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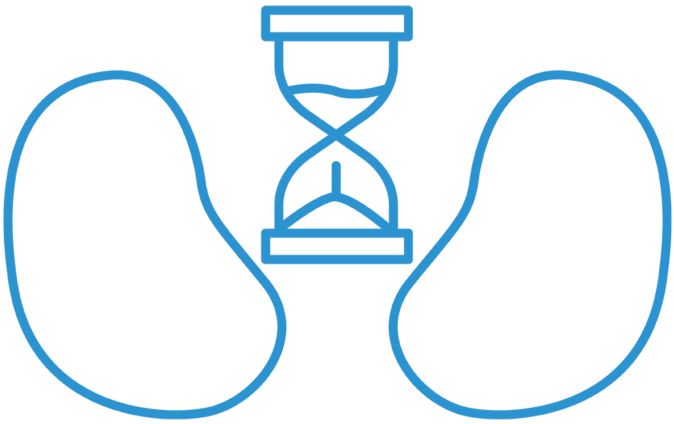

# Chronic Kidney Disease

drip 2

version 1

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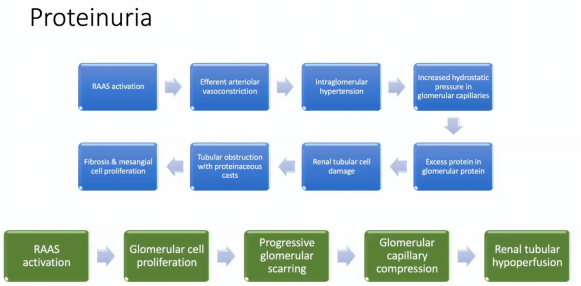
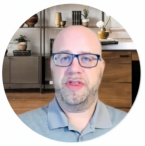



Proteinuria is very important in chronic kidney disease. We don't want it. And the reason that it's important is twofold, and it has to do with the different effects of activation of that RAAS system. The classic issue with RAAS system activation is, you get the efferent arteriolar vasoconstriction. So that backs things up at the level of the glomeruli.

So the pressure within those glomeruli increase. So hydrostatic pressure goes up, the glomerular capillaries are not happy at all. And so now, we have excess leakage of glomerular protein. And renal tubular cells don't like that. They can even become obstructed with proteinaceous casts. And when that happens, fibrosis sets in, and the mesangial cells begin to proliferate.

Besides mesangial cells proliferating because of RAAS activation, so do glomerular cells. And when that happens, we end up getting scarring in that region, and the capillaries end up getting smushed around the glomeruli. And now, those renal tubules aren't getting their typical blood supply. And those renal tubules will be damaged as a result of that hypoperfusion.



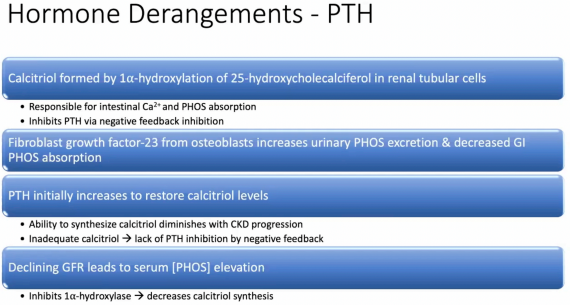
Hormone Derangements - Anemia

- Erythropoietin synthesized in inner cortex & outer medullar
  - Reduced in patients with CKD
- Anemia may contribute to CKD progression
  - Decreased renal blood flow → oxidative stress → decreased oxygen diffusion → induction of fibrosis
- Classic anemia: normochromic, normocytic, non-regenerative

We are all familiar with the fact that erythropoietin is synthesized in the inner cortex and the outer medulla of the kidneys. And so that capacity for erythropoietin production decreases with the progression of chronic kidney disease. And the anemia itself is very common in later stages of chronic kidney disease may contribute to CKD progression.

So it's this vicious cycle. Nephron loss, loss of functional kidney tissue contributes to the development of anemia through erythropoietin loss, but that anemia can contribute to the progression of chronic kidney disease through things like oxidative stress and, ultimately, the induction of scar tissue or fibrosis.

What’s the classic anemia for patients with chronic kidney disease? It is normochromic, normocytic, and non-regenerative, and that's because erythropoietin is not being secreted by the kidneys to travel to the bone marrow to stimulate effective or appropriate erythropoiesis.




Parathyroid hormone tends to be forgotten in chronic kidney disease, but it plays a meaningful role. Calcitriol is a very important hormone formed by a hydroxylation process of a cholecalciferol entity in renal tubules. And the reason we like calcitriol is that that is responsible for the intestines absorbing phosphorus and calcium. And calcitriol, through a negative feedback inhibition, also inhibits parathyroid hormone or PTH.

We're learning a lot more about Fibroblast Growth Factor 23 in terms of urinary phosphorus excretion and decreased GI phosphorus absorption. And this may become a value that we more routinely measure. Right now, it's experimental, but I wanted to measure it. I wanted to mention it, excuse me, as it relates to this process because I have a feeling that we're going to start seeing more about FGF-23 as it relates to chronic kidney disease in the near future.

Well, because the kidneys lose the ability to form calcitriol, PTH says, I'm going to increase so that I can help to restore those calcitriol levels. But the ability to make calcitriol continues to go down as the function of renal tubules or the sheer absolute number of renal tubules decreases.

So we get to a threshold where we don't have enough calcitriol. PTH is up, but we're not getting any calcitriol. Oh wait, calcitriol typically has a negative feedback inhibition on PTH secretion, but now there's not enough calcitriol. So PTH is going to be produced uninhibited.

We also are well aware that as glomerular filtration or GFR declines, serum phosphorus levels elevate. Well, it just so happens that our lovely friend phosphorus inhibits that hydroxylase reaction responsible for calcitriol synthesis in the first place, which is one of the reasons that phosphorus control, control of hyperphosphatemia as we'll talk about in treatment, is so important.