Describe the renal handling of sodium.

Total body Na⁺ content is regulated to within 2%. Regulation of any system is typically a balance between input and output, however sodium intake is essentially unregulated. Sodium is therefore regulated by adjusting methods of elimination.

Sodium is eliminated in:
- Sweat and GIT
  - Obligatory and not amenable to regulation.
    - Acclimatisation to hot environments improves the efficiency of sweating by reducing its tonicity, reducing sodium loss
- GIT
- Urine
  - Regulation of sodium is predominantly via adjusting renal elimination, and is mediated primarily by aldosterone.

Urinary Elimination of Sodium

\[
\text{Na excretion} = \text{Na filtered} - \text{Na reabsorbed} = (\text{GFR} \times \text{s-[Na]}) - \text{Na reabsorbed}
\]

∴ Urinary elimination can be adjusted if in two ways:
- Changes in GFR
  - Changes in GFR due to hyper or hypovolaemia will (indirectly) adjust sodium elimination.
  - Increased plasma volume increases GFR, and vice versa.
- Changes in sodium reabsorption
  - This is the main mechanism for controlling sodium in euvolaemia.
  - In terms of long term Na excretion; Na reabsorbed is more imp than GFR because:
    - GFR autoregulated
    - Glomerulotubular balance:
      - Changes Na reabsorption in response to primary change GFR
      - ie ~ 65% constant
      - intrarenal process
      - blunts changes in Na excretion caused by minor GFR changes
      - don’t confuse with TGF

Sodium Reabsorption

Given that:
- Normal glomerular filtrate is ~180L.day⁻¹
- The dominant osmole in glomerular filtrate is sodium
- Normal urine output is ~1.5L

The majority of filtered sodium must be reabsorbed. This is called bulk reabsorption and occurs in the PCT and LOH:
- PCT: 60% of total reabsorption is by the Na⁺-K⁺ ATPase pump
- LOH: 30% of total reabsorption is by the Na⁺-K⁺-2Cl⁻ co-transporter

The remaining 10% of sodium reabsorption occurs in the DCT and CD. As it is under the influence of aldosterone, it is the component which is important in regulation.

Aldosterone increases Na⁺ reabsorption by increasing the number or activity of these pumps:
- Na⁺-Cl⁻ pumps in the DCT
- Na⁺-K⁺ ATPase pumps in principal cells of the DCT
- Na⁺-H⁺ pumps in intercalated cells of the CT

Overall Control of Na reabsorption (∴ hence Excretion)

1. GTB
   - Decreased renal perfusion (eg secondary to hypovolaemia or hypotensing drugs) will reduce GFR and thus sodium excretion
2. Aldosterone - released from zona glomerulosa of the adrenal cortex to upregulate the activity of the CCD. Na/K ATPase and the ENaC channel to increase sodium resorption in exchange for K secretion.

3. SNS – direct – constrict arterioles → reduce GFR

4. AT2
Renin: secreted in response to sympathetic stimulation and direct stimulation from renal macula densa. Cleaves angiotensin 1 from angiotensinogen, AT1 then converted to AT2 which causes vasoconstriction especially of efferent arteriole, reducing the peritubular capillary hydrostatic pressure to increase the gradient for reabsorption of Na (and water and other electrolytes) in the tubules. AT2 also stimulates the activity of the Na/H exchanger in the proximal tubule and upregulates the Na/K ATPase throughout the tubule system.

5. ANP
secreted from the atria in response to stretching. Opposes Na resorption in the tubules, increases the filtration coefficient at the glomerulus, and inhibits the release of renin

6. ADH (indirect)

7. Intrarenal physical factors

8. Pressure natriuresis & diuretics

9. Misc
Other causes ↑Na reabsorb:
• Cortisol
• Oestrogen
• GH
• Thyroid hormone
• Insulin

Other cause ↓Na reabsorb:
• Glucagon
• Progesterone
• PTH
• Renal vasodilators:
  o PGs
  o Kinins

Examiner Comments:
46% of candidates passed this question.
A description of filtration and reabsorption, including amounts was required. Better answers described sodium handling in a logical sequence as it progressed through the nephron including the percentages reabsorbed in each segment. In addition to the amounts reabsorbed, the mechanisms of transport across the tubular luminal and basolateral membranes into interstitial space should have been described.