Casual Friday Series

CKD – Functional Implications

A Biogenetix Clinical Presentation

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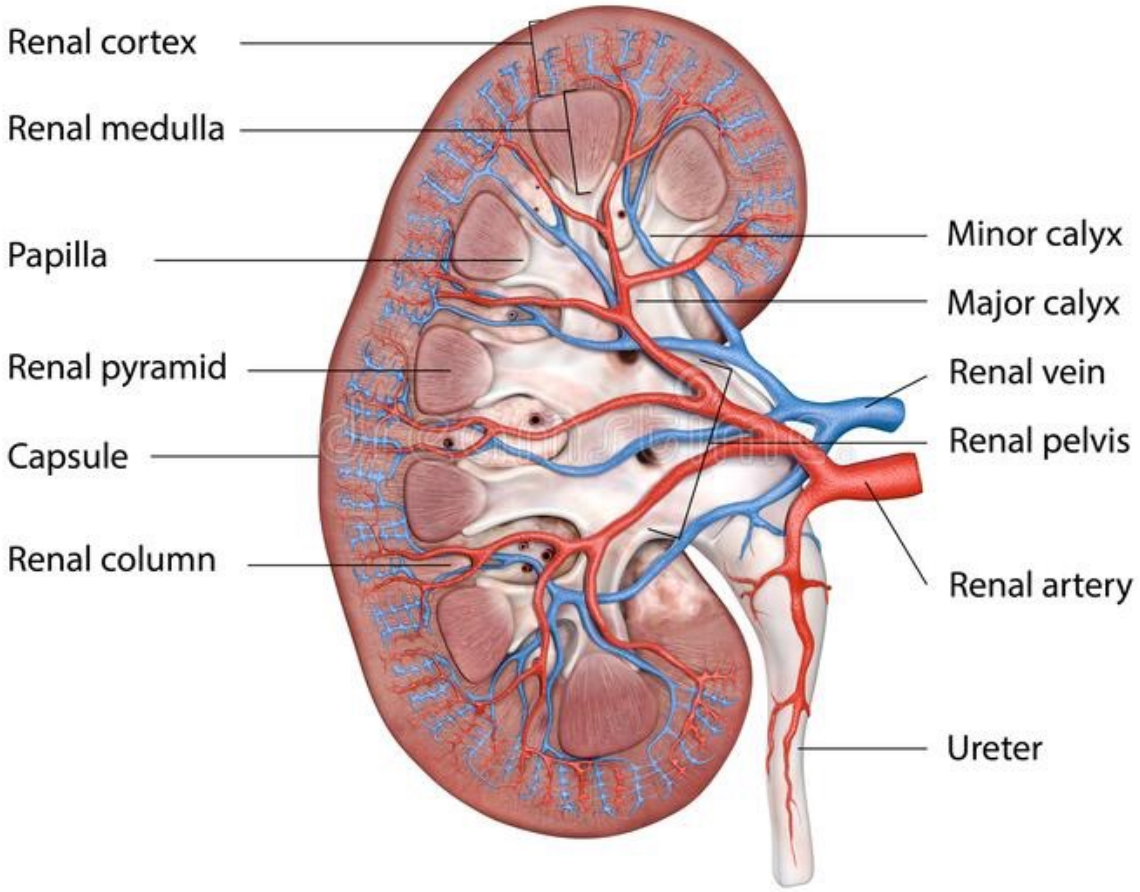
Disclaimer

- *Information in this presentation is not intended, in itself, to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*

Kidney Anatomy



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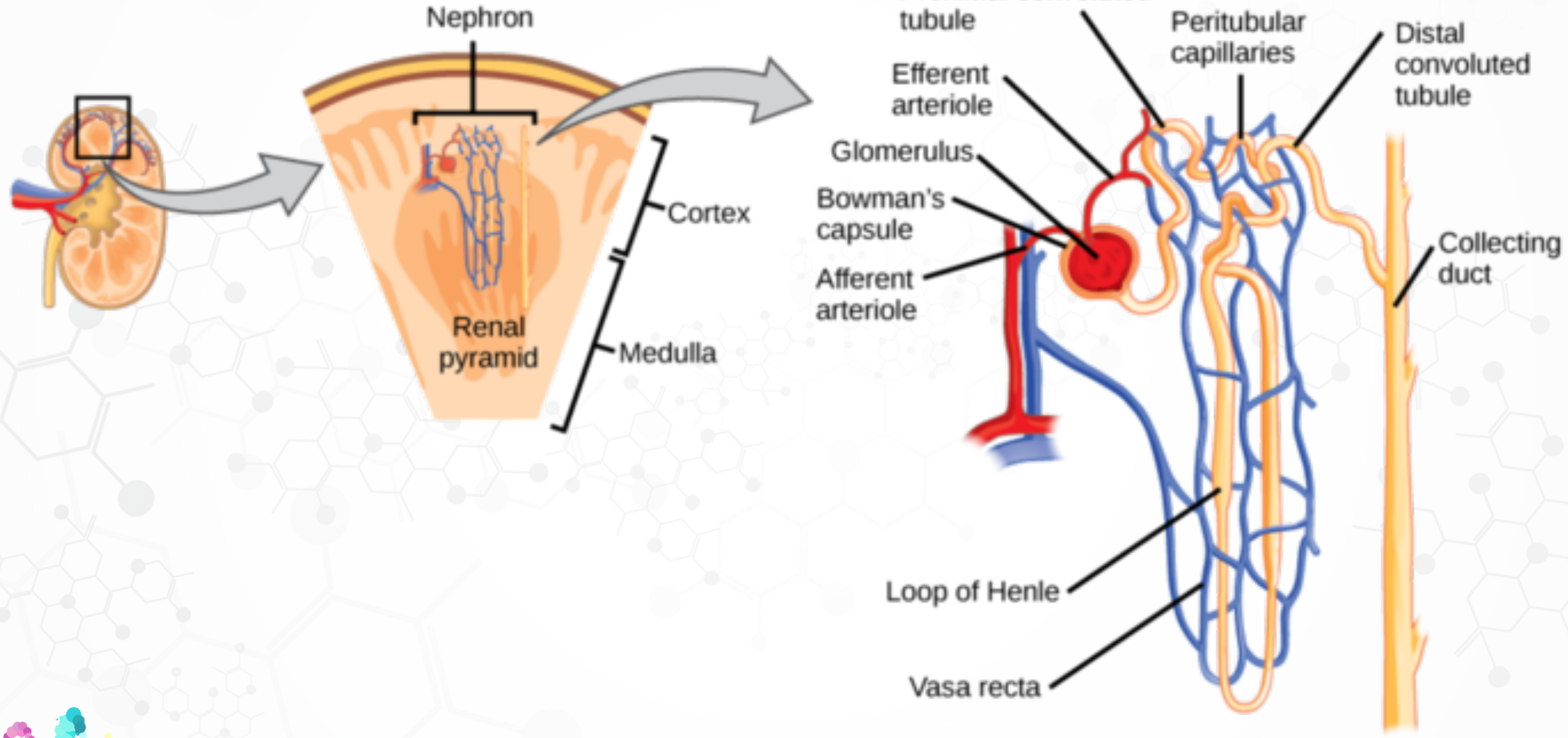

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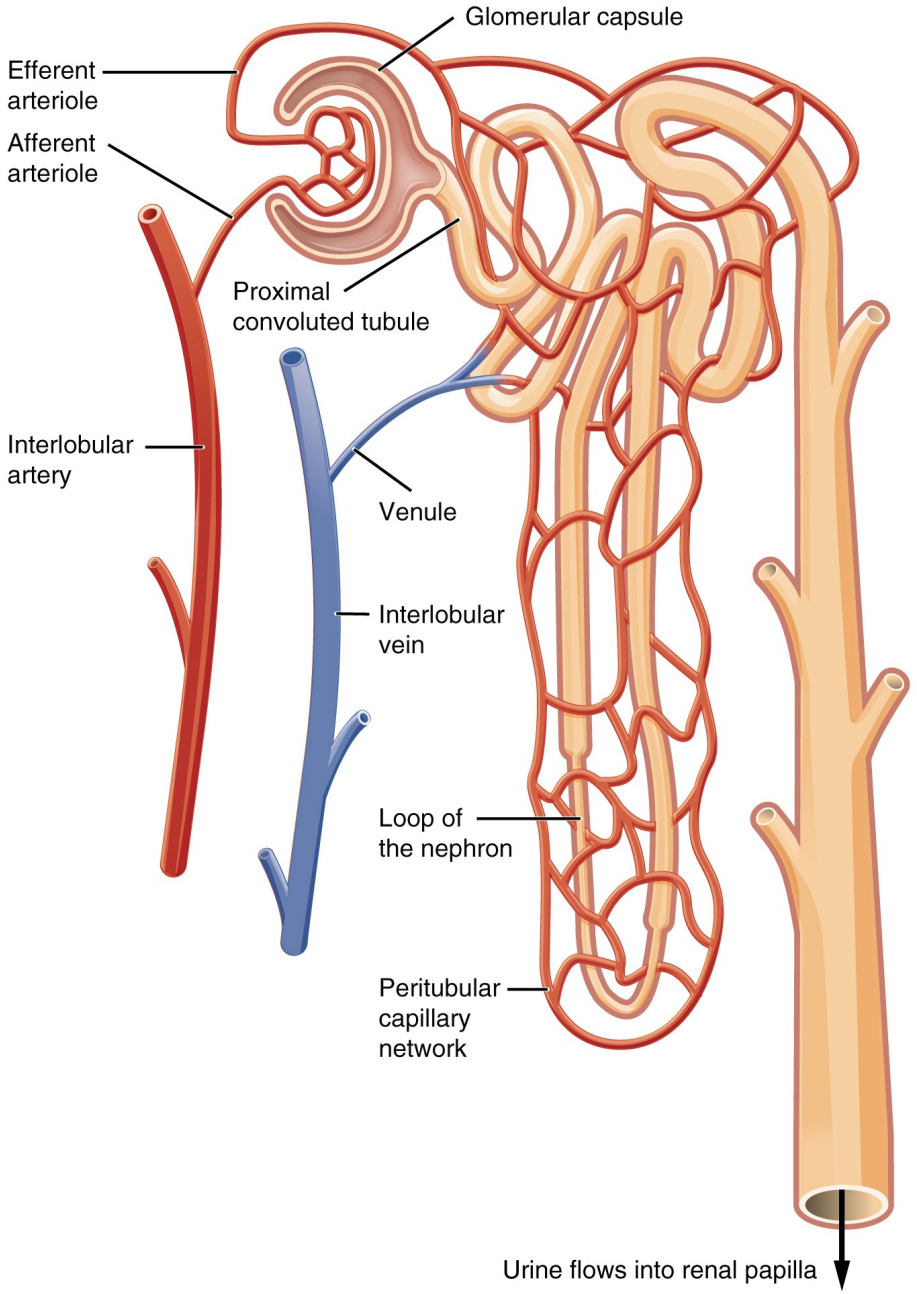

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Renin: an enzyme secreted by and stored in the kidneys which promotes the production of the protein angiotensin I.

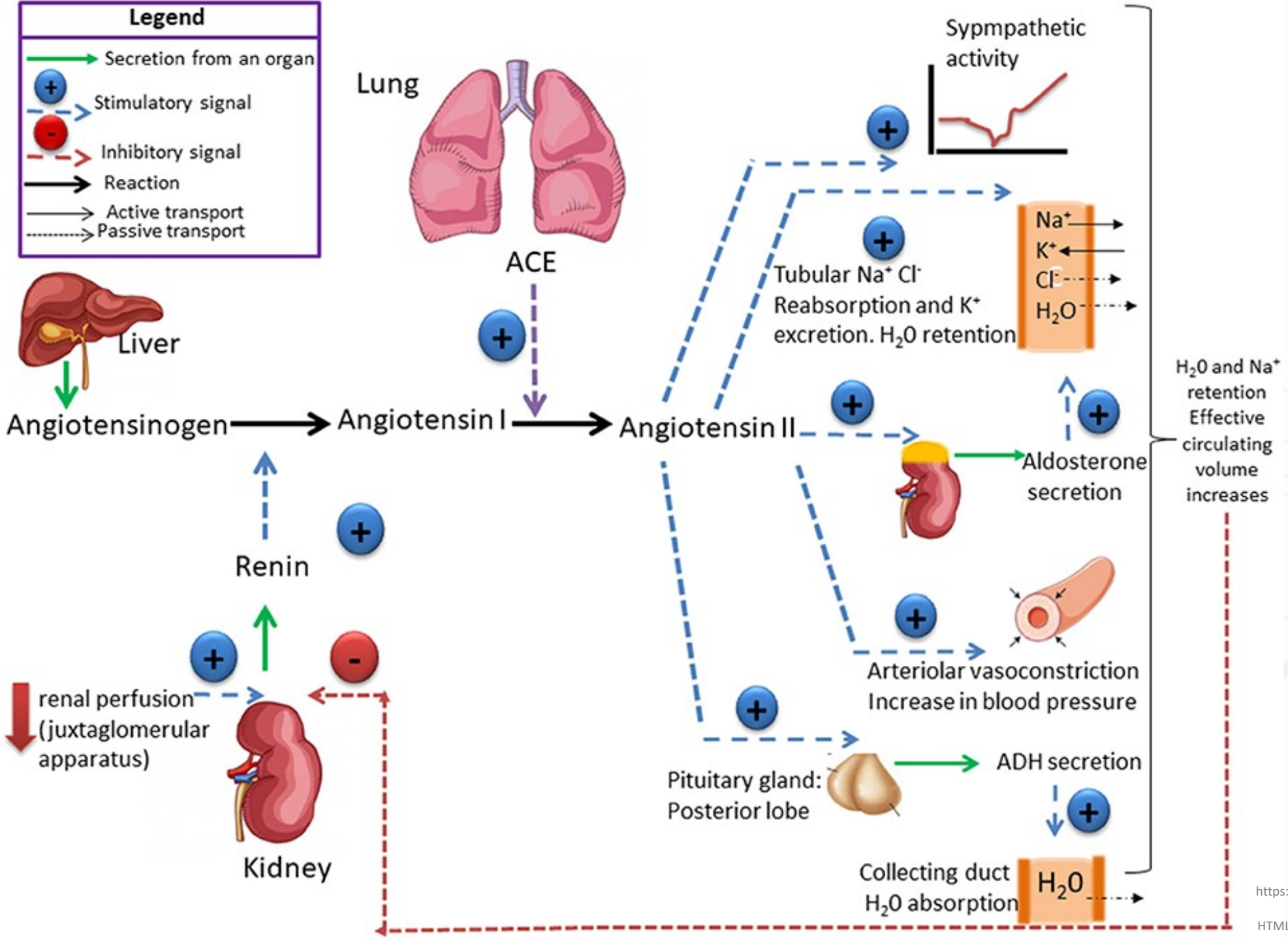
Angiotensin II: a protein with vasoconstrictive activity that increases blood pressure, stimulates the release of aldosterone. (ACE inhibitors act to block the conversion of angiotensin I to angiotensin II)

Atrial Natriuretic Peptide: a peptide hormone that is produced by the right atrium of the heart in response to elevated blood pressure and stimulates the excretion of sodium and water by the kidneys.

Parathyroid Hormone: a hormone that is made by the parathyroid glands and is critical to maintaining calcium and phosphorus balance. Deficiency of parathormone results in abnormally low calcium in the blood (hypocalcemia). Excessive parathormone leads to elevated calcium levels in the blood and calcium deposition in cartilage.

Aldosterone: a hormone produced by the outer portion (cortex) of the adrenal gland. Aldosterone regulates the balance of water and electrolytes in the body, encouraging the kidney to excrete potassium into the urine and retain sodium, thereby retaining water. It is classified as a mineralocorticoid hormone.

ADH (Vasopressin): a small peptide released by the pituitary gland. ADH has an antidiuretic action that prevents the production of dilute urine (and so is antidiuretic).



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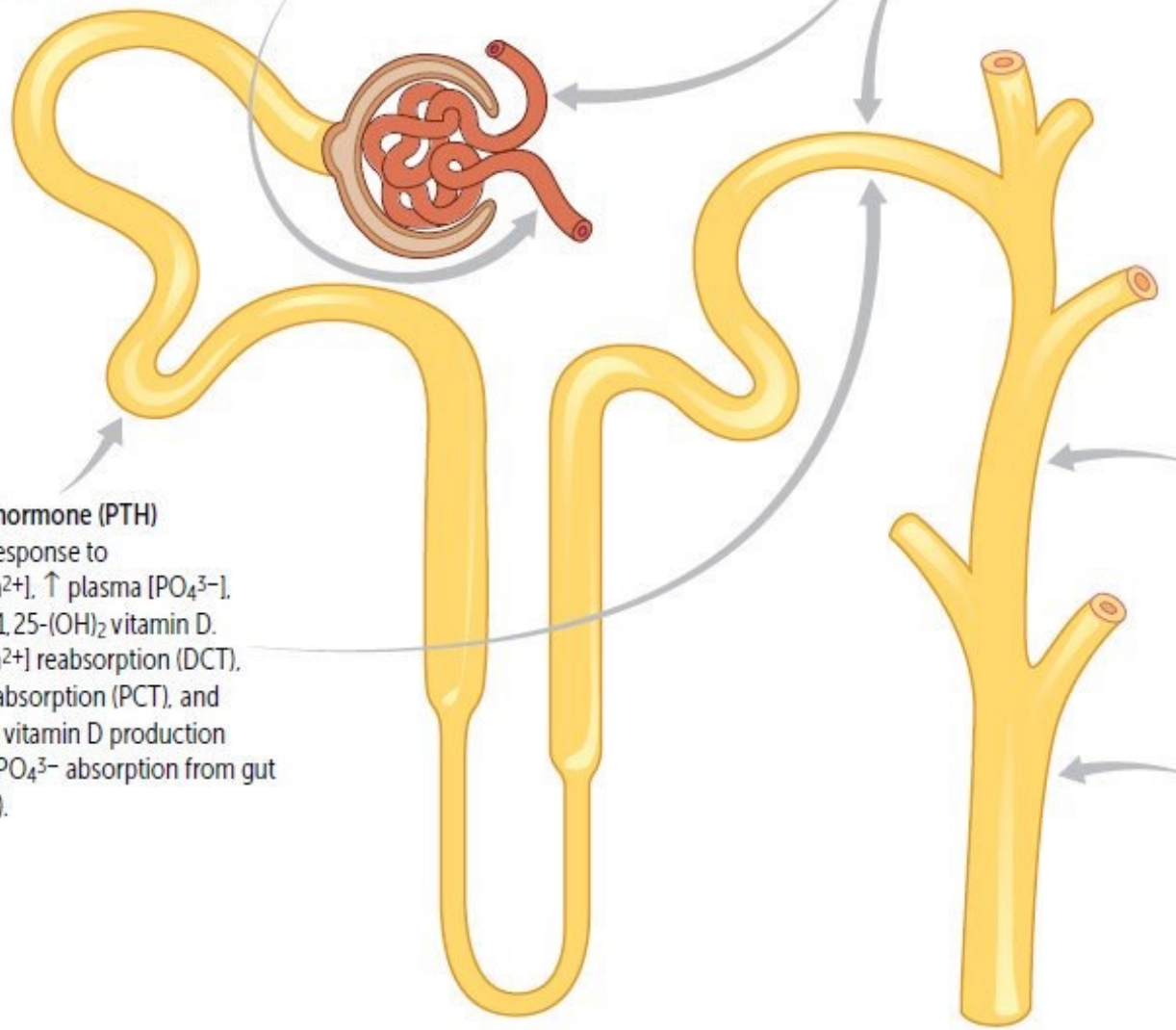
Hormones acting on kidney

Angiotensin II (AT II)
Synthesized in response to ↓ BP. Causes efferent arteriole constriction →↑ GFR and ↑ FF but with compensatory Na^+ reabsorption in proximal and distal nephron. Net effect: preservation of renal function in low-volume state (↑ FF) with simultaneous Na^+ reabsorption (both proximal and distal) to maintain circulating volume.

Atrial natriuretic peptide (ANP)
Secreted in response to ↑ atrial pressure. Causes ↑ GFR and ↑ Na^+ filtration **with no compensatory Na^+ reabsorption** in distal nephron. Net effect: Na^+ loss and volume loss.



Parathyroid hormone (PTH)
Secreted in response to ↓ plasma $[Ca^{2+}]$, ↑ plasma $[PO_4^{3-}]$, or ↓ plasma 1,25-$(OH)_2$ vitamin D. Causes ↑ $[Ca^{2+}]$ reabsorption (DCT), ↓ $[PO_4^{3-}]$ reabsorption (PCT), and ↑ 1,25-$(OH)_2$ vitamin D production (↑ Ca^{2+} and PO_4^{3-} absorption from gut via vitamin D).

Aldosterone
Secreted in response to ↓ blood volume (via AT II) and ↑ plasma $[K^+]$; causes ↑ Na^+ reabsorption, ↑ K^+ secretion, ↑ H^+ secretion.

ADH (vasopressin)
Secreted in response to ↑ plasma osmolarity and ↓ blood volume. Binds to receptors on principal cells, causing ↑ number of water channels and ↑ H_2O reabsorption.

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Front Immunol. 2015; 6: 340.
Published online 2015 Jul 8. doi: 10.3389/fimmu.2015.00340
PMCID: PMC4495338
PMID: 26217336

Cellular and Molecular Mechanisms of Chronic Kidney Disease with Diabetes Me… …norbidities

Prathibha Reddy Gajj…

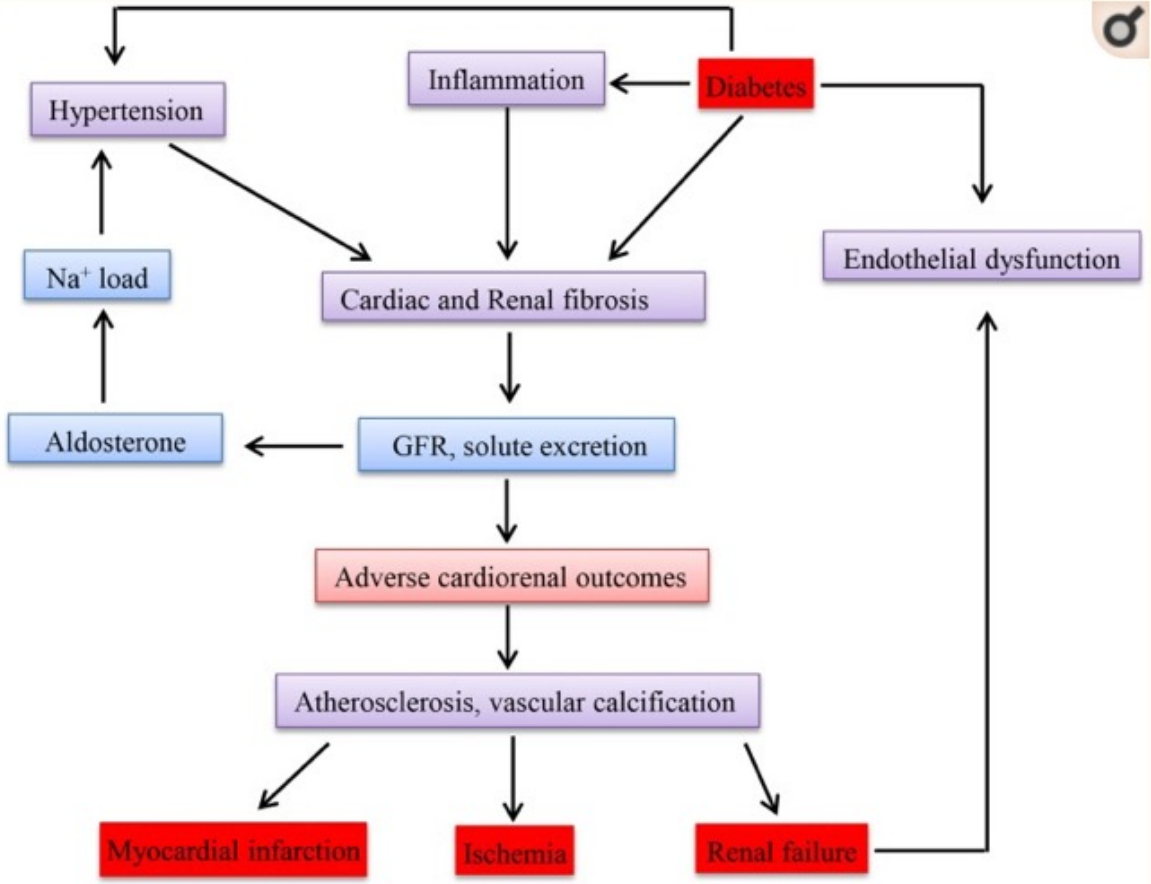


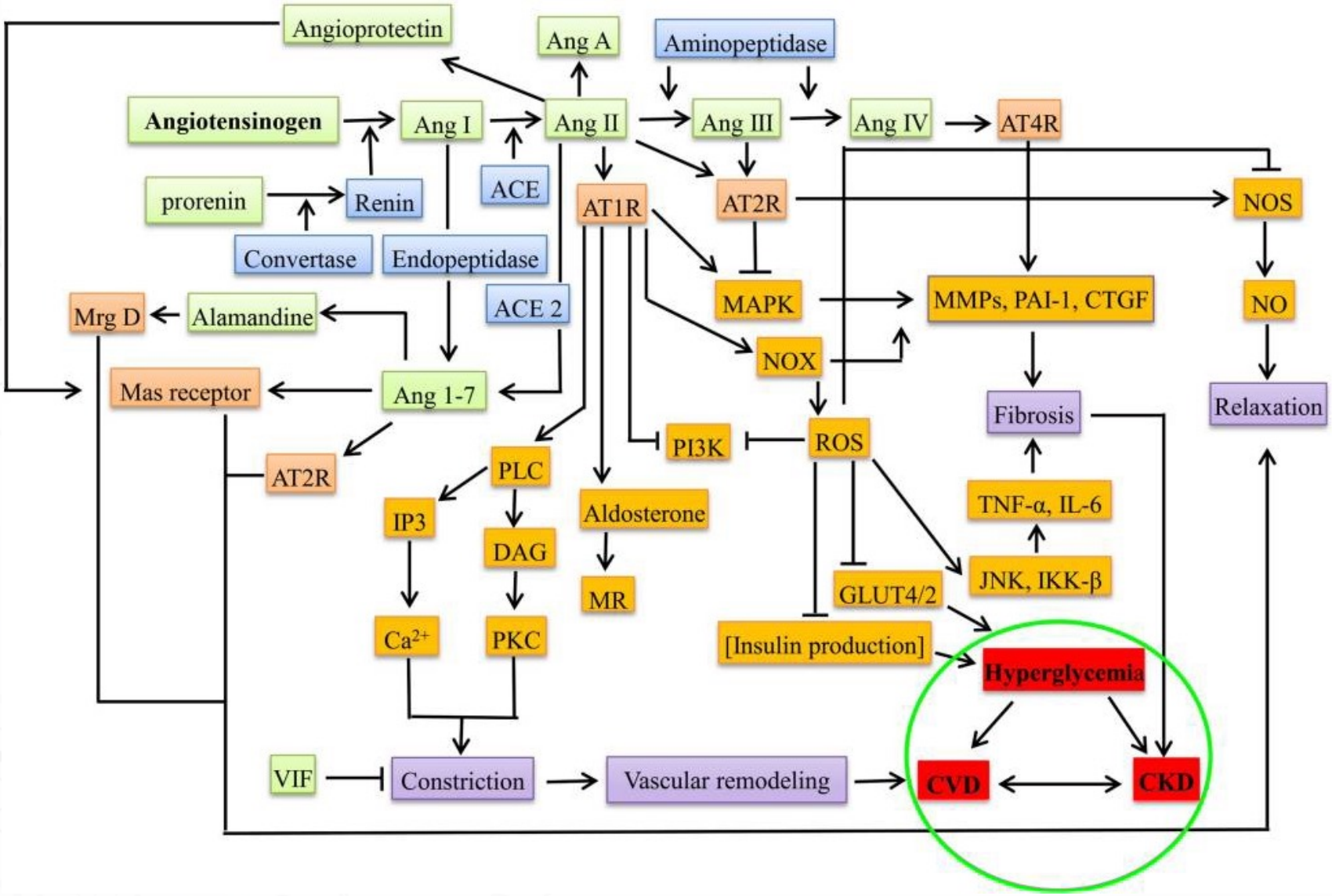
Figure 3

Schematic representation of clinical link between chronic kidney disease, diabetes mellitus, and cardiovascular disease.

5 Proposed Mechanisms of CKD

1. Dysfunction in the renin angiotensin-aldosterone system.
2. Inflammation
3. Fibrosis
4. Uremic Toxins
5. Vascular Calcification

1. Dysfunction in the renin angiotensin-aldosterone system.



3. Fibrosis

Fibrosis

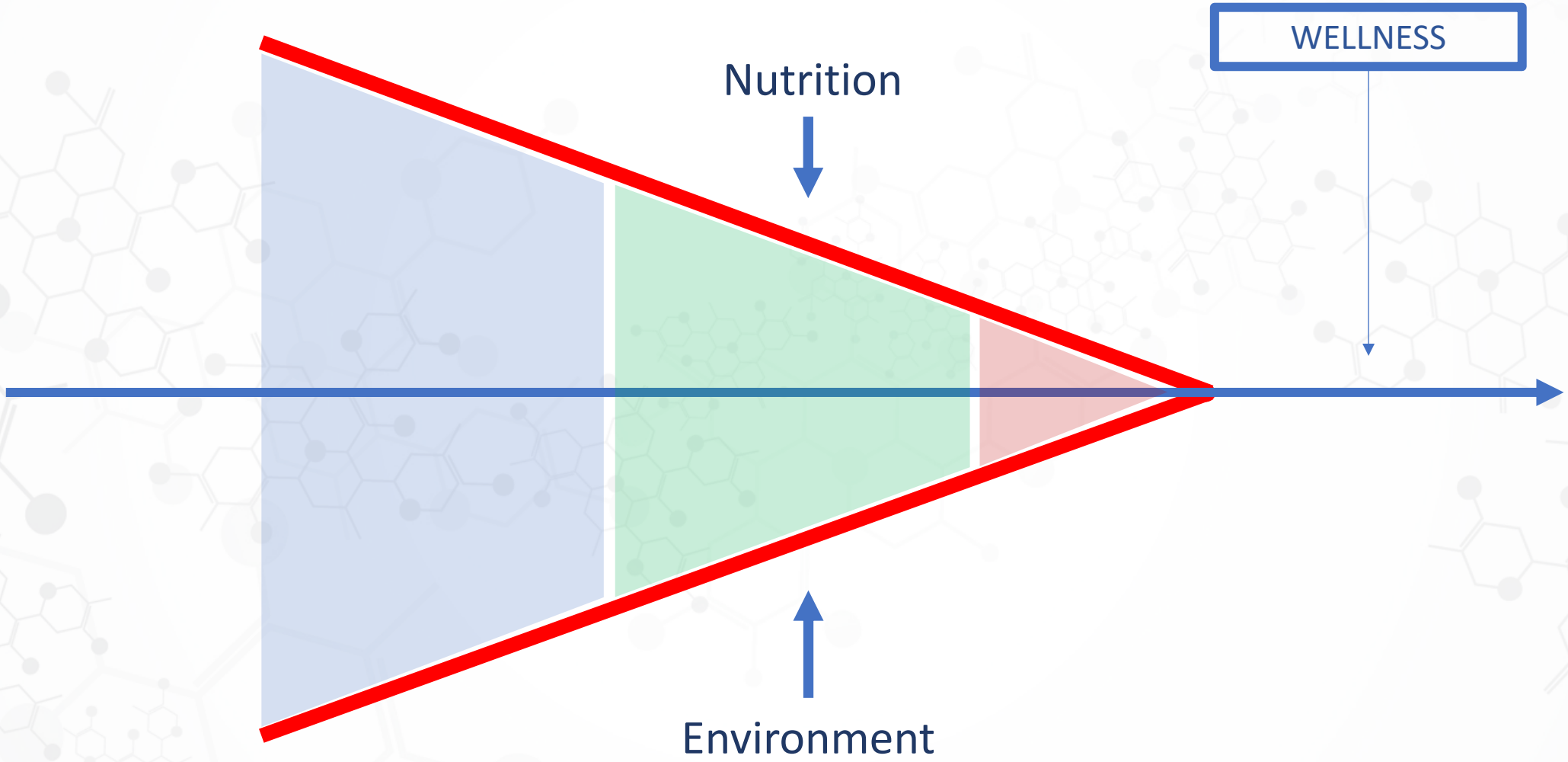
At the site of cell injury or tissue damage, the cells are replaced by the same cell type or with fibrous tissue after the clearance of the inflammatory response. The kidneys have an intrinsic capacity to repair cell death by the de-differentiation and proliferation of tubular epithelial cells. Failure of these processes results in fibrosis during infarction/ischemia or toxic insult (78, 79). Renal fibrosis is a prominent feature of every stage of CKD where an excessive accumulation and deposition of ECM are observed. At the beginning of inflammatory response in interstitium, infiltrates of macrophage population can be observed, which links inversely with the kidney function (80), that could be either deleterious (M1 macrophages) or advantageous (M2 macrophages). This is followed by transdifferentiation of interstitial cell population to

4. Uremic Toxins

Uremic toxins

Uremic toxins are in general the waste products that accumulate in the body fluid due to dysfunction of the kidney. They are divided into small water soluble compounds, middle molecules, and protein-bound uremic compounds (116). Among protein-bound uremic toxins, para-cresol sulfate (PCS) and indoxyl sulfate (IS) are linked to the cardiovascular comorbidities (117). p-cresol, a metabolite of p-cresol sulfate showed reduced contraction rates of cardiomyocytes, resulting in the irregular beating mediated by protein kinase C (PKC) by increasing the intracellular calcium levels (118). Furthermore, p-cresol is involved in the increased endothelial micro-particle shedding mediated by Rho-kinase in hemodialysis patients, leading to endothelial dysfunction, which is also observed in acute coronary syndromes, acute ischemic stroke, and venous thromboembolism (119–122).

Protocols



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