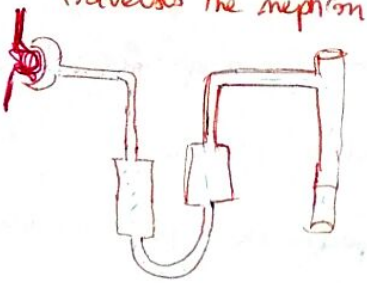
Urinary lithiasis: Campbell

Physicochemistry and pathogenesis:

Stone formation: physical process,
complex cascade of events occuring as the glomerular filtrate traverses the nephron



as the glomerular filtrate traverses the nephron
stone formation occur

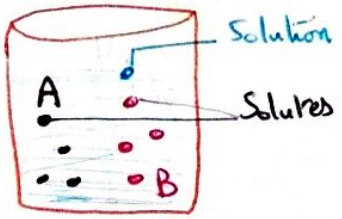
① Urine supersaturation with stone forming salts
② Nuclei formation (crystals)

Retained in kidney at anchoring sites → Promote → Growth and aggregation → Stone formation

Flow with urine

- State of saturation
- Nucleation, Crystal growth ~~and~~, aggregation and retention
- :
- :

State of saturation.



Salt AB: Concentration Product = $[A] \times [B]$

Example: CP (Concentration Product) of sodium chloride: $CP = [Na^+] \times [Cl^-]$

Pure aqueous solution of a salt:
Saturated ⇔ no further added salt crystals will dissolve
CP at saturation point = K_{sp} Thermodynamic Solubility product

K_{sp}: Thermodynamic Solubility Product

CP at the point of saturation (no more salt crystals will dissolve)

Dissolved and Crystalline components are in equilibrium

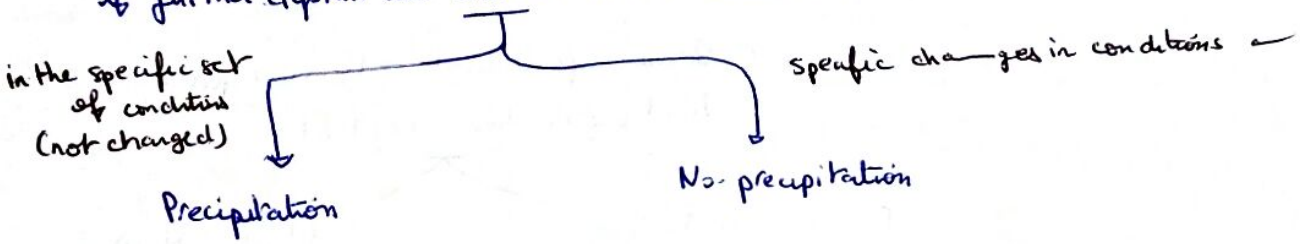
for a specific set of conditions: pH
temperature

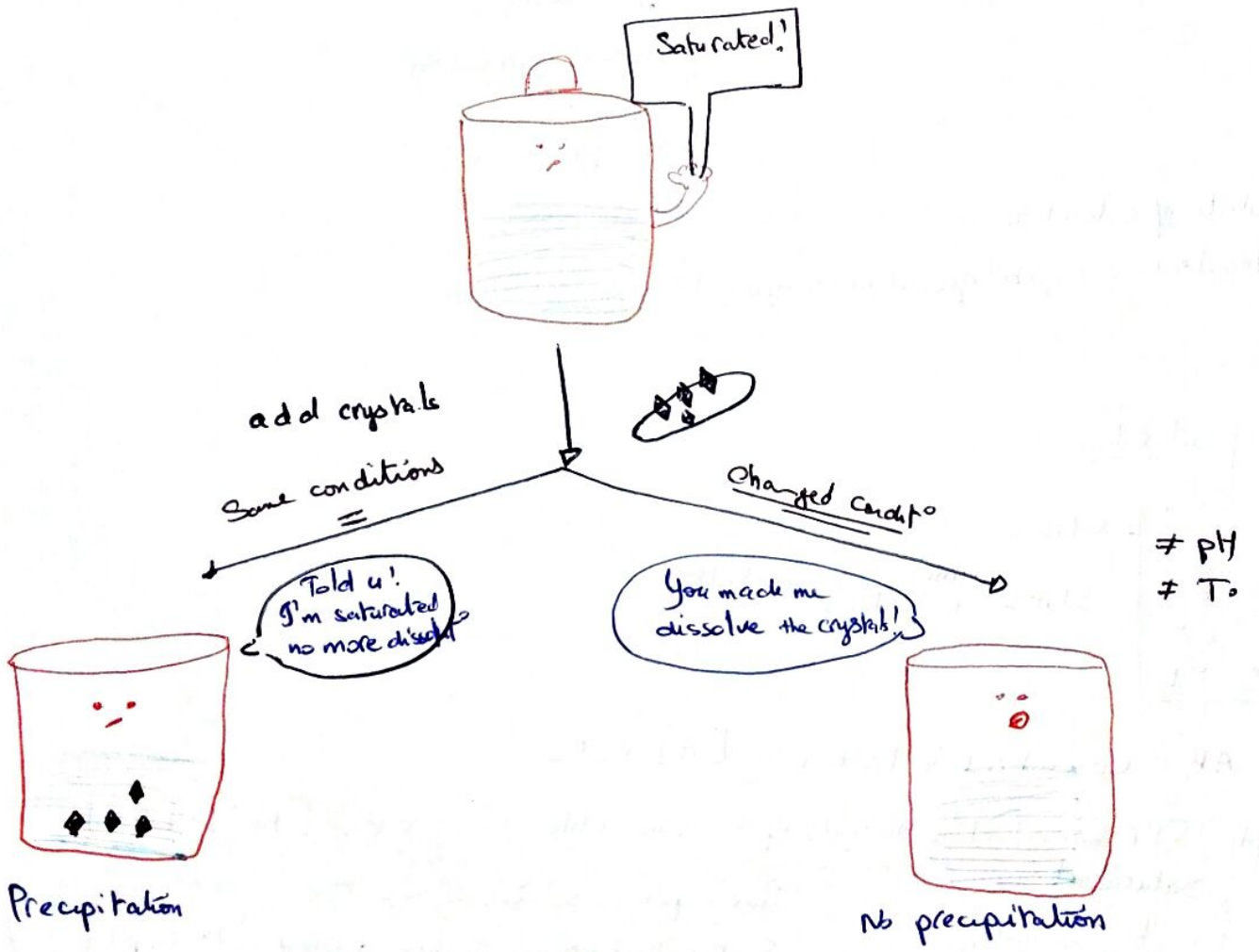
At the point of saturation:

CP = K_{sp} thermodynamic solubility product

dissolved vs crystaline compunds are in $\rightleftharpoons$ for a specific set of conditions: pH T°

if further crystals are added to the saturated solution





stone forming salt

components ↑CP

example: Calcium Oxalate

in urine

CP > K_{sp} but no crystallization

→ inhibitors
→ other molecules

Metastable

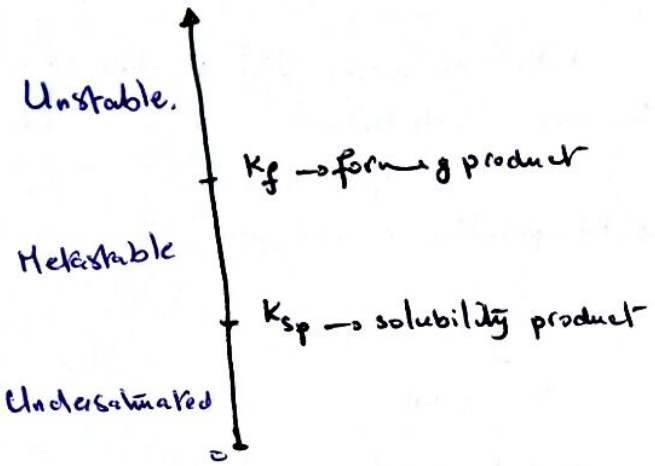
In urine

~~Satt~~ Stone forming salt

CP > K_{sp} but no crystalization → urine is metastable
- inhibitors

[ ] ↑↑↑ → crystals form : at this point CP → K_f : formation product

CP : Concentrat° product [ ] x [ ]



Undersaturated	K_{sp}	Metastable	K_f	Unstable
Crystals will not form under any circumstances Crystals dissolution possible		Supersaturated urine Nucleation Spontaneous de novo → no ✗ Under certain Circumstances → possible ✓ → Modulation factors act here. → Circumstances under which crystals can form: • Nephron: CP > K_{sp} for enough long time • UUT: obstruction / stasis → prolonged urinary transit • Urine: microscopic impurities other constituents → adsorption: heterogenous nucleation (↓ energy required.)		Crystals will form

Computer programs → urine solution measurements EQUIL 2. RSR, CPR
JESS more accurate

Historically: urinary oxalate > urinary calcium in influencing calcium oxalate stones
Later on → Conclusion both are important and equal contributors

Nucleation, Crystals growth, aggregation and Retention

Urine Water

[calcium oxalate] > 4 x Ksp

↓ volume, citrate
↑ calcium, oxalate, phosphate, uric acid } → ↑ calcium oxalate supersaturation → favoring stones formation

Calcium oxalate : CP > Ksp → crystallisation can occur but it doesn't because of inhibitors and other substances

CP > 7-11 x Ksp → Precipitation occur ✓

Nucleation

Homogeneous

in pure solution

nuclei formation

Heterogeneous

by adsorption onto existing surfaces of:
- epithelial cells
- cell debris
- other crystals

Nuclei: earliest crystals that will not dissolve

Threshold

small → size.

- unstable nuclei
- dissolution ++

depending on:
- supersaturation level
- lag time (nucleation time vs transit in nephron time)
- stability of the nuclei

destabilize → inhibitors

Stabilize - adsorpt° surface. → Promoters

min transit 5 - 7 min

[not enough for crystals to grow → size → luminal occlusion
but if enough nuclei form and grow → aggregation → larger particles → tubular lumen occlusion

Inhibitors: Prevent

- Growth
  - Uroponin
- Aggregation
  - Mg
  - Citrate.
  - Tamm. Horsfall mucoprotein
  - Bikunin (light chain of inter α trypsin)
- Both
  - Nephrocalcin

Urinary Stone Disease — Smith and Tan

UT afflictions : UTI → prostate conditions → urinary calculi

Speculative etiology : some wh ?

- 2 kidneys, same constituents → unilateral stones ?
- early in the dupt → small stones → why they don't pass ?
- Why some people form [multiple small stones / one large stone.

Advances : in surgical trt > understanding the etiology

Clinician : Dg
Trt
Metabolic evaluation → [lifestyle changes / medical therapy } → Prevent recurrence.
↑ effective prophylaxis needed

Renal and Ureteral stones

▷ Etiology:

In all biologic systems: Mineralization = (Crystals + Matrix) inter twined
Urinary stones = mineralization = crystalloid + organic matrix

Urine supersaturation : is required for stone formation

depends on urinary — [pH / ionic strength / solute concentration / Complexation

- pH : physiologic differences — first morning → relatively acid / after meals → alkaline
- ionic strength : Monovalent ion ~~concentration~~ relative concentration

[Mono V ion]relative

Ionic stright ↑ → activity coefficient ↓
[reflects the availability of particular ion

- Solute concentration : 2 ions

↑ [2 ions] → ↑ more likely to precipitate
↓ [ ] → undersaturation → ↑ solubility

[ions] ↑ → activity product → solubility product (K_{sp})

ions: A and B

A and B [ ] ↑ → $A_{activity} \times B_{activity}$ → solubility product (K_{sp})

[ ] > ↑ → metastable : capable of initiating crystal growth and heterogenous nucleation

A and B [ ] ↑↑↑ → activity product → formation product (K_{fp})

[ ] > ↑ → spontaneous homogenous nucleat°

Recap :

[ions] ↑ → solubility product (K_{sp}) → formation product (K_{fp})

> ↓ crystal growth nucleation heterogenous nucleation

> ↓ spontaneous homogenous nucleation

* Complexation
  - influences the availability of specific ions
  - Na^+ with oxalate → ↓ oxalate availability
  - Sulfate with calcium → ↓ calcium availability

* Other substances influencing crystal formation : in the urinary tract

Mg
Citrate
Pyrophosphate
Trace metals
} → inhibitors acting ↗ active crystal growth ↘ in solution (citrate)

Theories

Nucleation theory

Crystals / foreign bodies in supersaturated urine ↓ crystal formation

but:
Hyperexcretors
Risk of DSH
} not always form crystals

Stone formers : 24h urine collect°
- normal [ ] of stone forming units

Crystal inhibitor theory

Lack of natural inhibitors ↓ Crystal formation

but

People lacking inhibitors → never form stones
People with stones → abundant inhibitors