Snakes in the Grass

A critique of “Vitamin D: Bioenergetic Wunderkind or Arbiter of Doom?” by Danny Roddy

Warning, this is very long. The blue font text is taken from the paper, not to be confused with hypertext URL links that are also blue.

I committed to critiquing this piece in a Facebook post but I also said it would be the last time I would deal with any works from the Ray Peat followers who choose to attack me with the goal of proving me wrong and themselves right. There’s nothing worse than a rigid right fighter. These folks are dangerous to begin with but when they are masquerading as health advocates for sick people, which can prove deadly! Sick people need advocates for many reasons. Many lack the knowledge to research let alone sort out fact from fiction. Others have extreme fatigue, and many suffer from severe “brain fog.” The last thing these people need is to run into a charlatan that will literally lie to them in order to maintain the position of “being right.” This is exactly what you find in this piece of work I am critiquing if you take the time to drill down and follow through examining its content.

I began my critique by simply looking at the content and writing general comments about it. I will still include this but based upon what I discovered next I won’t being doing as full of a critique as I originally intended. You see, it goes beyond needing to educate and share science here. It is clearly impossible to make headway with this individual and you will see the why of it in the introduction below. After writing the cursory review I mention above, I decided to look deeper into one section I knew lacked any scientific merit, that 25D lowered 1,25D. On its face this is a ludicrous position to take. It would be like saying if you bring home flour it will eliminate bread from the house. (Flour being a substrate for bread like 25D is for 1,25D.) If you were to suggest the 25D stopped becoming bread and the bread slowly got used up that would at least be plausible, but the direct affect insinuation is absurd.

Below is the section I looked at next. The paper is linked below it.

25-D Lowers 1,25-D

“...With high dose cholecalciferol therapy... PTH is physiologically down-regulated and therefore the synthesis of 1,25-D and dietary calcium absorption are reduced.” — Vaidya, et al. (2015)

The Renin-Angiotensin-Aldosterone System and Calcium-Regulatory Hormones (nih.gov)

Naturally, I wanted to read the cited paper and initially I didn't notice his use of … in the citation. An ellipsis (…) is a set of three periods or dots in a row. In formal writing, it is used to indicate omitted text in a quotation. I haven't ever done this myself and it's not something I expected.

I retrieved the paper and I immediately saw why he did this. It made him right, by lies of omission, and me wrong which was his goal. He also changed the scientific realty to hide the true hypercalcemia axis which is calcium/PTH/1,25D. This is a well-known axis which is unfortunately overlooked by most medical practitioners today with the increased focus on the fake 25D deficiency due to the increased serum goal implemented in 2010.

Let's look at the entire paragraph and I will highlight the part he cherry picked to cite which resulted in a completely different statement that fit his agenda:

"Beyond large and longer trials, it is important to remember and consider that "vitamin D" is not a single metabolite, rather is colloquially used to refer to a complex hormone system that includes several important players, each requiring metabolism and regulation at different steps. One factor complicating this physiologic relationship is the fact that 25(OH)D has low affinity for the VDR when compared to 1,25(OH)2D, yet most vitamin D interventions in research and clinical settings use vitamin D3 to raise 25(OH)D levels. However, the continued conversion to the active VDR agonist 1,25(OH)2D by sheer substrate abundance may be down-regulated depending on other pertinent variables. For example, **with high dose vitamin D3 therapy** that increases serum calcium and 1,25(OH)2D, **parathyroid hormone is physiologically down-regulated and therefore the synthesis of 1,25(OH)2D and dietary calcium absorption are reduced.** In this scenario, normal physiology "buffers" the effect of sustained and chronic vitamin D3 supplementation until the elevations in 25(OH)D exceed this buffering capacity and create a substrate-driven PTH-independent augmentation of 1,25(OH)2D. Although circulating concentrations of these vitamin D metabolites may correlate with or dictate downstream biologic effect, it is well recognized that binding protein concentrations and genetic polymorphisms in the infrastructure governing this pathway play crucial roles in inter-individual responses to vitamin D therapy. Powe et al. demonstrated that black Americans had significantly lower 25(OH)D and vitamin D-binding protein concentrations when compared to white Americans; however, they had similar bioavailable 25(OH)D concentrations as a result (104, 105). This study points out a major weakness in the reliance on a circulating blood level of 25(OH)D to determine vitamin D status and correlations with downstream biologic activity. In most research studies that assess vitamin D interventions, the assessment of binding protein concentrations, bioavailable 25(OH)D, or 1,25(OH)2D to assess active metabolite levels, is not performed or considered."

Absolute dishonesty

Now I will highlight in green what supports my position and/or destroys his.

"Beyond large and longer trials, it is important to remember and consider that "vitamin D" is not a single metabolite, rather is colloquially used to refer to a complex hormone system that includes several important players, each requiring metabolism and regulation at different steps. One factor complicating this physiologic relationship is the fact that 25(OH)D has low affinity for the VDR when compared to 1,25(OH)2D, yet most vitamin D interventions in research and clinical settings use vitamin D3 to raise 25(OH)D levels. However, the continued conversion to the active VDR agonist 1,25(OH)2D by sheer substrate abundance may be down-regulated depending on other pertinent variables. For example, with

high dose vitamin D3 therapy that increases serum calcium and 1,25(OH)2D, parathyroid hormone is physiologically down-regulated and therefore the synthesis of 1,25(OH)2D and dietary calcium absorption are reduced. In this scenario, normal physiology "buffers" the effect of sustained and chronic vitamin D3 supplementation until the elevations in 25(OH)D exceed this buffering capacity and create a substrate-driven PTH-independent augmentation of 1,25(OH)2D. Although circulating concentrations of these vitamin D metabolites may correlate with or dictate downstream biologic effect, it is well recognized that binding protein concentrations and genetic polymorphisms in the infrastructure governing this pathway play crucial roles in inter-individual responses to vitamin D therapy. Powe et al. demonstrated that black Americans had significantly lower 25(OH)D and vitamin D-binding protein concentrations when compared to white Americans; however, they had similar bioavailable 25(OH)D concentrations as a result (104, 105). This study points out a major weakness in the reliance on a circulating blood level of 25(OH)D to determine vitamin D status and correlations with downstream biologic activity. In most research studies that assess vitamin D interventions, the assessment of binding protein concentrations, bioavailable 25(OH)D, or 1,25(OH)2D to assess active metabolite levels, is not performed or considered."

Now let's look more at this paper to show it had nothing to do with 25D controlling PTH.

INTRODUCTION

"Parathyroid hormone (PTH) and vitamin D are calcium-regulatory hormones that play a crucial role in skeletal health(4-6). PTH plays several key roles, including: 1) raising circulating calcium by mobilizing calcium from skeletal reservoirs; 2) promoting the 1-alpha-hydroxylation of 25-hydroxyvitamin D (25[OH]D); 3) indirectly increasing intestinal calcium absorption (via vitamin D receptor activation); 4) and increasing renal calcium absorption. Elevations in circulating calcium, in turn, negatively regulate PTH and synthesis of 1,25-dihydroxyvitamin D ($1,25[OH]_2D$). In addition to these known physiologic roles of PTH and vitamin D, high PTH and low vitamin D have been repeatedly associated with cardiovascular disease and mortality (7-15), although consistent and conclusive evidence from intervention studies to support these observations have yet to be reported.

The above section is talking about the Calcium/PTH/1,25D hypercalcemia axis. It also makes clear that calcium may be pulled from bone which is something I've been warning folks about as it relates to "vitamin D induced osteoporosis", that I call "non-lethal human rodenticide." It is the same biological action that kills rodents.

I looked at the studies cited to support: "…low vitamin D have been repeatedly associated with cardiovascular disease and mortality (7-15)". I want to make it clear what these papers are really showing us when they use 25D as the marker for deficiency by putting them in context for you. You will see it was worth the effort by the authors own admission in citation #14 as well as in the paragraph I shared in its entirety above that was selectively cited by Danny to alter its meaning and intent.

Citations #7 and #8 are about the PTH level, no mention of "vitamin D"

Citation #9 was a study involving Black people in winter and was 25D and looked at blood pressure in 250 individuals.

Citation #10 is about the J shaped all-cause mortality curve as it relates to serum 25D levels.

“Large population and clinical studies have implicated poor vitamin D status as a potential risk factor for a number of chronic and infectious diseases (1, 2). Moreover, several studies have found a nonmonotonic association between vitamin D status (3–8), as measured by circulating levels of serum total 25-hydroxyvitamin D (25[OH]D), and all-cause mortality (1, 2). The shape of this association appears to be asymmetric and in a reverse J-shape, with a clear upturn in the risk of death from all causes at low concentrations of 25(OH)D and possibly a shallow increase in the risk of death with higher serum 25(OH)D levels.”

“Conclusions:

A reverse J-shaped association between serum 25(OH)D and all-cause mortality appears to be real. It is uncertain whether the association is causal.”

I have posted at length and shared several papers showing that low 25D is a marker for illness and that they never measure the active form when calling these folks deficient.

Citation #11: “**Authors' conclusions:** Vitamin D3 seemed to decrease mortality in elderly people living independently or in institutional care.”

I’ve addressed the usage of the unscientific term “seem” numerous times.

Citation #12 Another J shaped curve for all-cause mortality as it relates to serum 25D levels.

“Conclusion: In this study from the general practice sector, a reverse J-shaped relation between the serum level of 25(OH)D and all-cause mortality was observed, indicating not only a lower limit but also an upper limit. The lowest mortality risk was at 50-60 nmol/liter. The study did not allow inference of causality, and further studies are needed to elucidate a possible causal relationship between 25(OH)D levels, especially higher levels, and mortality.” For context 50 nmol = 20 ng/ml and 60 nmol = 24 ng/ml. This falls in the insufficient category as it relates to the 2010 raised serum goal of 30+ ng/ml.

Citation #13 is the same author as the paper this piece began with, Vaidya.

Vitamin D and the RAS (renin-angiotensin system)

“Dietary sodium and increased activity of the RAS are known to contribute to hypertension; salt restriction and inhibition of RAS activity reduce blood pressure.[3–5] Li et al[6] provided convincing support for vitamin D as a proximal inhibitor of the RAS when they described a phenotype of excess plasma renin activity and hypertension in mice lacking the vitamin D receptor, which normalized after treatment with RAS antagonists. These vitamin D receptor–null mice also displayed an increased susceptibility to obstructive renal injury that could be prevented with RAS antagonism.[7] Mice with deficient 1α-hydroxylase activity were also found to have increased plasma renin activity and hypertension, and this unfavorable phenotype could be reversed with 1,25-dihydroxyvitamin D ($1,25[OH]_2D$).[8] Their collective experiments indicated that vitamin D may inhibit the RAS by reducing renin gene expression.[9]”

Please notice how the above issue was corrected by administering 1,25D.

Citation #14 Again, the original author I began with here, Vaidya.

“Introduction:

Vitamin D has long been known to be an important factor for normal calcium metabolism and skeletal health. In the past decade, resurging interest and new research has implicated vitamin D deficiency as a potential contributor to the pathophysiology of many extra-skeletal conditions, including vascular diseases such as high blood pressure and kidney disease (1). Recent experimental animal and observational human studies have repeatedly suggested that supplementation with vitamin D metabolites may lower the risk for hypertension and kidney injury, but definitive human trials favoring the adoption of vitamin D therapy for the primary or secondary prevention of these conditions are still pending.

One of the many challenges in evaluating the biologic role of vitamin D in influencing blood pressure and renal function is deciphering which circulating vitamin D metabolites to measure in cross-sectional studies (ie - 25-hydroxyvitamin D or 1,25-dihydroxyvitamin D) and what forms of vitamin D therapy to use for interventional studies (oral vitamin D_2, oral vitamin D_3, oral vitamin D receptor agonist, or ultraviolet radiation to promote cutaneous synthesis). **The typical clinical barometer of human vitamin D status is 25-hydroxyvitamin D_3 (25[OH]D), which is converted to the active vitamin D metabolite 1,25-dihydroxyvitamin D_3 ($1,25[OH]_2D$) in a tightly regulated manner by the 1-alpha-hydroxylase enzyme. Although 25(OH)D is a stable steroid metabolite in blood, and is easier to quantify and interpret than $1,25(OH)_2D$, it is $1,25(OH)_2D$ and not 25(OH)D that activates the vitamin D receptor (VDR) at the end-organ level. Thus, observational studies that measure 25(OH)D as a marker of overall vitamin D status may not always represent the full scope of biologic action. Moreover, the inferences drawn from trials that provide conventional over-the-counter vitamin D_2 or D_3 supplements, might differ from those drawn from trials that bypass the tightly regulated 1-alpha-hydroxylase reaction and provide $1,25(OH)_2D$ (or other VDR agonists) to illicit end-organ effects."**

Notice, as always, more trials are needed to sort this out as we remain fortified with Secosteroid Hormone D. Everything I bolded is damning to the Danny paper. Tightly regulated 1,25D, activates the VDR, NOT 25D, and that we may be looking at the wrong molecule. It's just the "typical barometer of human vitamin D status," more stable in blood, which is half-life related anyway.

Citation #15 Again the author is citing their OWN prior work.

"**Conclusion:**

Animal studies implicate vitamin D receptor agonist therapy to lower RAS activity as a potential method to reduce the risk of hypertension, kidney disease, and diabetes. There is a need for more well designed prospective interventional studies to validate this hypothesis in human clinical outcomes."

More studies needed to validate a HYPOTHESIS.

Citation #16. Although I didn't look at the full text version this study is "Calcium-phosphate levels and cardiovascular disease in community-dwelling adults: the Atherosclerosis Risk in Communities (ARIC) Study" and I didn't see any mention of vitamin D in the abstract. If these are the citations for "low vitamin D have been repeatedly associated with cardiovascular disease and mortality (7-15)", one would expect the abstract to contain information about "vitamin D".

Citation #17. Sorry if this is painful but this paper is the one Danny lied over its content, so I wanted to dig deep into the real paper and what it was calling "low vitamin D" to see if any of these papers even looked at 1,25D and I found a lot of support for the importance of 1,25D being checked within these

works cited even though none of the papers actually did! I won't bore you with drilling down into citations again, this one mattered because it's the one Danny decided to manipulate the content of to be right regardless of what the facts were.

Back to the original paper now.

THE RAAS (Renin-Angiotensin-Aldosterone System) AND VITAMIN D

"The conversion of 25(OH)D to the active metabolite and vitamin D receptor (VDR) agonist 1,25$(OH)_2$D is a process governed by PTH."

This makes clear that the ACTIVE metabolite is 1,25D. Notice this doesn't say that 25D is influencing PTH, it says PTH governs the creation of the 1,25D.

I will limit myself to the following large section of the paper and direct your attention to what I have bolded and spare you the interpretation. I think directing you to these parts is enough. This section includes a repeat of the paragraph Danny selectively cited from but sharing the parts before and after offer context for the paper as a whole.

"THE RAAS AND VITAMIN D

The conversion of 25(OH)D to the active metabolite and vitamin D receptor (VDR) agonist 1,25$(OH)_2$D is a process governed by PTH(4), yet vitamin D may have independent influences on the RAAS. Low vitamin D status has been **associated** with clinical outcomes that are also traditionally associated with excess RAAS activity, including hypertension, inflammation, and cardiovascular disease(13-15, 86). Animal studies and human genetic association studies have provided mechanistic support for these observations; however, **conflicting data exist, and there is a strong need for large-scale randomized studies to confirm the influence of vitamin D therapy on the RAAS and RAAS-mediated clinical outcomes.**

Animal studies (mice) have shown that the 1**,25$(OH)_2$D-VDR complex negatively regulates renin expression**, and that this vitamin D-induced reduction in RAAS activity can prevent adverse vascular outcomes to a similar extent induced by pharmacologic angiotensin-receptor antagonism(15, 87-93). Human studies have supported this **theory**, demonstrating that low circulating vitamin D concentrations are **associated** with higher plasma renin activity and angiotensin II concentrations(86, 94, 95), and that **vitamin D deficiency is associated with higher RAAS** activity that can be lowered following intervention with vitamin D_3 therapy(72, 94, 96). Extrapolation of these results suggests that vitamin D therapy **might** serve to lower RAAS activity and improve complications associated with excess RAAS activity such as hypertension, nephropathy, and insulin resisitance(15).

To date, there have been mostly unimpressive or negative results from human interventional studies. Many human vitamin D intervention studies have focused on blood pressure or albuminuria as primary outcomes, and since both of these outcomes are related to excessive RAAS activity, these studies are particularly interesting to the topic of this review. One recent randomized study showed that reasonably high doses of vitamin D_3 therapy over 3 months modestly lowered systolic blood pressure in blacks(9). In addition, morbidly obese individuals with vitamin D deficiency have been reported to have modest reductions in mean arterial pressure following 1 month of very high-dose vitamin D_3 therapy, and this phenomenon was associated with reductions in the local vascular-tissue renin-angiotensin

system(72). De Zeeuw *et al.*, Larsen *et al*., and Joergensen *et al*. have shown that paracalcitol therapy, a VDR agonist, can lower albuminuria in advanced chronic kidney disease with or without diabetes; however, whether this effect is attributable to RAAS activity reduction remains to be proved(14, 97-99).

In contrast, a number of well-conducted intervention studies have found no effect of vitamin D therapy on blood pressure. **Recently, Scragg *et al*. and Witham *et al*., in combination with several other small and short-term vitamin D_3 intervention studies(13, 14), have mostly reported no blood pressure lowering effect associated with vitamin D_3 therapy for time durations of 1 year and longer**(100, 101). **Perhaps the most notable vitamin D_3 intervention study to examine blood pressure lowering effects to date is the DAYLIGHT study. In this double-blinded, randomized, multi-center trial, including 534 individuals with stage I hypertension, 4,000 IU of daily vitamin D_3 for 6 months did not affect the mean 24-hour systolic blood pressure (primary endpoint) when compared to 400 IU of daily vitamin D_3**(102).

These contradictory human intervention studies raise doubt about the consistency of observations, or at a minimum, the relevance of vitamin D therapy related to blood pressure lowering and cardiovascular outcomes. At the very least, it can be concluded that vitamin D3 therapy in durations of 3-12 months does not dramatically lower blood pressure akin to pharmacologic anti-hypertensives; however, long-term studies are lacking. It should be noted that except for the DAYLIGHT study, none of these studies was particularly large, and on the same token none of these studies (including the DAYLIGHT study) were particularly long in duration; therefore**, larger and longer population-based interventional studies with more refined effect detection will be needed to satisfactorily determine whether vitamin D therapies can definitively modulate clinical outcomes related to excessive RAAS activity. Perhaps the best candidate for such a large study is the currently on-going VITAL study**(103).

Beyond large and longer trials, it is important to remember and consider that "vitamin D" is not a single metabolite, rather is colloquially used to refer to a complex hormone system that includes several important players, each requiring metabolism and regulation at different steps. One factor complicating this physiologic relationship is the fact that 25(OH)D has low affinity for the VDR when compared to $1,25(OH)_2D$, yet most vitamin D interventions in research and clinical settings use vitamin D_3 to raise 25(OH)D levels. However, the continued conversion to the active VDR agonist $1,25(OH)_2D$ by sheer substrate abundance may be down regulated depending on other pertinent variables. For example, with high dose vitamin D_3 therapy that increases serum calcium and $1,25(OH)_2D$, parathyroid hormone is physiologically down-regulated and therefore the synthesis of $1,25(OH)_2D$ and dietary calcium absorption are reduced. In this scenario, normal physiology "buffers" the effect of sustained and chronic vitamin D_3 supplementation until the elevations in 25(OH)D exceed this buffering capacity and create a substrate-driven PTH-independent augmentation of $1,25(OH)_2D$. Although circulating concentrations of these vitamin D metabolites may correlate with or dictate downstream biologic effect, it is well recognized that binding protein concentrations and genetic polymorphisms in the infrastructure governing this pathway play crucial roles in inter-individual responses to vitamin D therapy. Powe *et al*. demonstrated that black Americans had significantly lower 25(OH)D and vitamin D-binding protein concentrations when compared to white Americans; however, they had similar bioavailable 25(OH)D concentrations as a result(104, 105). This study points out a major weakness in the reliance on a circulating blood level of 25(OH)D to determine vitamin D status and correlations with downstream biologic activity. In most research studies that assess vitamin D interventions, the

assessment of binding protein concentrations, bioavailable 25(OH)D, or 1,25(OH)$_2$D to assess active metabolite levels, is not performed or considered."

The very last piece is vitally important!!!!!

Since this paper was published the VITAL study was conducted so I will share the information I gathered after its conclusion.

"From my perspective as an endocrine fellow, VITAL has made my job in clinic a bit easier. Now, at least to the best of our current knowledge, I can tell patients that the evidence indicates that vitamin D supplementation is not useful for the primary prevention of cardiovascular disease or cancer."

https://resident360.nejm.org/from-pages-to-practice/vitamin-d-supplements-and-prevention-of-cancer-and-cardiovascular-disease

D-Flating news

VITAL trial results were released in November in Chicago at the American Heart Association's annual scientific sessions and published in the New England Journal of Medicine. Fish oil supplements offered some benefits, preventing heart attacks, but not stroke. Extra vitamin D offered no heart protection (SN: 12/8/18, p. 9).

The VITAL results were the latest of a string of largely discouraging news. In 2017, scientists had reported the results of a study testing whether monthly high doses of vitamin D could prevent heart problems. About 5,000 people from the general population of New Zealand were randomly assigned to receive the vitamin D boost or a placebo. In JAMA Cardiology, the researchers reported that supplementation made no difference.

As a safeguard against bone fractures, vitamin D has not fared much better. Because the vitamin is necessary for bone health, many doctors recommend supplements for older people to help prevent breaks and falls. Yet the U.S. Preventive Services Task Force concluded last spring that the evidence for this advice was still inconclusive. Another blow came in October, when researchers reported in Lancet Diabetes and Endocrinology that a review and summary of studies so far "suggest that vitamin D supplementation does not prevent fractures or falls, or have clinically meaningful effects on bone mineral density."

https://www.sciencenews.org/article/vitamin-d-supplements-lose-luster?linkId=63205492

Now I will switch to my review of Danny's paper I did before I began reviewing the paper Danny manipulated to fit his agenda.

His paper never addresses how vitamin A is necessary for the 1,25D to create VDRE's when the VDR's and RXR's heterodimerize and enter the cell's nucleus. Vitamin D response elements are the chemical and biological warriors made after they are requested by the body.

Additionally, the work cited lacks data sets for 1,25D along with the 25D. It's all associations. That is all you can create using molecules with ZERO biological activity.

Now moving to the paper in the order it's presented.

"*For myself, I use liquid vitamin D made from lanolin only on my skin.* ***So, again, I'm not defending all the shitty vitamin D supplements out there***."

So where are the papers about topical use of D that support this?

"*This article is primarily about defending vitamin D against the laughable incoherent hyperbole that has developed over the last year or so ('vitamin D is as bad as fish oil and will calcify you')*."

Where is the information showing any of my work to be incoherent?

What aspect are you defending as well? That all the accolades belong to 1,25D, which is mentioned but never overcome. That there are at least fourteen distinctly different molecules of 25D and we measure only two? That serum isn't storage for fat solubles? Did you actually defend the use of topical D?

I have created a list of hurdles to compartmentalize the issues to help guide folks in learning about vitamin D. These would have helped him understand my position. And let's be clear, it's me he is after.

1. It harms. Starts in the womb. Kids make non-calcemic analogues from oral inputs.

2. Harms adults.

3. We're not low. Wrong molecule, wrong location-serum. No true test. A true test may reveal there's not even a 25D deficiency compared to the goal. Hard to say.

4. The sick are high in the active form, 1,25(Oh)2D3. Dihydroxy vitamin D.

5. The pathogens have evolved to block the action of vitamin D via ligands that occupy the VDR's.

6. Excess active D wreaks havoc on other nuclear receptor systems like thyroid, adrenal, and glucocorticoid.

7. You exhaust your ability to build bone in old age.

8. We're focused on the wrong molecules and pathway.

9. Distinct differences in oral versus UVB created D analogues as well as the carriers utilized.

10. Most are unaware there are two forms of the VDR and "cross talk."

11. We're promoting cancer. The feedbacks employed to breakdown/reduce 1,25D are oncogenic in nature/action.

12. We're avoiding the anticancer molecules by avoiding sun.

13. Dark Skin Myth.

14. We're focused on the wrong receptors.

"*The third important thing is that I'm addressing these points of contention from a* ***bioenergetic point of view"***.

How much of the paper actually did this? *"The organizing power of energy flow is* ***hypothesized*** *to be the origin of biological complexity and its decline the basis of "complex" diseases and aging..."*

Notice this is a hypothesis.

"I'm unaware of the context for health and disease of various anti-vitamin D people are on the internet…"

This sentence doesn't make sense first of all, but it shows that he's overlooked the vast majority of my work. Simply look at the emails I sent Georgi.

First email:

I appreciate your effort in your response but I'm not going to take the time to read very much of it. I've been researching it myself for almost 2 decades and unfortunately, and don't take this wrong, most people only have a vocabulary a couple molecules deep. The fact that you view the active form, and it is the active form, as bad it's kind of unbelievable. This is the form that is responsible for the slow genomic response that we are taking a vitamin D for.

Anyone trying to build a model around a molecule with the seasonal variation is very naïve and is feeding into the fake deficiency model of mainstream medicine today. I have agreed to stay out of the Ray Peat groups as if they were vitamin D deficiency groups.

You clearly haven't looked at any of the evidence of harm. I wish you luck, we have known for decades that the active form is in control of PTH and vice versa. You're feeding into the increased goal implemented in 2010.

You should research hormone imprinting. What we're doing to the children in the womb is disgusting.

Email #2:

The other thing I would add is you talked about a slow metabolism causing the low 25D. That's an oversight on your part because you can't have high 125D without it first passing through the 25D, therefore you had ample energy.

Email #3

I apologize, I will make this the last one, but I forgot to say something. You don't realize that the active form of vitamin D is the molecule of immune response. That's what drives it. I don't know how you think it appears but that's how and why it appears. That's why we turn to a vitamin D for our immune system, it's that molecule that all the accolades belong to. I know you think that the other one activates The VDR but go ahead and send me a paper that shows it does biological activity. One thing that will happen if you get your serum over 100, it will trigger bone resorption which is normally not its job. That's why it's a great rodenticide, resulting in osteoporosis in most people today.

I did send one more response.

Email #4:

You're welcome.

You know pregnenolone, I listened to you talk about it.

These aren't THE molecules. The cyp24a1 enzyme and FGF23 (Both involved with breaking down 1,25D and in the case of my concerns excess 1,25D) are both oncogenic in nature.

Look at cholesterol side-chain cleavage enzyme, the Cyp11A1 alternative pathway.

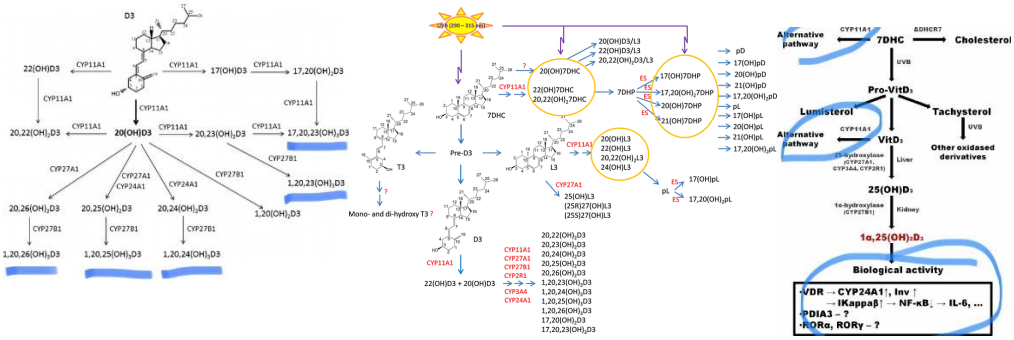
You're kinda looking at it. Now look at the vitamin D analogues it makes for the RORs. The orphaned retinoid eceptors. You will be at the heart of steroidogenesis like you know, but now you're looking at the glucose and circadian rhythm control as well. Tied to the suprachiasmatic nuclei (SCN).

In the one image the underlined molecules are trihydroxy vitamin D level molecules.

The second photo lacks any oral inputs of D2, they would have a distinctly different pathway.

There are two forms of the VDR's. Membrane and Nuclear. Membrane VDR's love nutritional ligands like curcumin. You should research it.

The ROR's membrane version is called cytoplasmic.



The Anti-Vitamin D Argument Steelman "*As I understand the basic argument, it goes a little something like this:*

There's a basic argument and you think you are able to capture it? Where did this come from??

"Vitamin D3 or cholecalciferol is converted into the non-biologically active storage form of vitamin D (calcifediol or 25-D) by the liver, which is converted again into the biologically active calcitriol (1,25-D) primarily by the kidneys."

The above statement is a well-recognized FACT.

"Since 1,25-D is barely ever measured, you could be sufficient in it already; thus, randomly supplementing with cholecalciferol to increase 25-D is risky and could cause harm."

Incorrect understanding of the basic argument here. The deficiency is never demonstrated in the active form, you are to assume it's true over falling below the man set SERUM goal which was raised, nearly tripled in 2010, and it's a serum test for a **stored** molecule. I've said this thousands of times. It's not a could type situation but this is where he needs to turn 1,25D into a bad thing in general, not over it being high. This is also where it becomes necessary for him to make it all about 25D. Additionally, this avoids the fact that low 25D is coupled with high active D and that the sick have high active D, not to

mention total denial of the necessary immune response, the pathogens, and their ability to block the action of vitamin D. This also helps dismiss them needing to look into you being sufficient since they are basically saying it's bad and you don't need it, even for the slow genomic creation of the chemical and biological warriors 1,25D creates.

1,25-D is the only form of vitamin D that activates the vitamin D receptor (VDR), which is responsible for all of vitamin D's useful biological functions. For instance, 1,25-D is essential for mounting an immune response.'

This is NEVER addressed scientifically in the paper. In fact, there's work cited that makes clear what this truly means yet no such evidence is offered to support 25D activating the VDR.

"Argument #1: "25-D is The Biologically Inactive Storage Form of Vitamin D"

"This one, in my estimation, is quite bizarre as 25-D has so many anti-stress, anti-inflammatory, and pro-mitochondrial energy effects."

The support for this will simply be associations made with the level of 25D regarding other molecules. This isn't the establishment of effects, nor is it support for "activating the VDR"

None of the work will include what is happening with 1,25D as well as 25D. There will only be discussion limited to 25D and another molecule. There's no discussion of retinol but since he's promoting 25D as the workhorse without any science the heterodimerization of the VDR/RXR is meant to be ignored to build his pseudoscience position.

"*Has been found to be*" lists are only based upon associations.

They never mention serum isn't storage. Huge piece to overlook.

25-D Lowers PTH

PTH Context: "PTH inhibited mitochondrial respiration… The reduction of oxidative phosphorylation may result in decreased ATP synthesis. These events may cause long-term adverse effects of PTH on the myocardium…" — Rodriguez, et al. (2009)

"Optimal vitamin D status, defined by estimated maximum PTH suppression, does not occur until at least 25-D levels ≥40 ng/ml [100 nmol/l]." — Ginde, et al. (2012)

"In healthy persons, the reference (normal) range for serum PTH is known to decline as serum 25-D levels increase. Therefore, the theoretical plateau in PTH, as 25-D increases, can be used as a determinant in establishing the adequacy of vitamin D status." — Muscogiuri G., et al. (2014)

Notice two out of the three papers are AFTER the goal for 25D was increased. Trying to prop up the raised level.

From the IOM report that says not to raise the goal above 20:

Measures that have been explored are the levels of serum 25OHD at which PTH levels rise as well as the level of serum 25OHD at which PTH levels no longer decline (Aloia et al., 2006a; Durazo-Arvizu et al., 2010). However, because serum PTH levels increase with age, it is not clear what level of PTH should be regarded as normal (Dawson-Hughes et al., 1997a; Vieth et al., 2003) or whether the relationship is meaningful for all age groups (Abrams et al., 2005). These studies have led some to suggest that a serum 25OHD level of 75 nmol/L is consistent with the PTH plateau point (Malabanan et al., 1998) and hence demarcates sufficiency and insufficiency for vitamin D. However, a review of the literature does not show widespread agreement on a plateau consistent with a serum 25OHD level of 75 nmol/L. In most cases, serum PTH level reaches a plateau at different levels of serum 25OHD varying between 37.5 and 125.0 nmol/L. Box 4-7 summarizes the study outcomes.

Race/ethnicity may be a factor in determining the relationship between serum 25OHD and PTH levels, although the measures used have focused on calcitriol rather than serum 25OHD concentrations. African American and dark-skinned populations have lower serum 25OHD and calcitriol levels compared with white populations (Bell, 1995, 1997). A study of more than 500 healthy women ages 20 to 80 years found that PTH and calcitriol levels were higher in black than in white women and that the black women had lower bone turnover rates compared with white women (Aloia et al., 1996b). Some evidence, however, suggests that PTH levels are similar in both populations (Benjamin et al., 2009).

“In healthy persons, the reference (normal) range for serum PTH is known to decline as serum 25-D levels increase. Therefore, the theoretical plateau in PTH, as 25-D increases, can be used as a determinant in establishing the adequacy of vitamin D status.” — Muscogiuri G., et al. (2014)BOX 4-7Studies Demonstrating PTH Plateaus at Various Serum 25OHD Levels

Serum 25OHD < 30 nmol/L:

Ooms et al. (1995a)

Serum 25OHD < 50 nmol/L:

Malabanan et al. (1998)

Levis et al. (2005)

Steingrimsdottir et al. (2005)

Aloia et al. (2006a)

Serum 25OHD < 75 nmol/L:

Vieth et al. (2003)

Holick et al. (2005)

Durazo-Arvizu et al. (2010)

Serum 25OHD ~ 88 nmol/L:

Kinyamu et al. (1998)

Serum 25OHD 100–125 nmol/L:

Krall et al. (1989)

Dawson-Hughes et al. (1997a)

No plateau:

Bates et al. (2003)

Benjamin et al. (2009)

No relationship:

Rucker et al. (2002)

Yes, those are less than symbols.

25-D Opposes Prolactin

"Cholecalciferol administered to patients with macroprolactinemia increased 25-D, reduced total prolactin and macroprolactin, as well tended to reduce PTH…" — Krysiak, et al. (2015)

"Female patients with prolactinoma have lower 25-D levels and have higher prevalence of 15-D insufficiency and deficiency among prolactinoma patients when compared with normal subjects. Also 25-D deficiency in prolactinoma patients associated with larger adenoma size and higher prolactin level." — Aboelnaga, et al. (2017)

This hinges on the deficiency but folks are given D3. It's not tracked to even see if it becomes 25D.

25-D Lowers Aldosterone

"The findings indicate that cholecalciferol supplementation significantly decreases [plasma aldosterone concentration] in patients with arterial hypertension and 25-D insufficiency." — Grübler, et al. (2016)

"Cholecalciferol repletion decreases aldosterone in patients with heart failure and low serum 25-D." — Boxer, et al. (2014)

"The co-existence of 25-D deficiency and elevated levels of aldosterone in benign prostate hyperplasia, presented for the first time in literature, strongly favors a link between the renin-angiotensin-aldosterone system, vitamin D and benign prostate hyperplasia pathogenesis." — Yalçınkaya, et al. (2014)

Again, giving D3 without tracking it, hinges on being deficient, and never says what the 1,25D is.

25-D Opposes Cortisol

"…In the present investigation we further confirmed the importance of sufficient 25-D availability in maintaining proper function of hepatic cells in normal and diseased conditions. It has been demonstrated that prednisolone-induced oxidative/nitrosative stress and liver injury may be related to established inadequate circulating level of 25-D, because prohormone repletion after cholecalciferol treatment

resulted in partial or complete normalization of the most detrimental alterations associated with glucocorticoid hepatotoxicity." — Lisakovska, et al. (2016)

You can go one by one, and they all unravel. Plus, they say 25D everywhere, but the tests only pick up two of at least fourteen distinctly different molecules of 25D. What about the other 12??? Were they low? And again, that's just serum. It's the STORAGE molecule and serum isn't storage for fat solubles. Basic biology.

C. Hepatic 25-Hydroxylation

"Vitamin D does not circulate for long in the bloodstream but, instead, is immediately taken up by adipose tissue for storage or liver for further metabolism. In humans, tissue storage of vitamin D can last for months or even years."

www.physiology.org/doi/full/10.1152/physrev.1998.78.4.1193

We don't drink salmon blood; we eat the flesh. Think about where D is stored.

The Role of Skeletal Muscle in Maintaining Vitamin D Status in Winter

Because of seasonal variation in intensity of solar UV light, vitamin D status falls in winter and rises in summer. It has been presumed that there is no functional store of vitamin D. Thus, to avoid deficiency, a nutritional supply would be required in winter. However, there is now evidence that the main circulating metabolite of vitamin D, 25-hydroxyvitamin D, accumulates in skeletal muscle cells, which provide a functional store during the winter months. The mechanism is mediated by muscle cell uptake of circulating vitamin D–binding protein (DBP) through a megalin-cubilin membrane transport process. DBP then binds to cytoplasmic actin to provide an array of high-affinity binding sites for 25-hydroxyvitamin D [25(OH)D]. The repeated passage of 25(OH)D into and out of muscle cells would account for its long residence time in blood.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6776467/#!po=0.694444

25-D Synergizes with Progesterone

"In this context something as simple as providing cholecalciferol supplementation could improve recovery and potentially enhance the neuroprotective benefits of progesterone (or any other) treatment." … "…Progesterone and 25-D each work through different pathways to reduce cellular injury and enhance the metabolic processes of repair…" — Cekic M., et al. (2009)

Giving D3 again. And it doesn't say they synergize. Each works through different pathways.

25-D Synergizes with Thyroid

"Our results indicated that patients with hypothyroidism suffered from hypovitaminosis D with hypocalcaemia. Moreover, the positive significant correlation between each of 25-D and calcium with thyroid hormones and that negative significant correlation with TSH levels, suggested that deficiency of serum 25-D and calcium levels were significantly associated with degree and severity of the

hypothyroidism which encourage the advisability of cholecalciferol supplementation. Screening for 25-D deficiency and serum calcium levels recommended for all hypothyroid patients." — Mackawy A., et al. (2013)

Deficiency BS again and they have a condition in the first place. What was 1,25D??

1,25-D Increases Prolactin:

"The results confirm the stimulating action of 1,25-D on prolactin secretion in healthy women..." — Zofkova, et al. (1988)

"Administration of prolactin to animals produces an increase in the 1a-hydroxylase activity and a rise in plasma 1,25-D. Consistent with a possible regulatory role of prolactin on 1,25-D biogenesis, the administration of bromocriptine, which suppresses prolactin secretion, lowers plasma 1,25-D values in lactating rats. These findings suggest prolactin-mediated modulation of 1a-hydroxylase activity..." — Rosen, et al. (1983)

"Because a high-calcium diet results in the suppression of 1,25-Dproduction, these results indicate that prolactin may require the presence of 1,25-D to exert its long-term stimulatory effect on intestinal calcium absorption…" — Charoenphandhu, et al. (2006)

"Possible" in second one "may" in third. Using nocturnal creatures, we kill with D.

Within this section he is attempting to establish 25D as an active molecule. He alleges that 25D lowers PTH and then goes on to say PTH increases other molecules. He hasn't even established 25D as active or controlling PTH but now he's moving away from 25D. Alleging what one molecule does something to another molecule and then saying what that molecule does to yet another is creating degrees of separation and doesn't support the beginning argument in the first place, that 25D is an active molecule. For example, saying 25D lowers PTH then pointing out PTH impact to prolactin but then speaking directly to 1,25D's effect on prolactin isn't accomplishing anything.

Plus looks at the diseases and conditions in his examples: macroprolactinemia, prolactinoma, arterial hypertension, heart failure, glucocorticoid hepatotoxicity, and hypothyroidism.

Most of the section also hinged on the 25D deficiency.

Argument #2: "Increasing 25-D Increases Active 1,25-D"

That's one pathway it can take but keep in mind these folks have a "vitamin D" vocabulary only 3 molecules deep.

"While viewing chemistry charts might make a person think that 1,25-D is the ultimate destination for 25-D, however, in the living organism, at physiological amounts, the 1a-hydroxylase enzyme that converts 25-D to 1,25-D tends to decrease when supplementing 25-D."

This is the section he used … to hide the truth of a citation he quoted that I began the paper with.

Again, he hasn't captured the argument at all. He is building a strawman to knock over. In the LIVING ORGANISM there are literally dozens and dozens of unique molecules of vitamin D, AND there are charts

of these as well. When you limit yourself to D3, 25D, and 1,25D this sounds great but it's actually total BS. It's important to understand the 1,25 referenced here is in control of the enzyme anyway. Notice the bulk of the argument here is a 1985 citation. Back then the serum goal was 12.5 and the RDA was 200IU. This is hilarious. The 2008 citation is speculating, just read it. *"…We speculate that the decrease in plasma 25-D….."*

1,25D is its own control, including its own production.

"1,25(OH)2D3 autoregulates the expression of the VDR gene through intronic and upstream enhancers.

The VDR is an absolute determinant of the biological activity of 1,25(OH)2D3 (1). Thus, the receptor's expression in cells is a requirement for response, and the receptor's concentration itself a key component of sensitivity to the hormone as well. While little is known of the molecular determinants of basal expression of the VDR in cells, the VDR gene is known to be regulated by a variety of hormones including PTH, retinoic acid, and the glucocorticoids (56). Perhaps most interesting is the ability of 1,25(OH)2D3 to increase the level of VDR gene expression itself.

1,25(OH)2D3 both suppresses the renal expression of Cyp27b1 (33), whose protein product is responsible for its synthesis, and induces Cyp24a1 (33, 34) whose product is responsible for its degradation to calcitroic acid. In addition to these activities, 1,25(OH)2D3 also autoregulates the expression of its own receptor gene (Figure 3), thus modulating not only levels of the ligand, but of the VDR as well (5, 35)."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2879406/

1,25-D Causes Hypercalcemia and Calcification

"Severe hypercalcemia is mainly caused by inappropriately high concentrations of compounds which promote bone resorption, in particular PTH, PTHrP, or 1,25-D." — Schmind, C. (1994)

"Replacement therapy with calcitriol… often produces hypercalcaemia… In addition, these vitamin D compounds can aggravate the hyperphosphataemia in these patients." — Brown, et al. (2002)

It's quite ironic this is used as support against me when it in fact is a huge piece of my work and the problem I am seeking to expose. THANK YOU for including this since it shows your absolute failure to capture the anti-D position in the first place. Let's not forget it's seldom measured which is another tenet of the anti-D position.

Calcium Lowers 1,25-D

"Oral calcium supplementation in these men was also accompanied by a reduction in the plasma concentration of PTH and 1,25-D…" — Lijnen, et al. (1995)

Use of … here again to hide the fact that 25D was unaffected. The rest of the sentence is included here:

"Oral calcium supplementation in these men was also accompanied by a reduction in the plasma concentration of intact parathyroid hormone and 1,25-dihydroxyvitamin D3**, an increase in 24-h urinary calcium excretion but no change in the plasma total Ca2+ concentration, serum ionized Ca2+ level and plasma phosphate or 25-hydroxyvitamin D3**."

Argument #4: "You Need The Active Form of Vitamin D to Activate The Vitamin D Receptor (VDR)"

Getting into cellular receptors is beyond my pay grade, but I will this one time.

Firstly, both 25-D and 1,25-D activate the vitamin D receptor, so this argument is a bit of a moot point.

Notice he is unable to show 25D activates the VDR's and he in fact cited work that says only 1,25D does this.

This is what he offers in this section: *"the association-induction hypothesis"*

What does any of this have to do with 1,25-D activating the vitamin D receptor?

Firstly, it shows that overfocusing on a specific receptor is going to lead a person down a weird path — neglecting how a drug or hormone can change the activity of a cell's affinity for water, or shift the balance of intracellular and extracellular ions, or act on mitochondria to impair energy production, or produce free radicals, or cause inflammation, etc.

Secondly, given my understanding of the hair follicle's growth cycle and the vitamin D receptor's (or cardinal site's) involvement in the activation and proliferation of stem cells, I would infer that the vitamin D receptor is a type of regulatory material that supports cellular division— similar, to nitric oxide, histamine, and estrogen.

A weird path? Speaking of neglecting how a hormone works you leave out any creation of VDREs in your work.

Let's look at the hair follicle growth cycle now. I will share science rather than infer! It involves 1,25D to begin with. The article will also correctly point out the hypercalcemia control axis.

CONCLUSION

"The 1,25(OH)2D3-FGF23-phosphate axis is as important pathophysiologically as the 1,25(OH)2D3-PTH-calcium axis in bone and mineral homeostasis. FGF23 appears to be a novel mediator of 1,25(OH)2D3-VDR action that prevents ectopic calcification and reduces cardiovascular mortality.

1,25(OH)2D3 is both anabolic and catabolic to bone, providing an explanation as to how vitamin D-VDR is associated with dynamic maintenance of the skeleton and reduced osteoporotic fractures.

The modern bone, calcium, and phosphate homeostatic functions of VDR evolved from a primitive detoxification role.

1,25(OH)2D3 functions molecularly via VDR-RXR in either a cyclical progressive fashion of coactivator attraction or a "cloverleaf " model, wherein DNA in chromatin is looped out and remote VDRE enhancers are clustered to nucleate a gene transcription machine that simultaneously recruits HATs, SWI/SNFs, DRIP/Mediator, TFIIB, etc., to initiate and process mRNAs that are translated into vitamin D-induced effector proteins.

Naturally occurring, novel, low-affinity agonist VDR ligands, (e.g., lithocholic acid, curcumin, and PUFAs) may trigger VDR actions in specific tissues such as colon and skin, lowering the risk of cancer and mediating the hair cycle, respectively.

Hair cycle signaling by VDR involves neither vitamin D nor transactivation, and is apparently mediated through Hr/HDACs and the repression of Wise, which results in the stimulation of Wnt/LRP/b-catenin."

https://asbmr.onlinelibrary.wiley.com/doi/pdf/10.1359/jbmr.07s216

Another hair cycle paper. Notice this one mentions other ligands but not 25D. It also talks about the immune system he says you don't want to activate.

"The nutritional analogy can be drawn between fat-soluble vitamins A and D. The well-recognized role of vitamin A (retinal-dehyde) in vision represents just a small fraction of the effects of vitamin A when one considers the pleiotropic influence of its retinoic acid metabolites on growth, development, and reproduction. Similar to retinoic acid and RAR/RXR, 1,25(OH)2D3 exerts a wide array of effects beyond bone. These actions are all mediated by VDR, consistent with the broad cellular distribution of VDR expression. Many of the extraosseous effects of VDR appear to be triggered by locally produced 1,25(OH)2D3, again similar to the scenario with retinoic acid liganding of RAR/RXR. Numerous tissues besides the kidney express the1a-OHase enzyme, including cells of the immune system (e.g., T-cells), the pancreas, skin, etc. This locally produced 1,25(OH)2D3 does not contribute significantly to circulating 1,25(OH)2D3, but it retains the capacity to be active in a cell- and tissue-specific manner. Examples of local 1,25(OH)2D3-VDR actions include repression of IL-2 in T-cells,14 induction of defensin and cathelicidin as local antimicrobial effectors,44 stimulation of involucrin synthesis in skin,45 CYP3A4, and p21 induction in epithelial cells (especially in the colon),20 and promotion of insulin secretion from the b-cells of the pancreas.46 By locally stimulating the above-mentioned genes, the Vitamin D/VDR system emerges, likely redundantly with other regulators, as an immunomodulator that stimulates the innate and suppresses the adaptive immune system to effect both antimicrobial and anti-autoimmune actions, detoxifies xenobiotics to be chemoprotective, controls cell proliferation and regulates apoptosis to reduce cancer, and moderates type II diabetes by promoting insulin release as well as possibly enhancing fatty acid b-oxidation via induction of FOXO1 (Table 1). A second possibility obviating the need to generate1,25(OH)2D3 locally would be for VDR to function unliganded. As indicated above, VDR but not vitamin D is required to sustain the mammalian hair cycle. Thus, as depicted in Figure 8 (lower center), the Hr corepressor could function as a surrogate VDR "ligand" to suppress Wise or other genes that normally keep the hair cycle in check. Also, unlike the case of intestine, kidney, and bone, calbindin induction by VDR does not require Vitamin D in brain.47 VDR is widely expressed in the central nervous system, as is Hr, raising the possibility that unliganded VDR, along with Hr, acts in select neurons. Notably, it has been reported recently that VDR-null mice exhibit behavioral abnormalities including anxiety, etc.48. The ability of VDR to function unliganded is difficult to justify physicochemically because the tertiarystructure of VDR and its functionally interactive surfaces cannot be stabilized unless the hydrophobic binding pocket is occupied by a lipophilic ligand. We therefore suggest that VDR binds one or more naturally occurring non-vitamin D ligands to effect its extraosseous actions. As discussed above, we have identified several potential examples of non-vitamin D-related VDR ligands, including LCA, g-tocotrienol, and PUFAs. Because VDR is capable of binding these lipids, albeit with low affinity, the receptor may have retained its promiscuity for ligand binding that presumably originated with its

primitive detoxification function. Also, the ligand binding pocket of VDR is second only to PXR in volume among the crystallized nuclear receptor ligand binding domains, suggesting (but not proving) that it can accommodate a broad array of lipids. The question remains whether in the course of its evolution VDR co-evolved higher affinity local ligands that would explain the broad health benefits of vitamin D and other lipid nutrients beyond bone. For example, 1,25(OH)2D3-VDR is anti-inflammatory and suppresses NFkB.49 This action would be desirable for instance in preventing atherosclerosis. Is there, perhaps, a local novel VDR ligand in endothelial cells that could trigger the anti-inflammatory influence of VDR? Combined with the anti-calcification effect of FGF23, VDR would then be able to exert a two-pronged attack in preventing arteriosclerosis. Only the future will reveal the actual mechanisms for the apparent cardiovascular benefits of vitamin D/VDR. Clearly, VDR will emerge as a versatile therapeutic and preventative target once we fully understand the pleiotropic extraosseous effects of vitamin D. No doubt the faces of vitamin D and VDR will again change to reflect new frontiers in health and disease."

https://www.researchgate.net/publication/51434311_Vitamin_D_receptor_Molecular_signaling_and_actions_of_nutritional_ligands_in_disease_prevention

Argument #5: "You Need The Active Form of Vitamin D to Activate The Immune System"

This is another argument that seems compelling before you find out that you probably don't want to activate your immune system.

This one's hilarious. We don't want to activate our immune system. Too stupid to comment on beyond the fact that this is how we create our chemical and biological warriors, the IMMUNE SYSTEM.

Argument #7: "You're Only Supposed to Get Vitamin D From The Sun"

As far as I know, it has never been claimed that a supplement of cholecalciferol can replace or is better than sunlight. For what it's worth, for over a year, I've been climbing a rickety old ladder on the side of the casita I live in to layout whenever possible. If I fall off this ladder, I will likely break my neck — but to me, regular sunlight is worth the risk.

My only response here is that he thinks the sun only makes D3 when it makes literally dozens and dozens of unique "vitamin D" molecules.

For example, he went on and on about 25D controlling PTH yet he never mentioned 24,25D when he talked about PTH as well as when he talked about 25D becoming 1,25D. He in fact cited a paper that mentions 24,25D!! This shows how little he understands the metabolism.

This is from his second citation meant to show 25D decreases 1,25D, even though it says the absolute opposite. And remember, so did the first citation that he used the … in and lied by leaving out the part that said 1,25D actually increases. Again, it's what I opened the paper with.

Gigantic Cholecalciferol Dose Causes Transient Increase in 1,25-D

"Twenty-five patients with vitamin D deficiency… randomly received either 540,000 IU of cholecalciferol… or matched placebo…" … "As serum PTH and total calcium levels, which both modulate CYP27B1 activity, remained unchanged during that period, it seems that this transient rise in 1,25-D was mainly attributable to the boost of suddenly available 25-D substrate. A plausible reason for the subsequent decrease in 1,25-D levels following day 3 may be the induction of CYP24 hydroxylase gene that shifts 25-D more towards the production of inactive 24,25 (OH)2D thus limiting the rise of 1,25-D levels." — Amrein, et al. (2011)

A little more about 24,25D, said to be an inactive molecule made instead of 1,25D.

"24,25(OH)2D3 significantly enhance bone mineralization, significantly decreases PTH secretion in humans."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3213838/#!po=0.387597

Argument #8: "25-D Deficiency is Actually A Magnesium Deficiency"

This is a derivative of the 'you need active vitamin D because the storage form is not biologically active' argument:

"Vitamin D needs to be converted from its storage or inactive form 25-D to an active form 1-25-D before exerting its biological functions. These various stages of vitamin D conversions are actively dependent on the bioavailability of magnesium." — Uwitonze, et al. (2018)

Right there it calls the storage form, 25D, inactive. Thanks for including it. It's not a derivative of anything, it's a FACT. Danny goes on to tell you how to get magnesium still unable to deal with the fact that 25D is inactive and fails miserably to address that taking excess D tanks your magnesium and it's a very common deficiency. He would have been better off leaving this one out since he didn't address it at all.

If I were going to predict the anti-vitamin D people's response to this article, I would guess that the context will immediately be ignored, followed by the addition of overwhelming complexity and obfuscation.

Sorry I have to add complexity to your limited three analogue vocabulary based view of a complex topic. It's obvious you don't understand it so you create a ton of esoteric unscientific writings that are mostly supported by pill based studies on people already suffering from a disease or condition. The very folk with high active D. Not to mention a total denial of how the immune system works and how pathogens seek to disable it via the VDRs when you actually acknowledge the receptors existence.

And to say I'm anti-D is the biggest mistake. Vitamin D is wonderful, BUT it's a vast array of molecules and the body decides which ones it wants. The body is WICKED smart. The immune system isn't built around a SEASONAL VARIATION molecule; we would have died out as a species eons ago if that were the case. It's unfortunate he's completely unaware of the other molecules and the work they do, compared to inactive STORAGE substrate 25D. And like every other person saying I'm wrong, Danny can't produce a single study where people are actually low in the active form without a defect activating 25D. May be that's why he seeks to completely dismiss the active form as being the ACTUAL goal.

There are other arguments I am not going to address. I've done plenty to show his piece is "Much Ado About Nothing." I often respond to folks carrying on like this simply with "blah blah blah" because that is all they are saying in the first place. And in the case of this author, I choose to not engage EXPOSED liars.