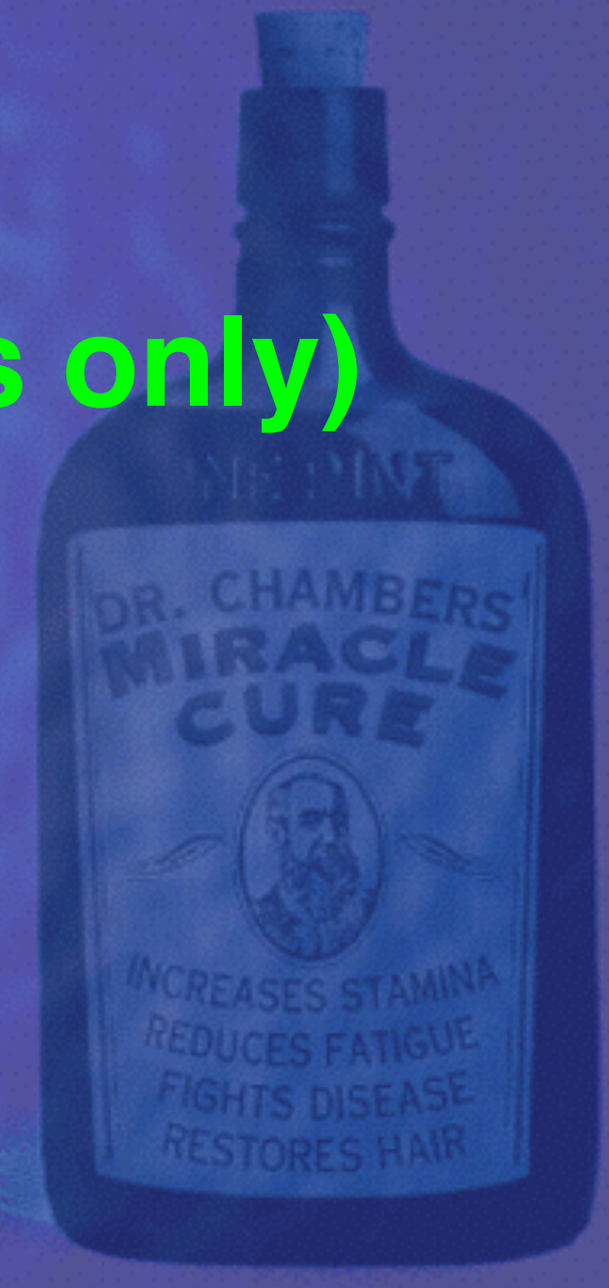

ECF
urine
K+
sodium
pump
Na+
indirectly
ALDOSTERONE
H2O
Cl-
K+
H+
Na+
indirectly
SPIRONALACTONE
ALDOSTERONE
AMILORIDE
TRIAMTERINE
ANTIDIURETIC
HORMONE

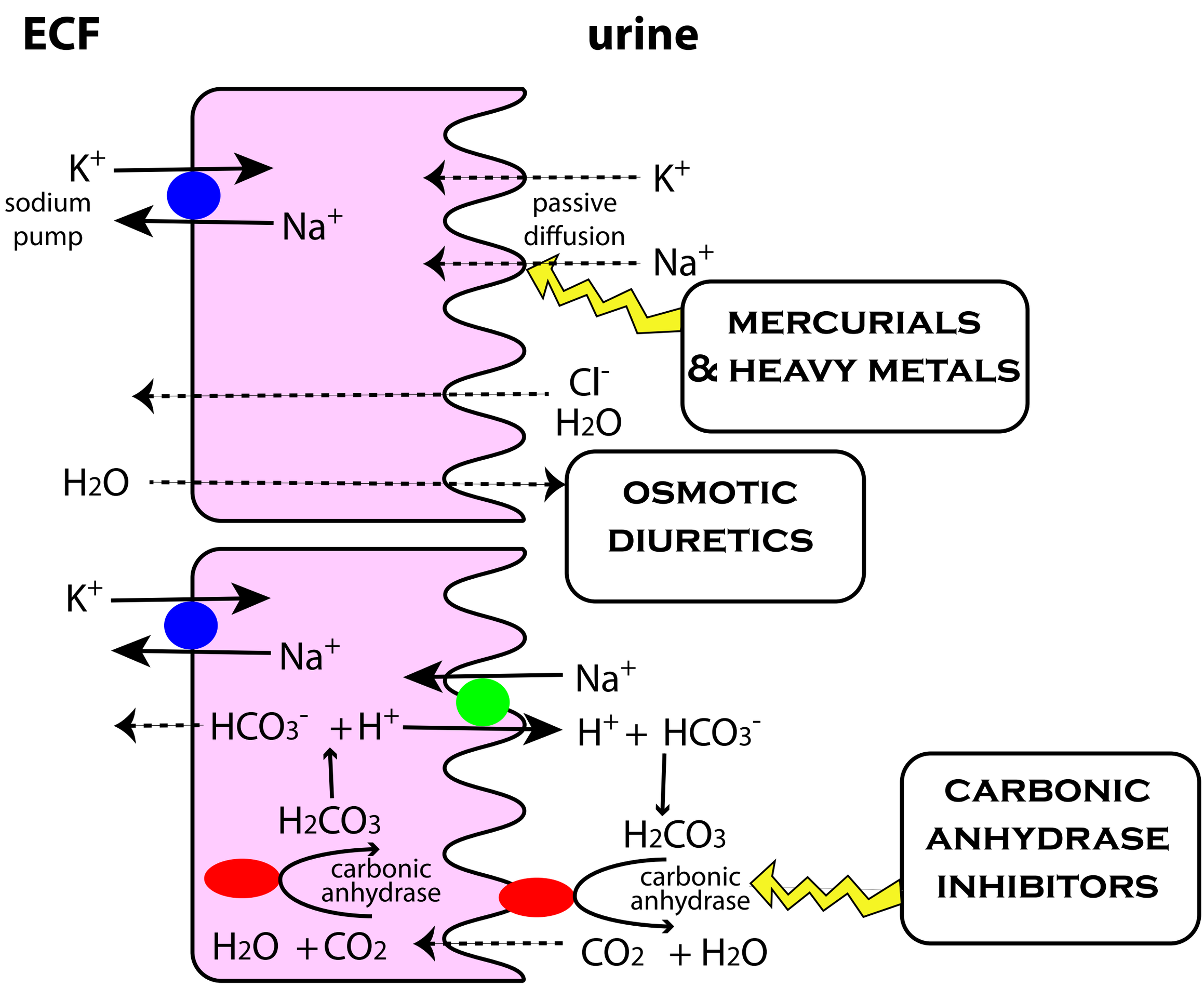
K^+ sparing diuretics

- weak diuretics
- expensive
- caution with ACE inhibitors
- rarely used in animals

CA inhibitors

- acetazolamide
- (dorzolamide - eye drops only)

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HCO3- +H+
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H2CO3
carbonic
anhydrase
H2CO3
carbonic
anhydrase
CARBONIC
ANHYDRASE
INHIBITORS
H2O +CO2
CO2 + H2O

CA inhibitors

- **weak diuretics**
- **rarely used as diuretics**
  - –used for glaucoma
- **cause mild metabolic acidosis**

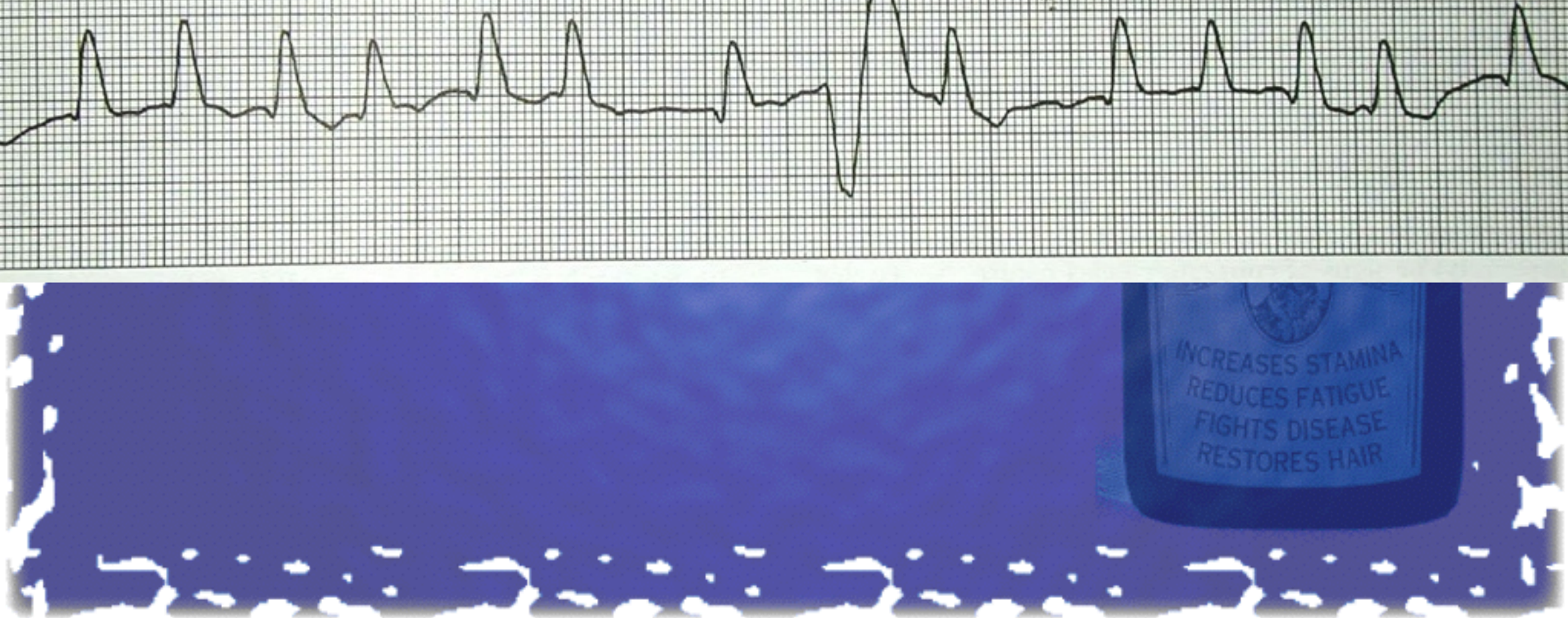
7 yr old Doberman

- cough
- lethargy / exercise intolerance
- anorexia
- ascites
- sudden onset 1 week ago

examination

- soft systolic murmur
- heart rate 148
- harsh lung sounds

ECG lead II


INCREASES STAMINA
REDUCES FATIGUE
FIGHTS DISEASE
RESTORES HAIR

diagnosis

- dilated cardiomyopathy

normal

R

L

dilated

R

L

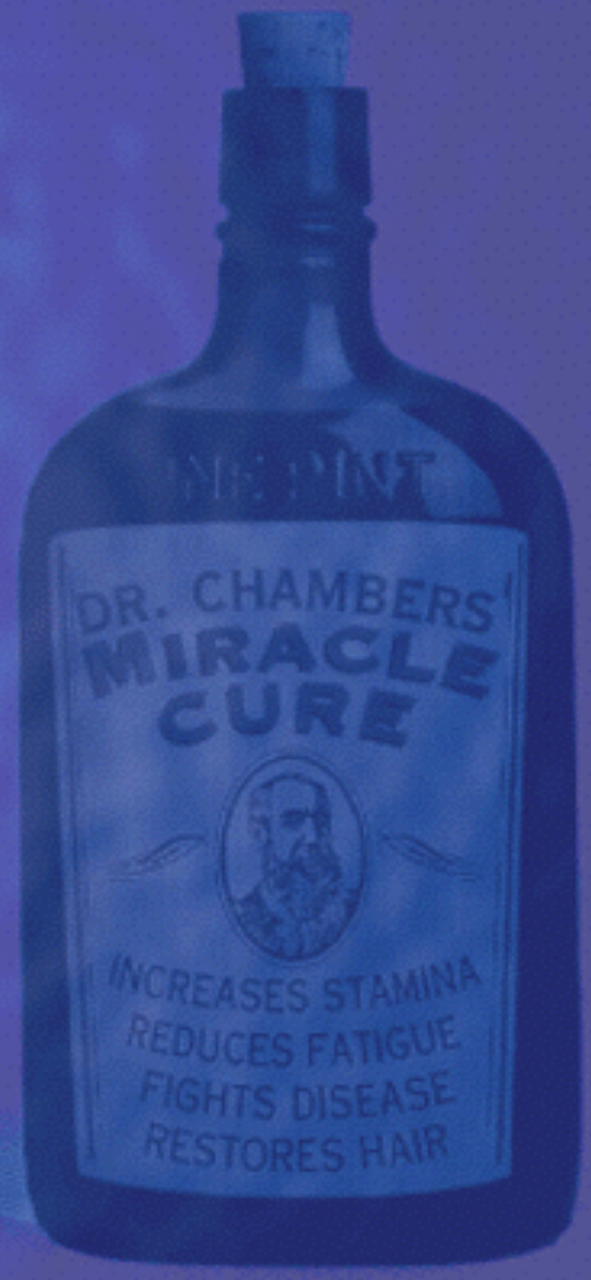
hypertrophic

R

L

Dobermann DCM

- frusemide
- digoxin
- pimobendan?
- beta blocker?



congestive heart failure

- digoxin binds competitively to potassium binding site of sodium pump
- low potassium increases effect
- positive inotrope, negative chronotrope
- side effects - vomiting & anorexia, ventricular tachycardia
- indications - atrial fibrillation with tachycardia, congestive heart failure
- phosphodiesterase inhibitors are useful and safe in mild / moderate CHF