Question: What has anyone heard about Cholecalciferol? I have read that it is not a final metabolite and has been connected to Vit D toxicity in Vit D Resistant Rickets.

Response: Cholecalciferol (which is vitamin D_3) is the vitamin obtained from the **diet** or from vitamins and is the same form of Vitamin D produced in the **skin** in response to sunlight (UV radiation) **FIGURE 1**. It gets its name because it is made (synthesized) in the body by a form of cholesterol (7-Dehydrocholesterol). However, Cholecalciferol is physiologically inactive (has no biological activity) and needs to be converted to an active hormone that can then help the body to reabsorb phosphate (and calcium) from the intestine. This involves 2 steps:

1. The first step is when cholecalciferol is delivered to the liver. In the **liver**, there are enzymes that convert cholecalciferol to a new compound called 25-hydroxy-cholecalciferol (which is still inactive). It gets this new name because a hydroxyl group has been added to cholecalciferol at a carbon at position 25. It is also called 25-hydoxy-vitamin D_3.

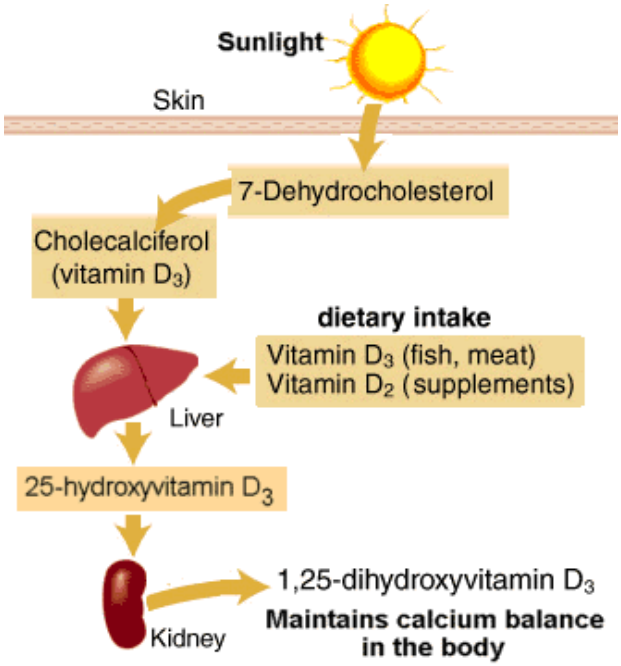
2. The final step is when 25-cholecalciferol is delivered to the **kidney** where it is then converted to 1,25-cholecalciferol. Here, another hydroxl group is added; now at the carbon at position 1. This is where we get the name 1,25 dihydroxy-cholecalciferol. It is also called 1,25 dihydroxy-vitamin D3 or Calcitriol.

Calcitriol = 1,25 dihydroxy-cholecaciferol = 1,25 dihydroxy-vitamin D_3

Now, this is the active form of Vitamin D. Its primary role is to stimulate intestinal reabsorption of phosphate (and calcium)*.

So, when you take oral cholecalciferol, it has to be converted in the liver and then the kidney to be biologically active to form 1,25 dihydroxy-cholecaciferol. The problem with patients with XLH is that the final step in the kidneys is suppressed, so 25-cholecalciferol delivered from the liver cannot be converted to 1,25 dihydroxy-cholecaciferol. This is why patients are treated directly with calcitriol (1,25 dihydroxy-cholecaciferol).

FIGURE 1



*Vitamin D also affects phosphate and calcium resorption from bone and, in the kidney, it also decreases the excretion (loss) of phosphate and calcium into the urine.

In terms of toxicity, the most commonly reported problem is nephrocalcinosis and calcification of soft tissues. This is an intrinsic problem for all therapies using vitamin D because it also stimulates calcium reabsorption. This, as well as other important reasons, is why your clinician should closely monitor treatment.

On a footnote, shown if Figure 1, oral Vitamin D can also come in another form called Vitamin D_2. Both increase levels of 25-hydroxy-cholecalciferol.