The Vitamins

FUNDAMENTAL ASPECTS IN NUTRITION AND HEALTH

GERALD F. COMBS, JR.

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PREFACE

I have found it to be true that one learns best what one has to teach. And, because I have had no formal training either in teaching or in the field of education in general, it was not for several years of my own teaching that I began to realize that the good teacher must understand more than the subject matter of his or her course. In my case, that realization developed, over a few years, with the recognition that individuals learn in different ways and that the process of learning itself is as relevant to my teaching as the material I present. This enlightenment has been for me invaluable because it has led me to the field of educational psychology from which I have gained at least some of the insights of the good teacher. In fact, it led me to write this book.

In exploring that field, I came across two books that have influenced me greatly: A Theory of Education[1] by another Cornell professor, Joe Novak, and Learning How to Learn[2] by Prof. Novak and his colleague Bob Gowin. I highly recommend their work to any scientific "expert" in the position of teaching within the area of his or her expertise. From those books and conversations with Prof. Novak, I have come to understand that people think (and, therefore, learn) in terms of *concepts* - not facts. Therefore, for the past few years I have experimented in offering my course at Cornell University, The Vitamins, in ways that are more concept-centered than I (or others, for that matter) have used previously. While I regard this experiment as an ongoing activity, it has already resulted in my shifting away from the traditional lecture format to one based on open classroom discussions aimed at involving the students, each of whom, I have found, brings a valuable personal perspective to discussions. I have found this to be particularly true for discussions concerning the vitamins; while it is certainly possible in modern societies to be misinformed about nutrition, it is virtually impossible to be truly naive. In other words, every person brings to the study of the vitamins some relevant conceptual framework and it is, thus, the task of the teacher to build upon that framework by adding new concepts, establishing new linkages and modifying existing ones where appropriate.

It quickly became clear to me that my own notes, indeed, all other available reference texts on the subject of the vitamins, were insufficient to support a concept-centered approach to the subject. Thus, I undertook to write a new type of textbook on the vitamins, one that would be maximally valuable in this kind of teaching. In so doing, I tried to focus on the key concepts and to make the book itself useful in a practical sense. Because I find myself writing in virtually any book that I really use, I gave this text margins wide enough for the reader to do the same. Because I have found the technical vocabularies of many scientific fields to present formidable barriers to learning, I have listed what I regard as the most important technical terms at the beginning of each chapter and have used each in context. Because I intend this to be an accurate synopsis of present understanding but not a

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[1] Cornell University Press, Ithaca, N.Y., 1977, 324 pp.

[2] Cambridge University Press, New York, 1984, 199 pp.

definitive reference to the original scientific literature, I have cited only current major reviews that I find useful to the student. Because I have found the discussion of real-world cases to enhance learning of the subject, I have included case reports that can be used as classroom exercises or student assignments. I have designed the text for use as background reading for a one-semester upper-level college course within a nutrition-related curriculum. In fact, I have used draft versions in my course at Cornell as a means of refining it for this purpose.

While The Vitamins was intended primarily for use in teaching, I recognize that it will also be useful as a desk reference for nutritionists, dieticians and many physicians, veterinarians and other health professionals. Indeed, I have been gratified by the comments I have received from colleagues to that effect.

It is my hope that The Vitamins will be read, re-read, written in and thought over. It seems to me that a field as immensely fascinating as the vitamins demands nothing less.

G.F. Combs, Jr.

Ithaca, New York
August, 1991

HOW TO USE THIS BOOK

The Vitamins is intended as a teaching text for an upper-level college course within a nutrition-related curriculum; however, it will also be useful as a desk reference or as a workbook for self-paced study of the vitamins. It has several features that are designed to enhance its usefulness to students as well as instructors.

To the student:

Before reading each chapter, take a few moments to go over the ***Anchoring Concepts*** and ***Learning Objectives*** listed on the chapter title page. ***Anchoring Concepts*** are the ideas fundamental to the subject matter of the chapter; they are the concepts to which the new ones presented in the chapter will be related. The ***Anchoring Concepts*** identified in the first several chapters should already be very familiar to you; if they are not, then it will be necessary for you to do some background reading or discussion until you feel comfortable in your understanding of these basic ideas. You will find that most chapters are designed to build upon the understanding gained through previous chapters; in most cases, the ***Anchoring Concepts*** of a chapter relate to the ***Learning Objectives*** of previous chapters. Pay attention to the ***Learning Objectives***; they are the key elements of understanding that the chapter is intended to support. Keeping the ***Learning Objectives*** in mind as you go through each chapter will help you maintain focus on the key concepts.

Next, read through the ***Vocabulary*** list and *mark* any terms that are unfamiliar or about which you feel unsure. Then, as you read through the text, look for them; you should be able to get a good feel for their meanings from the contexts of their uses. If this is not sufficient for any particular term, then you should consult a good medical or scientific dictionary.

As you go through the text, note what information the layout is designed to convey. First, note that the major sections of each chapter are indicated with a bold heading above a bar, and that the wide left margin contains key words and phrases that relate to the major topic of the text at that point. These are features that are designed to help you *scan* for particular information. Also note that the footnoted information is largely supplementary but not essential to the understanding of the key concepts presented. Therefore, the text may be read at two levels: at the basic level, one should be able to ignore the footnotes and still get the key concepts; at the more detailed level, one should be able to pick up more of the background information from the footnotes.

Chapters 5-17 are each followed by a ***Case Study*** comprised of one or more clinical case reports abstracted from the medical literature. For each case, use the associated questions to focus your thinking on the features that relate to vitamin functions. As you do so, try to ignore the obvious connection with the subject of the chapter; put yourself in the position of the attending physician who was called upon to diagnose the problem without prior knowledge that it involved any particular nutrient, much less a certain vitamin.

Take some time and go through the ***Study Questions and Exercises*** at the end of each chapter. These, too, are designed to direct your thinking back to the key concepts of each chapter and to facilitate integration of those concepts with those you already have. To this end, you are asked in this section of several chapters to prepare a *concept map* of the subject matter. Many people find the *concept map* to be a powerful learning tool; therefore, it you have had no previous experience with this device, then it will be well worth your while to consult Learning How to Learn[1].

At the end of each chapter is a reading list. With the exception of Chapter 2, which lists papers of landmark significance to the discovery of the vitamins, the reading lists consist of key reviews in prominent scientific journals. Thus, while primary research reports are not cited in the text, you should be able to trace research papers on topics of specific interest through the reviews that are listed.

Last, but certainly not least, have *fun* with this fascinating aspect of the field of nutrition!

To the instructor:

I hope you will find this format and presentation useful in your teaching of the vitamins. To that end, some of my experiences in using **The Vitamins** as a text for my course at Cornell may be of interest to you.

I have found that *every* student comes to the study of the vitamins with *some* background knowledge of the subject, although those backgrounds are generally incomplete, frequently with substantial areas of no information and mis-information. This is true for upper-level nutrition majors and for students from other fields, the difference being largely one of magnitude. This is also true for instructors, most of whom come to the field with specific expertise that relates to only a subset of the subject matter. In addition, I have found that, by virtue of having at least *some* background on the subject and being motivated by any of a number of reasons to learn more, *every* student brings to the study of the vitamins a unique perspective which may not be readily apparent to the instructor. I am convinced that meaningful learning is served when both instructor and students come to understand each others' various perspectives. This has two benefits in teaching the vitamins. First, it is in the instructor's interest to know the students' ideas and levels of understanding concerning issues of vitamin need, vitamin function, etc., such that these can be built upon and modified as may be appropriate. Second, I have found that many upper-level students have interesting experiences (through personal or family histories, their own research, information from other courses, etc.) that can be valuable contributions to classroom discussions, thus, mitigating against the "instructor knows all" notion, which we all know to be false. To identify student perspectives, I have found it useful to assign on the first class period for submission at the second class a written autobiographical sketch. I distribute one I wrote for this purpose and I ask each student to write "as much or as little" as he or she cares to, recognizing that I will distribute copies of whatever is submitted to each

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[1] Novak, J.D. and D.B. Gowin, 1984, Learning How to Learn, Cambridge University Press, New York, 199 pp.

student in the class. The biographical sketches that I see range from a few sentences that reveal little of personal nature, to longer ones that provide many good insights about their authors; I have found *every one* to help me get to know my students personally and to get a better idea of their understandings of the vitamins and of their expectations of my course. The exercise serves the students in a similar manner, thus, promoting a group dynamic that facilitates classroom discussions.

I have come to use **The Vitamins** in my teaching as the text from which I make regular reading assignments, usually a chapter at a time, as preparation for each class which I generally conduct in an open discussion format. Long ago, I found it difficult, if not impossible, to cover in a traditional lecture format all of the information about the vitamins I deemed important for a nutritionist to know. Thus, I have put that information in this text and have shifted more of the responsibility for learning to the student for gleaning it from reading. I use my class time to assist the student by providing discussions of issues of particular interest or concern. Often, this means that certain points were not clear upon reading or that the reading itself stimulated questions not specifically addressed in the text. Usually, these questions are nicely handled by eliciting the views and understandings of other students and by my giving supplementary information. Therefore, my class preparation involves the collation of research data that will supplement the discussion in the text and the identification of questions that I can use to initiate discussions. In developing my questions, I have found it useful to prepare my own concept maps of the subject matter and to ask rather simple questions about the linkages between concepts, e.g., *"How does the mode of enteric absorption of the tocopherols relate to what we know about its physio-chemical properties?"* If you are unfamiliar with concept mapping, then I strongly recommend your consulting Learning How to Learn[1] and experimenting with the technique to determine whether it can assist you in your teaching.

I have found it useful to give weekly written assignments for which I use the ***Study Questions and Exercises*** or ***Case Studies***. In my experience, regular assignments keep students focused on the topic and prevent them from letting the course slide until exam time. More importantly, I believe there to be learning associated with the thought that necessarily goes into these written assignments. In order to support that learning, I make a point of going over each assignment briefly at the beginning of the class at which it is due, and of returning it by the *next* class with my written comments on *each* paper. You will find that the ***Case Studies*** I have included are abstracted from actual clinical reports; however, I have presented them without some of the pertinent clinical findings (e.g., responses to treatments) that were originally reported, in order to make of them learning exercises. I have found that students do well on these assignments and that they particularly enjoy the ***Case Studies***.

I evaluate student performance on the basis of class participation, weekly written assignments, a review of a recent research paper, and either one or two examinations (i.e., either a final or a final plus a mid-term). In order to allow each student to pursue a topic of specific individual interest, I ask them to review a research paper published within the last year, using the style of Nutrition Reviews. I evaluate each review on its criticalness as well as on the importance of the paper that was selected, which I ask them to discuss. This assignment has also been generally well received. Because many students are inexperienced in research and thus feel uncomfortable in criticizing it, I have found it helpful

to conduct in advance of the assignment a discussion dealing with the general principles of experimental design and statistical inference. Because I have adopted a concept-oriented teaching style, I long ago abandoned the use of short-answer questions (e.g., *"Name the species that require dietary sources of vitamin C"*) on examinations. Instead, I use brief case descriptions and actual experimental data and ask for diagnostic strategies, development of hypotheses, design of means of hypothesis testing, interpretation of results, etc. Many students may prefer the more traditional short-answer test; however, I have found that such inertia can be overcome by using examples in class discussions or homework assignments.

The Vitamins has been of great value in enhancing my teaching of the course by that name at Cornell. Thus, it is my sincere wish that it will assist you similarly in your teaching. Whatever your experiences with it are, please let me know about them.

G.F. Combs, Jr.

Ithaca, New York
August, 1991

CONTENTS

SECTION I

PERSPECTIVES ON THE VITAMINS IN NUTRITION

CHAPTER 1 *WHAT IS A VITAMIN?*

"Imagination is more important than knowledge." A. Einstein

Anchoring Concepts:

i. Certain factors, called ***nutrients***, are necessary for normal physiological function of animals including man. Some nutrients cannot be synthesized adequately by the host and must, therefore, be obtained from the external chemical environment; these are referred to as ***dietary essential nutrients***.

ii. ***Diseases*** involving physiological dysfunction often accompanied by morphological changes can result from insufficient intakes of dietary essential nutrients.

Learning Objectives:

i. To understand the classical meaning of the term ***vitamin*** as it is used in the field of nutrition.

ii. To understand that the term vitamin describes both a ***concept*** of fundamental importance in nutrition as well as any member of a rather heterogeneous array of nutrients any one of which may *not* fully satisfy the classical definition.

iii. To understand the concepts of a ***vitamer*** and a ***pro-vitamin***.

Vocabulary:

vitamin
vitamer
pro-vitamin

A REVOLUTIONARY CONCEPT

everyday word or revolutionary idea?

The term **vitamin**, today a common word in everyday language, was born of a revolution in thinking about the interrelationships of diet and health that occurred at the beginning of the twentieth century.

That revolution involved the growing realization of two phenomena that are now so well understood that they are taken for granted even by the lay person:

> *i.* Diets are sources of more nutrients than the few then recognized by physiologists, those being *protein*, *fat*, *carbohydrate*, *"ash"* and *water*, which accounted for very nearly 100% of the mass of most foods;
>
> *ii.* Low intakes of specific nutrients can cause certain diseases.

In today's world, each of these concepts may seem self-evident; but in a world still responding to and greatly influenced by the important discoveries in microbiology of the nineteenth century, each represented a major departure from contemporaneous thinking in the area of health. With this view, it is understandable that, at the turn of the century, experimental findings which now can be seen as indicating the presence of hitherto unrecognized nutrients were interpreted instead as substantiating the presence of natural antidotes to unidentified disease-causing microbes.

Important discoveries in science have ways of directing, even entrapping, one's view of the world - a tendency resistance from which depends upon critical and constantly questioning minds. That such minds were involved in early nutrition research is evidenced by the spirited debates and frequent polemics that ensued over discoveries of apparently beneficial new dietary factors. Still, the systematic development of what emerged as nutritional science depended upon a *new* intellectual construct for interpreting such experimental observations.

vitamin or vitamine?

The elucidation of the nature of what was later to be called thiamin occasioned the proposition of such a new construct in physiology[1]. Aware of the impact of what was a departure from prevailing thought, its author, the Polish biochemist **Casimir Funk**, chose to generalize from his findings on the chemical nature of that ***"vital amine"*** to suggest the term

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[1]This is a clear example of what T.H. Kuhn has called a "scientific revolution" (The Structure of Scientific Revolutions, 1968), i.e., the discarding of an old paradigm with the invention of a new one.

'vitamine' as a generic descriptor for many such ***'accessory factors'*** associated with diets. That the factors soon to be elucidated comprised a somewhat chemically heterogeneous group not all of which were nitrogenous does not diminish the importance of the introduction of what was first pronounced as the ***'vitamine theory'***, later to become a key concept in nutrition: ***the vitamin.***

The term *vitamin* has been defined in various ways. While the very concept of a vitamin was crucial to progress in understanding nutrition, the actual definition of a vitamin has evolved in consequence of that understanding.

AN OPERATING DEFINITION

For the purposes of the study of this aspect of nutrition, a vitamin is defined as follows:

A vitamin . . .

is an ***organic compound*** distinct from fats, carbohydrates and proteins;

is a ***natural component of foods*** where it is usually present in minute amounts;

is essential, also usually in minute amounts, for ***normal physiological function*** (i.e., maintenance, growth, development and/or production);

causes, by its absence or under-utilization, a ***specific deficiency syndrome***;

is ***not synthesized by the host*** in amounts adequate to meet normal physiological needs.

This definition will be useful in the study of the vitamins, as it effectively distinguishes this class of nutrients from the others (i.e., proteins and amino acids, essential fatty acids, minerals) and indicates the needs in various normal physiological functions. It also points out the specificity of deficiency syndromes by which the vitamins were discovered. Further, it places the vitamins in that portion of the chemical environment upon which animals (including humans) must depend for survival, thus distinguishing vitamins from hormones.

some caveats It will quickly become clear, however, that, for all of its usefulness, this operating definition has serious limitations, notably with respect to the last clause, for many species can indeed synthesize at least some of the vitamins.

Four examples illustrate this point:

i. Most animal species have the ability to synthesize ascorbic acid. Only those few which lack the enzyme l-gulonolactone oxidase (e.g., the guinea pig, humans) cannot; only for them can ascorbic acid properly be called ***vitamin C***.

ii. Individuals exposed to modest amounts of sunlight can produce adequate amounts of cholecalciferol which for them functions as a hormone. Only individuals without sufficient exposure to ultraviolet light (e.g., livestock raised in indoor confinement, people spending most of their days indoors) require a dietary source of ***vitamin D***.

iii. Most animal species have the metabolic capacity to synthesize choline; however, some (e.g., the chick, the rat) may not be able to employ that capacity if they are fed insufficient amounts of methyl-donor compounds. In addition, some (e.g., the chick) do not develop that capacity fully until several weeks of age. Thus, for the young chick and for individuals of other species fed diets providing limited methyl groups, ***choline*** is a vitamin.

iv. All animal species can synthesize nicotinic acid mononucleotide (NMN) from the amino acid tryptophan. Only those for which this metabolic conversion is particularly inefficient (e.g., the cat, fishes) and others fed low dietary levels of tryptophan require a dietary source of ***niacin***.

With these counter-examples in mind, the definition of a vitamin can be understood as having specific reference to animal species, stage of development, diet or nutritional status, and physical environmental conditions.

Thus, it will be seen that:

some compounds are vitamins for one species and not another;
and
some are vitamins only under specific dietary or environmental conditions.

the vitamins

Thirteen substances or groups of substances are now generally recognized as vitamins; others have been proposed[2]. In some cases, the familiar name is actually the *generic descriptor* for a family of chemically related compounds having qualitatively comparable metabolic activities. For example, the term *"vitamin E"* refers to those analogues of tocol or tocotrienol[3] that are active in preventing such syndromes as fetal resorption in the rat and myopathies in the chick. In these cases, the members of the same vitamin family are called **vitamers**. Some carotenoids can be metabolized to yield the metabolically active form of vitamin A; such a precursor of an actual vitamin is called a **pro-vitamin**.

Study Questions:

i. What are the key features that define a vitamin?

ii. What is the fundamental difference between a vitamin and a hormone?

iii. List the recognized vitamins.

[2]These include such factors as inositol, carnitine, bioflavinoids, pangamic acid and laetrile, for some of which there is evidence of vitamin-like activity (*see* Chapter 19).

[3]Tocol is 3,4-dihydro-2-methyl-2-(4,8,12-trimethyltridecyl)-6-chromanol; tocotrienol is the analog with double bonds at the 3',7' and 11' positions on the phytol side chain. See Chapter 7.