Vitamin D

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Editors D. Feldman, F. Glorieux

CHAPTER 61

The Pharmacology of Vitamin D, Including Fortification Strategies

Reinhold Vieth
Dept Laboratory Medicine and Pathobiology, University of Toronto, and Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Canada M5G 1X5,

INTRODUCTION

The use of vitamin D has never been approached in the same way that we would expect to see for any modern drug. Unlike other nutrients, we have never had dietary intakes of vitamin D as a reasonable reference point for deciding on how much of this nutrient/drug that people should be consuming. The ambiguity between "nutrient" and "drug" is reasonable when it comes to vitamin D, because there were no meaningful amounts of vitamin D in the kinds of foods that Paleolithic humans would likely have been consuming.

Our biology was designed by evolution for life in equatorial Africa. Therefore, consumption of those rare foods that do contain a meaningful amount of vitamin D, like ocean fish, could not have played a role in determining human vitamin D requirements. Requirements for vitamin D were satisfied by the life of the naked ape that became the species, *homo sapien*, in its native, tropical environment. Since our culture and environment no longer match the conditions that defined our biology, we modern humans might benefit if we could compensate for the biological consequences of modern life. One such consequence may be an endemic lack of vitamin D that can be corrected by appropriate supplementation.

My perspective is the North American one, where vitamin D is primarily regarded as a nutrient. However, in Europe and the rest of the world, use of even small doses of vitamin D usually falls into the realm of a prescription drug. That perspective has the advantage of imposing a higher expectation on our understanding of the use of vitamin D. Before approving the clinical use of any new drug, government regulators expect to see the answers to some relatively standard questions. Pharmaceutical firms need to anticipate these issues as they plan the research necessary for implementation of new products. These questions include, but are not limited to, the following:

1a. What is the disease indication for the drug?

1b. What kind of clinical or health effects should we be looking for, based on preclinical animal and laboratory research?

2a. What are the most useful approaches to delivering the drug to people: the vehicle?

2b. What is the appropriate dosage, route of administration, and interval between doses?

3. What is the desirable target for the plasma concentration, what dose would be needed to attain or ensure this?

4. What, if any, are the biological markers to monitor toxicity, and what are our criteria for determining therapeutic effectiveness? What is the "therapeutic index" the ratio between toxic vs beneficial dose levels?

When it comes to plain and simple, nutritional vitamin D, the answer to each of these questions is that we have just started to address it in the past decade. Any opinion about vitamin D here is controversial. In an effort to provide some answers to the preceding questions, I will present perspectives about the vitamin D system that relate to pharmacological aspects of vitamin D in the adult context.