Describe the endocrine functions of the kidney.

**Vitamin D**
Vitamin D has a complex metabolic pathway which meanders through a number of organ systems:
- Vitamin D$_2$ (ergocalciferol) only in diet
- Vitamin D$_3$ (cholecalciferol) absorbed in diet or produced in skin by the action of UV light
  - 7-dehydrocholesterol $\rightarrow$ 7-dehydroxycholecalciferol $\rightarrow$ cholecalciferol
- Liver: Cholecalciferol hydrolysed $\rightarrow$ 25-hydroxycholecalciferol (25-OH$_D$$_3$)
  - Enzyme: Vitamin D25-hydroxylase (CYP450 enzyme)
- Released into plasma, binds to Vitamin D-binding protein ($\alpha$ globulin carrier protein)
- Kidney: 25-OH$_D$$_3$ hydrolysed $\rightarrow$ 1,25-dihydroxycholecalciferol (calcitriol – active form)
  - in the proximal tubule, Enzyme: 1alpha hydroxylase
  - Released into circulation
  - Transported by Vitamin D binding enzyme to intestine, kidney, bone

**Erythropoietin**
Secretion of EPO to stimulate RBC production
Erythropoiesis is stimulated by EPO release:
- In adults, EPO is released from the:
  - Peritubular capillary fibroblasts (85%)
  - Liver (15%)
- EPO is released in response to:
  - Hypoxia (near the secretory cells which lie in between the cortex and medulla)
  - Hypotension
  - Low Hct
- Erythropoiesis is inhibited by:
  - High red cell volume

Production of EPO is decreased in renal failure, which is why patients with end-stage renal disease require exogenous EPO.

**Prostaglandins**: Production of prostaglandins esp PGE2 and prostacyclin – potent renal vasodilators
**Bradykinin**: Production of bradykinin – potent renal vasodilator

**Renin-Angiotensin-Aldosterone System**
The RAAS is a signaling pathway involved in blood pressure control. It involves a number of hormones:

- **Angiotensinogen** is produced by the liver
- **Renin** is a protease enzyme (Half-life 80mins)
  - produced by the kidneys
  - stored by the granular cells of the juxtaglomerular apparatus, which lies close to the glomerulus and distal tubule
  - Secretion is stimulated by:
    - Pressure changes in the afferent arteriole
    - Stimulation of the macula densa when changes occur in tubular NaCl concentration
    - Renal sympathetic nerve activity (a direct β1 effect)
    - Baroreceptor reflexes
    - Negative feedback from AT II
  - Exists to cleave hepatic angiotensinogen to the 10-AA peptide angiotensin I
  - Note: Renin is rate-limiting step for activation of RAAS
- **Angiotensin I**
  - has mild vasoconstrictor properties, but not enough to cause significant changes in circulation
- **Angiotensin Converting Enzyme (ACE)**
  - Found mainly in pulmonary vascular endothelial cells - converts angiotensin I to angiotensin II
  - Also cleaves bradykinin into inactive metabolites
- **Angiotensin II**
  - Effects include a general reduction in sodium and water excretion, and maintenance of circulating blood volume, GFR and blood pressure.
  - Rapidly removed from circulation in 1-2mins, presumably by tissue peptidases (Angiotensinases)
- **Aldosterone**
  - is secreted from the zona glomerulosa of the adrenal cortex
  - It acts in the renal CCD to enhance the activity of ENaC and K+ secretion by principal cells.
  - increases Na+ (and water) reabsorption in exchange for K+ (kidney, gut, salivary, sweat)

**Examiner Comments:**
39% of candidates passed this question.

It was expected that candidates would discuss the major hormones produced (or activated) by the kidney. These included erythropoietin, renin and calcitriol. Good answers included the following: the area where the hormone is produced or modified; stimuli for release; factors which inhibit release; and the subsequent actions / effects. Marks were not awarded for hormones that act on the kidney.