Diuretics and RAAS case study

- Sonia, a 65 year old female has been taking HCTZ (50 mg/day) for 5 months. You see her for the 1st time in a clinical and decide that her BP is under control - 125/82 mmHg. You decide to draw blood and test for possible side effects.

Which side effects would you test for? Motivate your answer.

- Hypokalaemia
  - Thiazides are not K^+-sparing diuretics and may decrease K^+ levels
  - If levels are to low it may trigger arrhythmias in patients taking digoxin
- Hyperglycaemia
  - Diabetics and patients with moderately high glycaemia may become hyperglycaemic and have difficulty in maintaining normal blood sugar levels
  - Due to impaired pancreatic cell function, ↓ insulin release and ↓ glucose utilisation
  - Rarely develops with low doses (12.5 mg/day)

Which side effects would you test for? Motivate your answer.

- Serum uric acid
  - Thiazides ↓ uric acid excretion by the kidneys
  - May cause gout in predisposed individuals
- Hyperlipidaemia
  - Thiazides cause ↑ in LDL / triglycerides and ↓ HDL, unwanted in patients with hypercholestrolaemia
  - Does not outweigh beneficial BP effects
- Hypercalcaemia
  - Thiazide ↓ Ca^{2+} excretion → dangerous if patient on digoxin
  - May help with osteoperosis

Which side effects would you test for? Motivate your answer.

- Hyponatraemia
  - Thiazides cause excretion of Na^+ → necessary for therapeutic effect

How would you minimise these side-effects?

- Reduce dosage from 25 mg to 12.5 mg per day
- K^+ supplementation
- Low Na^+ diet may reduce K^+ loss
- Reduce Na^+ loss by decreasing H_2O intake

- Change therapy to Indapamide which has less side effects

- 6 months later you see Sonia again, her BP was raised and she was started on perindopril 4 mg daily

Describe the possible interaction between ACEIs and Thiazide diuretics. Are these interactions beneficial / toxic?

- ACEIs ↓ aldosterone secretion → K^+-sparing effect

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- Thiazides cause K^+ depletion

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- K^+ maintainence
- **Beneficial effect**

What would the possible interactions be if Sonia was taking Moduretic® (amiloride + HCTZ) along with perindopril? Beneficial / toxic?

- Amiloride would already compensate for K^+ depletion due to HCTZ.
  - K^+ levels would be maintained with Moduretic®
- Using Moduretic® in combination with perindopril (any ACEI) may cause dangerous hyperkalaemia
- Don't use K^+-sparing drugs / K^+ supplements with ACEIs