TABLE 25-3 SOME ENDOCRINE HORMONES ELABORATED BY THE KIDNEY

HORMONE	SOURCE	FUNCTION	DRUGS
Renin	JGA	Converts angiotensinogen to angiotensin I as an integral part of the renin-angiotensin-aldosterone system	Renin inhibitor ACE inhibitor Angiotensin receptor blocker Mineralocorticoid receptor blocker
$1,25(OH)_2$ vitamin D	Mostly proximal tubule	Converts the precursor 25(OH) vitamin D to its active form, $1,25(OH)_2$ vitamin D	25-Hydroxyvitamin D 1,25-Dihydroxyvitamin D Synthetic vitamin D analogues
Erythropoietin	Renal interstitial cells	Stimulates erythropoiesis in the bone marrow	Recombinant human erythropoietin Glycosylated recombinant human erythropoietin Other "epomimetic" erythropoiesis-stimulating agents

ACE, Angiotensin-converting enzyme; JGA, juxtaglomerular apparatus.

factors such as vitamin D and the Klotho protein. Conversion of the precursor 25(OH)-hydroxyvitamin D to its active form, $1,25(OH)_2$dihydroxyvitamin D, is achieved not exclusively but substantially in the kidney and is mediated by 1α-hydroxylase. Vitamin D deficiency is an important complication in chronic kidney disease. Replacement of vitamin D is efficacious in reducing the complications of chronic kidney disease and may even improve survival.

Erythropoietin

Erythropoietin, which is produced mainly in the kidney, stimulates erythropoiesis. The erythropoietin-producing cells are strategically located in the cortical interstitium to sense the balance between oxygen delivery and consumption. The current model suggests that upregulation of renal erythropoietin production (mainly by anemia and hypoxia) occurs via an increase in the number of latent erythropoietin-producing cells. The mechanism of erythropoietin deficiency in kidney disease is not definitively known, although it does not involve destruction of renal erythropoietin-producing interstitial cells. One possible mechanism is decreased renal oxygen consumption as a consequence of reduced GFR; this results in higher renal tissue oxygen tension and suppression of erythropoietin production. Resetting of the oxygen-sensing mechanism has also been conjectured. Another theory is direct inhibition of the erythropoietin-producing cells by inflammatory cytokines. Others have proposed transdifferentiation of erythropoietin-producing cells into myofibroblasts and a decrease in the number of interstitial cells that can be recruited to produce erythropoietin.

The use of erythropoiesis-stimulating agents (ESAs) has revolutionized the treatment of anemia associated with chronic kidney disease, but because of incomplete understanding of erythropoietin and erythropoietin receptor biology, the clinical outcome is far from ideal due to inability to tailor the optimal hematocrit for individual patients and uncertainty about possible extra-erythropoietic effects of erythropoietin.

SUGGESTED READINGS

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