

# Nephrology (Renal Medicine)



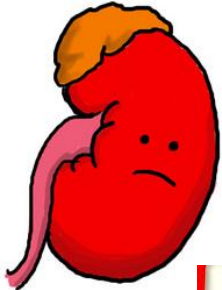
**Dr Shabbir Moochhala**

Consultant Nephrologist,  
Royal Free Hospital, London

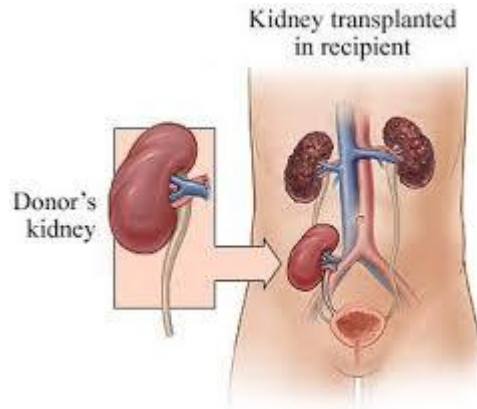


**Cystinuria Patient Day**  
**1<sup>st</sup> Feb 2014**

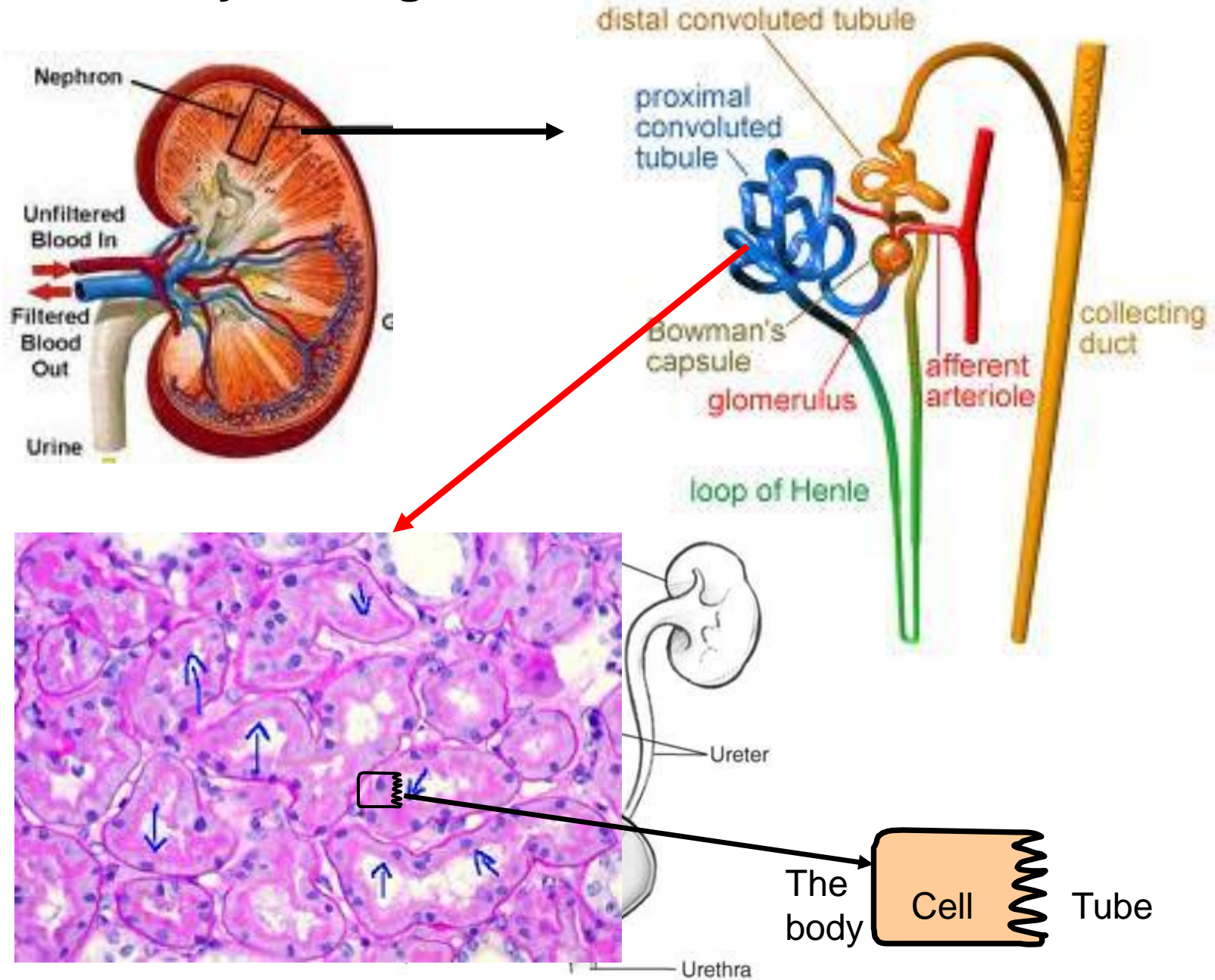
# Nephrologist



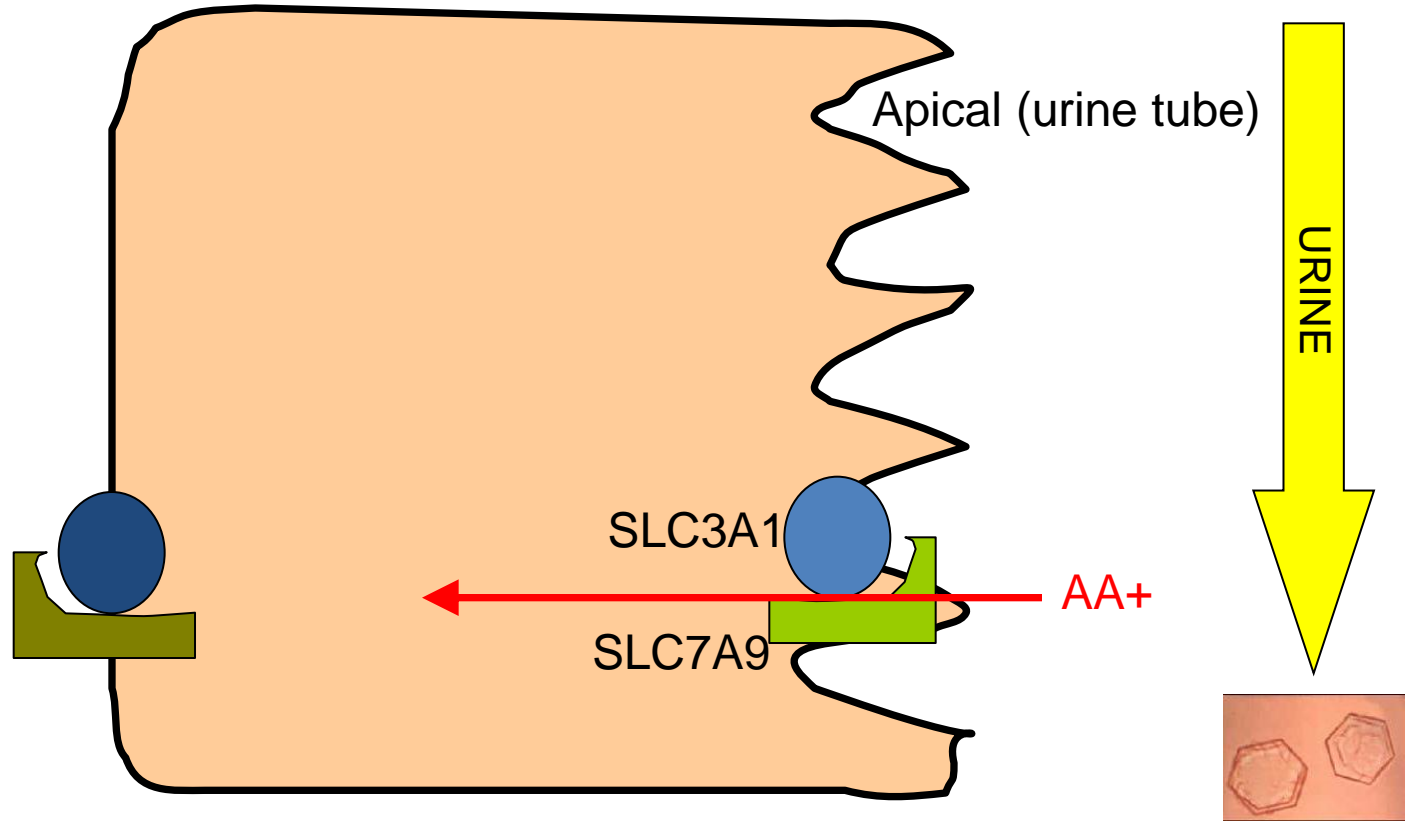
# Urologist



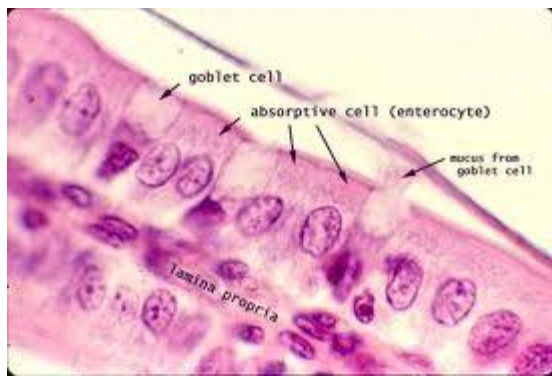
# The Kidney – designed for the job



# Reabsorption (reclaiming) in the proximal tubule

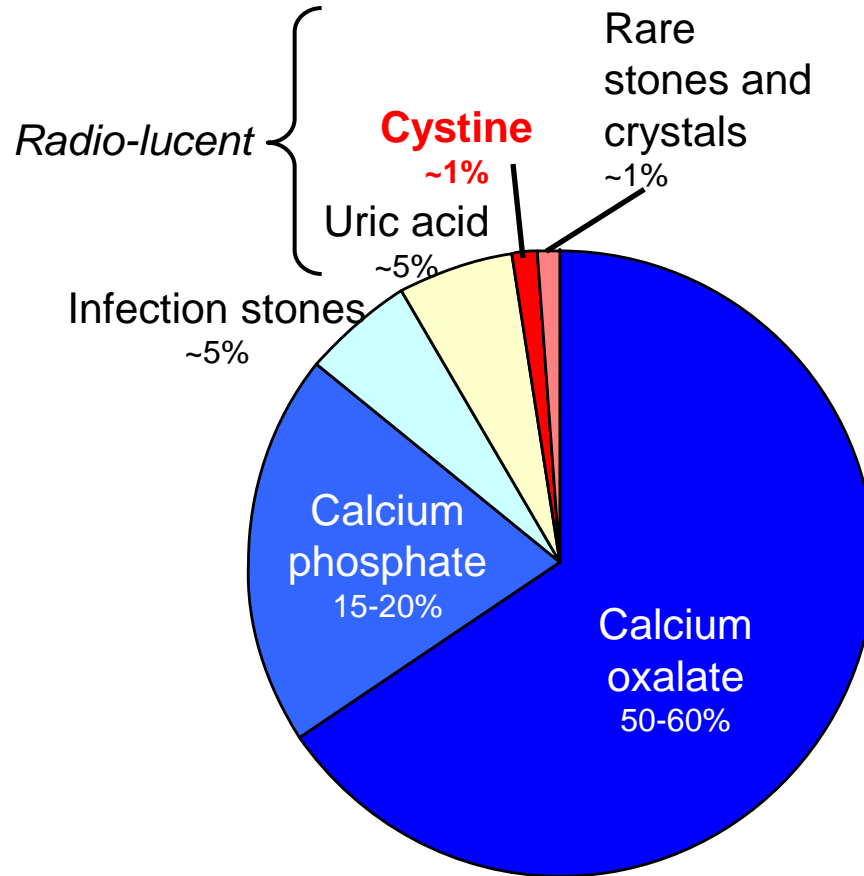


**99% efficient!**



**Same transport process in the gut!**

# The easiest stone disease to treat?



# eGFR

Stage	Description	GFR
1	Kidney damage, N or ↑GFR	≥90
2	Kidney damage, mild ↓GFR	60-89
3A	Moderate ↓GFR	45-59
3B	Moderate ↓GFR	30-44
4	Severe ↓GFR	15-29
5	Kidney failure	<15 (or dialysis)

**Denote proteinuria with a “p”**



# Clinical assessment (adult)

- Urinary tract symptoms
- Age of onset
- Unilateral or bilateral
- Previous stone episodes and procedures
- Anatomical abnormalities
- Job
- Fluid intake & pattern
- Salt intake
- Renal function

# What are we measuring?

Amino acid	umol/L	umol/24Hr	mmol/ mol Creat.
===== Cystine	226	860	78.6 [ 3-12 ]
Ornithine	707	2689	245.8 [0.5-2.0]
Lysine	2576	9799	895.7 [ 6-41 ]
Arginine	1536	5843	534.1 [ 0-3.7]
Pen-Cys disulphide	328	1248	114.0

:

Consistent with treated dibasic aminoaciduria  
(cystinuria). No generalised aminoaciduria.



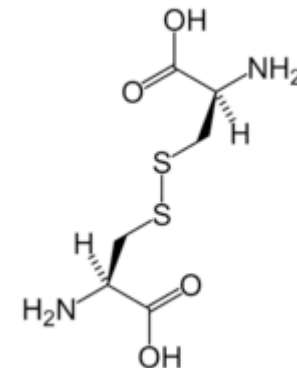
# Cystinuria - management

- Can't reabsorb dibasic amino acids in proximal tubule
- **DILUTE**
- **ALKALINISE**
- **SOLUBILISE**

Look out for other conditions: Fanconi  
Also hypercalciuria, hyperuricosuria, frequent UTIs etc  
can coexist.

Liaise with urological colleagues!

Enter into Patient Registries



Dimerised cysteine

# Summary

- We understand the physiology but not all the genetics
- Can coexist with other stone conditions/risk factors
- We work as a team!



# Diagnosis

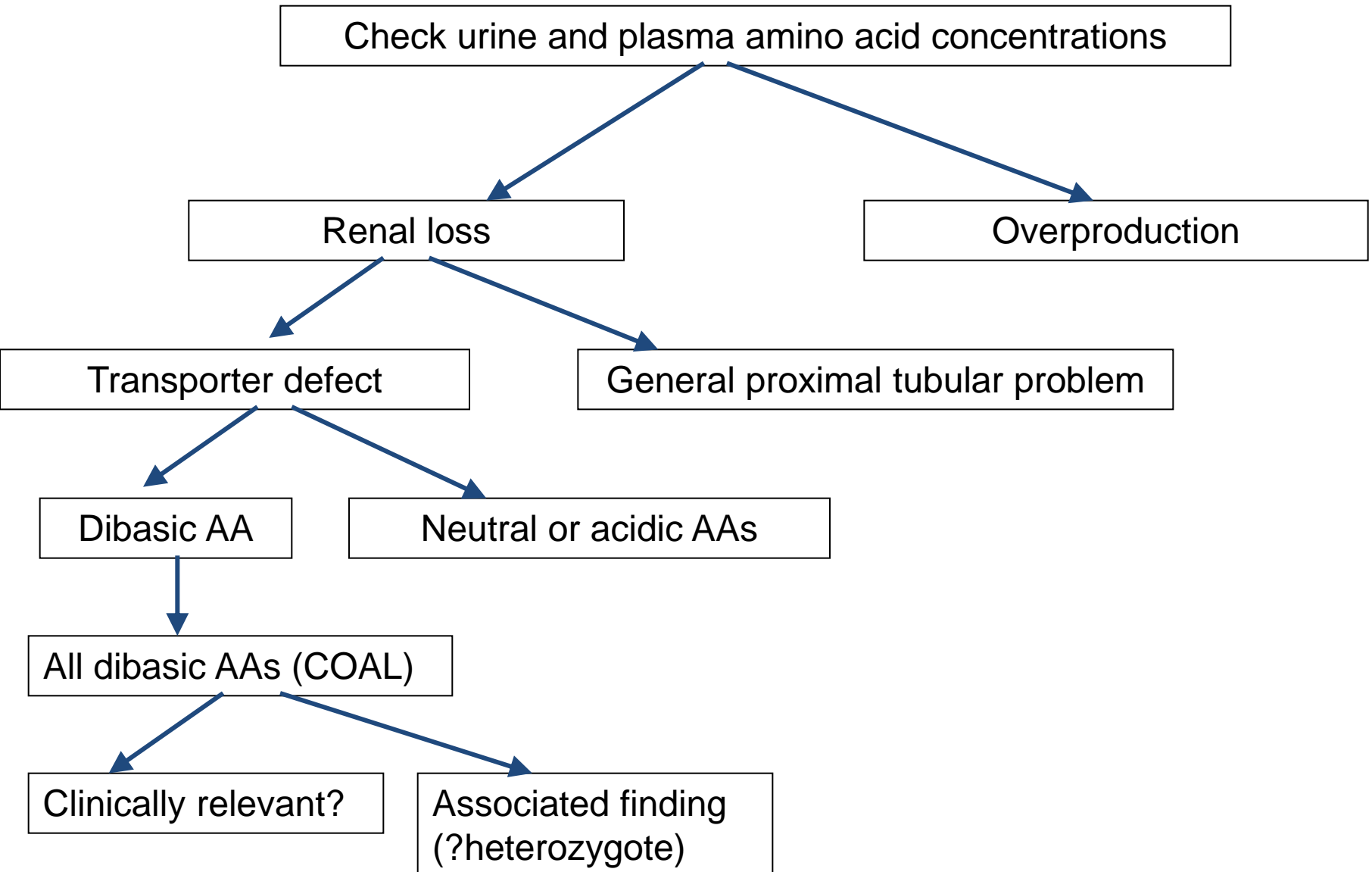
## Diagnostic clues

- Mildly radioopaque stone, autosomal recessive
  - (DD: xanthinuria, adenosine phosphoribosyltransferase deficiency)
- Bladder stones in a child
- Classic hexagonal crystals on urine microscopy
- Sulphurous smell on laser vapourisation of stone
- Positive screen on nitroprusside test

## Confirmation

- Ion exchange chromatography/HPLC
- AA + ninhydrin: detect light at 570nm
- Very high urinary levels but plasma levels not too low
- Mutation analysis: Not done!
- Stone analysis of (staghorn) stone

# Diagnostic method for aminoacidurias



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Consistent with treated dibasic aminoaciduria (cystinuria). No generalised aminoaciduria.

- Target cystine concentration <0.5 mmol/l ?
- Cystine:creat ratio ?
- Underestimate cystine when it precipitates out, so use acidified and plain (to measure pH) collection?

## Assays

- **Colorimetric assays** measure free sulphhydryl groups (nitroprusside)
  - Can't distinguish cystine v soluble thiol drug-cysteine complexes
- **Chromatographic** methods can distinguish
  - But drug-cysteine complexes can be disrupted by sample prep which also leads to overestimation of cystine
- pH affects all of these and pH effect on cystine solubility varies between individuals
- Dissolved solute and solid component: Need to know both for treatment purposes
- One way is to add a known amount of solid cystine crystals and incubate for 48h at 37C (Goldfarb, Kidney International 2006)
- Hence measure capacity of urine to dissolve cystine, without knowing total amount

# Successful management in an 18 yr old F

- 18 F
- L PCNL Aug 2010 (10x7 mm stone left lower pole)
- BMI 28.7
- Creat 57  $\mu\text{mol/l}$
- BP 120/60
- Potassium citrate 10 ml bd (= 30 mmol K bd)
- Annual imaging at UCH
  
- Often forgets the potassium citrate
- Average 24 h U cystine conc >500  $\mu\text{mol/l}$
- Average U Osm 100 mOsm/kg
- Overnight hydration and nocturia
- Plasma sodium 142 mmol/l
- Spot U Osm 252 mOsm/kg, spot U pH 6.9



THE END