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Chapter

Introductory Chapter: Overview of Vitamin D Facts and Fads

Edward T. Zawada

1. Introduction

The importance of vitamin D has risen from a narrow focus on bone health to a major concern for individual and population survival due to possible extraskeletal pharmacologic effects. The latter is derived from alterations in vascular tone and multi-organ physiologic changes resulting from deficiency and restored by repletion. However, the literature is controversial because there are studies pro and con for these latter effects. Thus, there has arisen a need to try to dissect fact from fad.

I began my clinical and research interest in vitamin D measurement, physiology, and therapeutic replacement nearly 50 years ago while in training in nephrology at the University of California, Los Angeles (UCLA). It was as though the influence of Hollywood, the beach, and the star-laden music industry created a stereotype of young, beautiful, tanned, physically fit population that naturally lead to a concern with a vitamin which is activated by being outdoors, from the sunlight, from the exposure at beach. As it were, nephrology at UCLA at that time was still a newborn specialty descended from the original specialty called "metabolism." Gathered together at UCLA were many clinicians who were interested in vitamin D. Names such as Jack Coburn, Charles Kleeman, David B. N. Lee, Morton Maxwell, Nostratola Vaziri, Arnold Brickman, Francesco Llach, and Joel Koppel were those who lured me into the arena of calcium balance in health and disease. My first publication was a collaboration on a very detailed review of "The pathophysiology and clinical aspects of hypercalcemic disorders" [1]. Also developing at that same time was knowledge of the variety of hormonal and other factors that determined proper intake and serum levels of calcium, phosphorus, and vitamin D. Finally, much was being explored about the pharmacokinetics, pharmacodynamics, and excretion of these factors and the impact on bone and skeletal health.

Dialysis and transplantation would eventually emerge to consume the interest of subsequent nephrology trainees, but this was the time of the transition from the endocrinology of fluids and electrolytes controlled by the kidney and disturbed by kidney diseases to the explosion of kidney replacement strategies. The above predecessors attracted their like-minded academicians from around the world to come and lecture which included Shaul Massry, Eduardo Slatopolsky, Hector DeLuca, Ralph DeFronzo, and others. They often presented annually at the "vitamin D meeting" on the Monterey Peninsula. I was able to observe the dialog among these pioneers which filled my mind with knowledge but also questions for future investigation. What was most interesting about science that time was the indirect nature of proving that vitamin D and parathyroid hormone played such a variety of roles in kidney and other organ function and disease since both were not easily, if at all, measurable in those days. Bioassays and extractions from the liver and kidney and parathyroid glands were used in pharmacologic and dietary studies of

electrolyte balance and organ physiologic measurements to search for perturbation of physiology, response to animal models of human disease, and observations intended to detect restoration of failed homeostasis.

2. Evolution of studies

By exposure to a large number of patients with calcium and vitamin D disorders, almost inadvertently I began to pursue a slightly different direction from my mentors. I was initially working in blood pressure management and prostanoid metabolism [2] when I observed a variety of hemodynamic disturbances in these "calcium" patients [3–9]. I questioned mechanisms and consequences of my observations. I began recording case reports and performing animal physiology studies and finally dietary studies in animals and then humans. The result was an idea that calcium and vitamin D influenced the heart, the blood vessels, and the physiology of circulation. This was the beginning of considerations of extraskeletal effects of calcium and vitamin D perturbations. Of course, in my mind I feel that I was in part responsible for discovering the impact of calcium and vitamin D on multi-organ, total body physiology, and homeostasis which confers survival benefit when deficiency is corrected and supplementation is provided. From my time in the 1970s, there has been a logarithmic accumulation of observations and research trials worldwide which has expanded the horizon of calcium and vitamin D metabolism from strictly bone health to multiple organ and total body health. I will review my original studies as well as the consequences of such hemodynamic and systemic effects of calcium and vitamin D in the last chapter of this book dealing with their role in the management of ICU patients.

3. Conclusion

Why is there a gap between the fads and facts with regard to vitamin D and health? For one thing, detailed pharmacokinetic measurements of vitamin D and its numerous metabolites in various populations are a relatively recent phenomenon. Secondly, it is likely that vitamin D plays a contributory role but not the primary role in disease and health beyond the known requirement to prevent rickets or osteomalacia, the main vitamin D-deficient bone diseases of children and adults, respectively. Finally, I believe more randomized controlled trials are needed to evaluate fad from fact.

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