

Nutrient Interrelationships Minerals — Vitamins — Endocrines

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Nutritional therapeutics has largely been directed toward the recognition and correction of nutritional deficiencies. It is now becoming evident that a loss of homeostatic equilibrium between the nutrients can also have an adverse effect upon health. A loss of this vital balance, particularly between the trace elements, can lead to subclinical deficiencies.

Nutrient interrelationships are complex, especially among the trace elements. A mineral cannot be affected without affecting at least two other minerals, each of which will then affect two others, etc. Mineral relationships can be compared to a series of intermeshing gears which are all connected, some directly and some indirectly. Any movement of one gear (mineral) will result in the movement of all the other gears (minerals). The extent or effect upon each gear (mineral) will depend upon the gear size (mineral quantity), and the number of cogs in the gear (number of enzymes or biochemical reactions the mineral is involved in). This meshwork of gears goes beyond just the mineral relationships, extending to and affecting the vitamins, hormones and neurological functions.

Extensive research involving tissue mineral analysis (TMA) of human hair and other tissues has led to significant advancements in the understanding of mineral relationships. This knowledge can now be further applied to the vitamin and endocrine relationships, resulting in a comprehensive, integrative approach to nutritional therapeutics.

Mineral Antagonisms

Two relationships exist among the trace elements, antagonistic and synergistic, which occur at two levels, metabolic and absorptive. Antagonism at the absorptive

1. Trace Elements, Inc., P.O. Box 514, Addison, Texas 75001.

level is due to inhibited absorption; that is, excess intake of a single element can decrease the intestinal absorption of another element. As an example, a high intake of calcium depresses intestinal zinc absorption, while an excess intake of zinc can depress copper absorption.¹ Figure 1 (p. 14) is a mineral wheel indicating the mineral antagonisms. Antagonisms at the metabolic level occur when an excess of one element interferes with the metabolic functions of another or contributes to its excretion due to compartmental displacement. This is seen with zinc and copper, cadmium and zinc, iron and copper, calcium, magnesium and phosphorus.²

Mineral Synergisms

Synergism between the elements occurs largely on a metabolic level. As an example, iron and copper are synergistic in that sufficient copper is required for iron utilization.³ Magnesium also functions in concert with potassium by enhancing its cellular retention.¹ The synergism between calcium, magnesium and phosphorus is well known due to their requirement in the maintenance and structure of osseous tissue. Other mineral synergisms include:

Element	Synergist Minerals
Ca	Mg-P-Cu-Na-K-Se
Mg	Ca-K-Zn-Mn-P-Cr
Na	K-Se-Co-Ca-Fe-Cu-P
K	Na-Mg-B ₁₀ -Mn-Zn-P-Fe
Cu	Fe-Co-Ca-Na-Se
Zn	K-Mg-Mn-Cr-P
P	Ca-Mg-Na-K-Zn-Fe
Fe	Cu-Mn-K-Na-Cr-P-Se
Cr	Mg-Zn-K
Mn	K-Zn-Mg-Fe-P
Se	Na-K-Cu-Mn-Fe-Ca

A third relationship is also noted, wherein a deficient intake of an element can allow toxic accumulation of another ele-

ment. Small amounts of cadmium intake can accumulate to a point of toxicity in the presence of marginal or deficient zinc intake.⁵ Lead toxicity can occur with insufficient calcium or iron intake,^{6,7,8,9,10,11} and iron toxicity can develop in the presence of a copper deficiency.¹²

A fourth relationship can also be seen when an excessive intake of a single element produces a deficiency of a synergistic element. This can result in an excess accumulation of an element, as seen with excessive zinc intake contributing to a copper deficiency. Such an imbalance can cause excessive iron to build up in storage tissues. Manganese by interfering with magnesium can result in excessive potassium and sodium accumulation.

Vitamin Antagonisms

Vitamins also have synergistic and antagonistic relationships which are not often considered. The vitamin wheel in Figure 2 depicts some of the known and observed theoretical antagonistic relationships of vitamins. The antagonism may not be direct but, as a result of excessive intake, may increase the requirements of other vitamins. Examples of some of these antagonisms follow: Vitamin A reduces the toxic effects of vitamin D.¹³ Vitamins A and D are mutually antagonistic. It has been reported that B₁ can have an antagonistic B₁₂ action.¹⁴ It should be noted that the antagonistic relationship depicted between vitamin C and vitamin B₁₂ is an indirect one. It has been confirmed (by Hoffer, Pauling and others), that vitamin C does not directly affect B₁₂, nor destroy this vitamin. The antagonism is via iron, in that iron is known to antagonize cobalt, which is an integral part of vitamin B₁₂.^{15,16,17,18} Vitamin C by enhancing iron absorption can therefore indirectly affect B₁₂ status. This is however a rare occurrence and may only affect a small segment of the population who may suffer from iron overload disorders.

In Figure 2, the known antagonisms among the vitamins are indicated by solid lines.^{19,20,21,22,23} Theoretical antagonisms are indicated by broken lines. These relationships are based upon their effects with minerals as determined through TMA research. As an example, vitamin D en-

hances the absorption of calcium; therefore, excessive intake of vitamin D by increasing calcium absorption would then produce a decrease in magnesium, potassium or phosphorus retention, or absorption.²⁴ The effects of vitamin A which enhances potassium and phosphorus absorption or retention, would then be reduced in the presence of high vitamin D intake.

Vitamin Synergisms

Vitamins are involved in many reactions. They act as coenzymes and are involved synergistically in many enzymatic reactions. They can also protect against deficiencies of other vitamins. The following is a list of vitamin synergisms:

Vitamin	Synergistic Vitamins
A	B ₂ -C-E-B ₃ -B ₁ -B ₆
D	B ₁₂ -E
E	A-B ₆ -C-B ₁₂ -B ₁ -B ₅ -B ₃ -B ₁₀ -D
B ₁	E-C-B ₆ -B ₁₂ -B ₃ -B ₅ -A-B ₁₀ -B ₂
B ₂	A-B ₃ -B ₁₀
B ₆	E-A-B ₁ -B ₃ -B ₅ -B ₁₂ -B ₁₀
B ₁₂	B ₁ -B ₃ -B ₆ -E-B ₅ -C-B ₁₀ -D
C	A-E-B ₆ -B ₃ -B ₅
B ₃	B ₁ -B ₂ -B ₆ -A-B ₅ -E-B ₁₀
B ₅	C-E-A-B ₁ -B ₃ -B ₆ -B ₁₀

Vitamin-Mineral Synergisms

Vitamins are closely associated with the metabolic functions of minerals. It is well known that a vitamin deficiency can interfere with mineral utilization or absorption, and vitamin supplementation may also be required to correct a mineral deficiency. Classic examples of vitamin requirements and mineral deficiencies are rickets and vitamin D. Vitamins C and/or B₆ and vitamin A may often be required to correct iron deficiency anemia which would not respond to iron supplementation.²⁶ A zinc deficiency can be related to vitamin A deficiency that would not respond to vitamin A supplementation. Zinc is required for mobilization of stored vitamin A from the liver.

The following is a list of vitamin-mineral synergists:

Vitamin	Mineral Synergists
A	Zn-K-P-Mg-Mn-Se
D	Ca-Mg-Na-Cu-Se

E	Na-K-Ca-Fe-Mn-Zn-P-Se
B ₁	Se-Co-Na-K-Fe-Mn-Mg-Cu-Zn-P
B ₂	Fe-P-Mg-Zn-K-Cr
B ₆	Zn-Cr-Mg-Na-K-P-Fe-Mn-Se
B ₁₂	Se-Cu-Ca-Co-Na
C	Fe-Cu-Ca-Co-Na
B ₃	Zn-K-Fe-P-Mg-Mn-Na-Cr-Se
B ₅	Cr-Na-K-Zn-P

Vitamin-Mineral Antagonism

Less recognized are the vitamin-mineral antagonistic relationships. Excessive intake of a single vitamin can lead to mineral disturbances by either producing a deficiency or increasing the retention of a mineral. High vitamin C intake will contribute to copper deficiency as a result of decreasing its absorption or producing a metabolic interference.²⁷ Since vitamin C is antagonistic to copper and copper is required in sufficient amounts for the metabolic utilization of iron, excess intake of vitamin C can lead to iron toxicity. A deficiency of copper results in the inability to utilize iron; therefore, iron will accumulate in storage tissues if an adequate supply of copper is not available.²⁸ Copper and vitamin C are synergistic in many metabolic functions, but due to their antagonistic effects upon each other, we can see that excessive intake of copper can cause a vitamin C deficiency.²⁹ Excess amounts of vitamin C in the presence of marginal copper status can contribute to osteoporosis³⁰ as well as cause a decrease in immune response.³¹ Excessive intake of vitamin D can produce a magnesium and potassium deficiency by its action of enhancing the absorption and/or retention of calcium.³² Excessive intake of vitamin A can contribute to calcium loss. Other vitamin-mineral antagonistic relationships are shown in the vitamin-mineral antagonism wheel in Figure 3.

Nutrient-Endocrine Relationships

Little consideration has been given to the nutritional effects upon the endocrine glands. Hormones are known to influence nutrients at several levels including absorption, excretion, transport and storage. Nutrients in turn can exert an influence on hormones. Trace elements are known to be involved in hormone secretion, the activity of hormones, and target tissue

binding sights. Trace metals, depending upon concentrations within the body (either too little or too much) can affect the hypothalamus-pituitary and thyroid-adrenal axis.³³

As with mineral and vitamin synergisms and antagonisms, endocrine synergisms and antagonisms also exist. Figure 4 shows the hormonal antagonistic relationships between some of the major endocrine glands.

Endocrine Classification

As early as 1930 Dr. Francis Pottenger commented on the relationship between the endocrine glands and the nervous system.³⁴ Later Dr. Melvin Page brilliantly categorized the endocrine glands according to neurological control, either sympathetic or parasympathetic.^{35 36} He described the sympathetic group as the "speed-up" endocrines and the parasympathetic group as the "slow-up" group. The sympathetic group consists of the thyroid, anterior pituitary, adrenal medulla and the androgen producing gonads. The parasympathetic group includes the pancreas, posterior pituitary, estrogen producing gonads, parathyroid and adrenal cortex. Dr. Page observed that if the phosphorus content of the blood is elevated, the sympathetic group is dominant and if calcium is elevated over phosphorus, the parasympathetic neuroendocrine group is dominant. He also keenly observed that the mineral composition of the body is dependent not on food intake directly but on the efficiency or inefficiency of neuroendocrine function.

Understanding of this classical work by Dr. Page can aid in the classification of nutrients from any source into two basic groups, sympathetic ("speed-up"), or parasympathetic ("slow-down") categories. These classifications are based on their nutrient-endocrine, or endocrine-nutrient influence upon neuroendocrine function.

Nutrient Classification Via Endocrine Dominance

As stated by Dr. Page, phosphorus can be considered sympathetic or stimulatory. Calcium is considered parasympathetic or sedative. The sympathetic and parasympathetic neuroendocrine systems have an

Figure 1
Mineral Antagonists

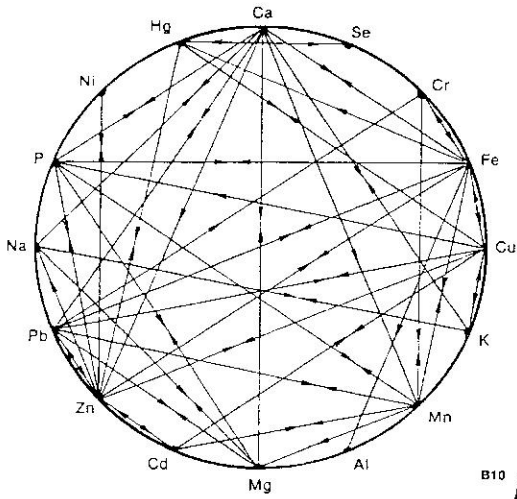


Figure 2
Vitamin Antagonists

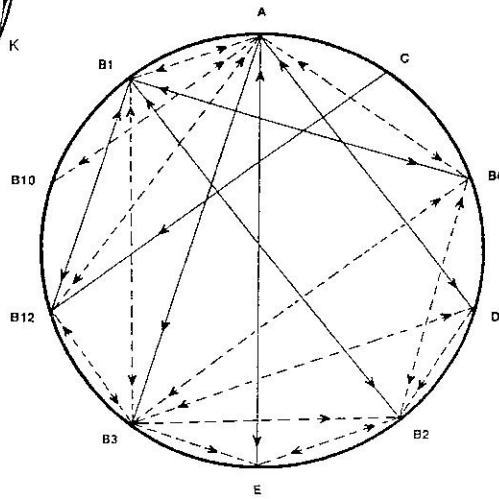


Figure 3
Vitamin-Mineral Antagonists

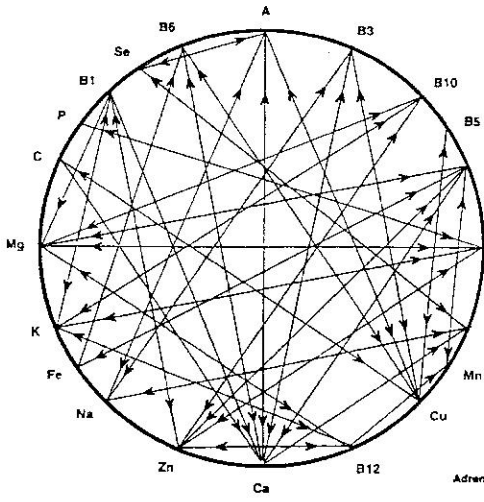


Figure 4
Hormonal Antagonists

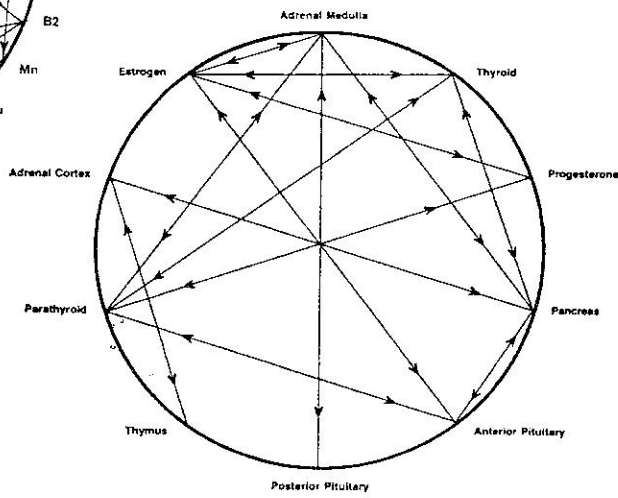


Figure 5

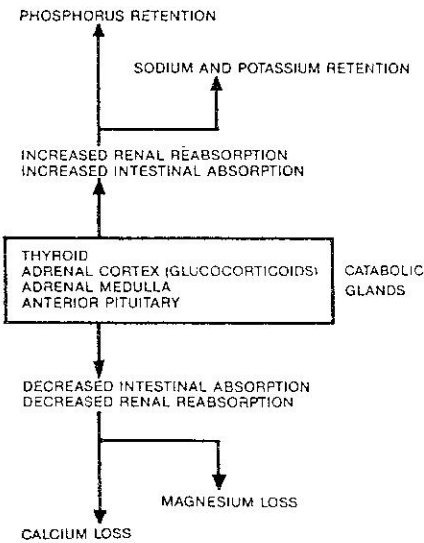
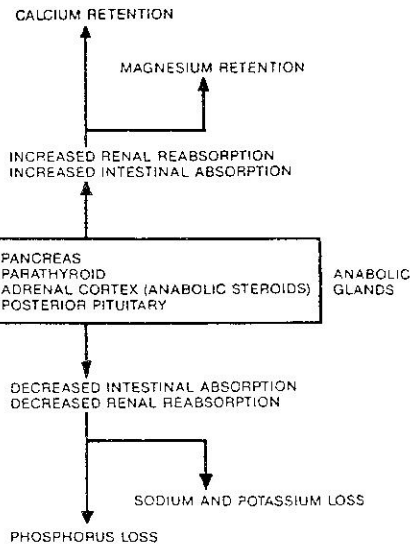


Figure 6



effect on minerals other than calcium and phosphorus, which can also be classified as either stimulatory or sedative.

Figure 5 shows the sympathetic glandular influence on calcium and phosphorus. The catabolic glands increase the intestinal absorption and renal reabsorption of phosphorus while decreasing the absorption and reabsorption of calcium. Along with an increase in phosphorus retention, there is also a corresponding increase in sodium and potassium retention. With a loss of calcium there is usually a corresponding loss of magnesium.^{37 38 39 40 41 42 43 44 45 46 47} Therefore, phosphorus, sodium and potassium are considered sympathetic or stimulatory nutrients.

Figure 6 represents the minerals affected by parasympathetic neuroendocrine dominance.^{48 49 50 51 52 53} Calcium and magnesium are retained relative to phosphorus. Sodium and potassium will usually be excreted along with the increased excretion of phosphorus.

We can therefore classify some of the major minerals into sympathetic and parasympathetic categories due to the neuroendocrine influence.

The vitamins can also be classified due to their influence upon mineral metabolism or absorption. Some vitamins and minerals, as shown below, can be considered transitional in that they can produce either a stimulatory or sedative effect depending upon their enzymatic and coenzymatic involvement.

Stimulatory Nutrients Sedative Nutrients

Minerals

P-Na-K-Fe-Mn-Se Ca-Mg-Zn-Cu-Cr

Transitional Minerals

Zn-Cu-Se

Vitamins

A-E-B₁-B₆-B₁₀ D-B₂-B₁₂-choline

Transitional Vitamins

B₅-B₆

Sympathetic and Parasympathetic Classification of Foods and Water

By understanding the neuroendocrine influence of nutrients, especially the trace elements, any substance can then be categorized. Foods, water, herbs and drugs

will all fall into either a stimulatory (sympathetic) or sedative (parasympathetic) category. Foods and water are classified according to their predominant mineral content or inhibitory mineral absorptive effects. Drug classification can be based upon their sympathomimetic-sympatholytic or parasympathomimetic-parasympatholytic effects as well as their effect upon mineral metabolism, absorption and excretion.

Food Classification

Naturally occurring substances in foods can inhibit the absorption of minerals. For example, oxalic acid found in foods such as spinach, beet greens and others can combine with calcium in the intestinal tract, rendering it unabsorbable. Phytic acid reduces calcium and zinc absorption and is prevalent in cereal grains and wheat. Soaking these foods to reduce their acid content is often advocated. However, in looking at their mineral content, we find that they are still high in stimulatory minerals relative to the sedative minerals and can be classified as stimulatory (sympathetic) in nature. The mineral content of foods will vary according to that of the soils in which the food is grown, as well as processing methods and type of cooking utensils used in preparing it (copper, aluminum, etc.).

Protein Foods

Protein has the highest Specific Dynamic Action (SDA), and therefore produces the greatest increase in the metabolic rate (sympathomimetic). Part of the effect is due to the calcium and magnesium excretion produced by protein. High density proteins have a higher SDA than low density proteins, with beef having a greater action than fish or fowl, and vegetable protein having the lowest SDA.

Water-Herbs

Hard water, which has a high total hardness is usually alkaline. The sedative minerals calcium and magnesium are also usually high relative to the stimulatory minerals, and therefore, is considered sedative (parasympathetic).⁵⁴

Softened water is considered stimulatory (sympathetic)⁵⁵ as it has low total solids

and is generally acidic while dominant in the stimulatory minerals, especially sodium.

The use of herbs can also be made more specific based upon their stimulatory or sedative effects. Continuing research on herbs has revealed their high mineral content, and they are being classified accordingly. An example of a sedative (parasympathetic) herb is horsetail. Its mineral content is high in calcium and magnesium relative to sodium and potassium. As with foods, the mineral content of herbs will vary depending upon the soils in which they are grown.

Drugs

Drugs can be categorized by their sympathomimetic or parasympathomimetic action, which mimics sympathetic or parasympathetic nervous system activity. Some of the sympathetic inducing drugs include epinephrine, phenylephrine and methoxamine.⁵⁶ Other drugs produce a sympathetic action by affecting neurotransmitter release. These include ephedrine, tyramine and amphetamines. These drugs are commonly used in the treatment of bronchial spasms associated with manifestations of asthma and allergies.

Sympatholytic drugs can be considered sedative in that they block sympathetic activity centrally or peripherally by inhibiting or blocking neurotransmission. Centrally acting sympathetic inhibitors include clonidine and methyl dopa. Their common trade names are Catapres, Aldomet and Aldoril. Reserpine and rauwolfia are alkaloids that prevent the synthesis and storage of norepinephrine, while guanethidine blocks its release. Some trade names are Diupress, Harmony and Ismelin. Alpha and beta receptor blockers are prazosin, phenoxybenzamine, propranolol, nadolol and metoprolol. Their common trade names are Minipress, Dibenzylin, Lopressor, Corgard and Inderal. These drugs are commonly used in the treatment of hypertension.

Parasympathomimetic drugs include, acetylcholine, muscarine, pilocarpine, methacholine and carbamylcholine. Other drugs that potentiate the effects of acetylcholine are neostigmine, physostigmine, pyridostigmine and carbamylmethylcho-

line chloride. These drugs are commonly used in the treatment of neurological or neuromuscular disturbances such as myasthenia gravis. For a further listing of sympathetic and parasympathetic drugs consult the *Physicians' Desk Reference*.

Drugs also interfere with nutrient absorption and retention. As an example, antacids, laxatives, anticonvulsants, corticosteroids and antibacterial agents are known to produce a deficiency of calcium and vitamin D.⁵⁷ They exert a chelating action upon calcium and antagonize the metabolic effects of vitamin D. Prolonged use can lead to rickets, osteomalacia and other calcium deficiency disorders. An individual's nutritional status in turn can also affect the metabolism of drugs.^{58 59 60}

Classification of Disease Processes

In order to be able to use the above information, we should become aware of disease conditions that manifest as sympathetic or parasympathetic disorders. The following is a partial list of conditions that can be classified accordingly. This list is compiled as a result of clinical research and evaluation of over 100,000 TMA profiles submitted by doctors throughout the country. This list should not be considered complete or absolute as there are always exceptions. For instance, hypertension can occur both sympathetically and parasympathetically due to different causative factors. An increase in sympathetic stimulation does contribute to hypertension, but arterio and athero-sclerosis can also produce hypertension, either sympathetically or parasympathetically.

Sympathetic	Parasympathetic
Anxiety	Arthritis (osteo)
Arthritis	Allergies
(rheumatoid)	(low histamine)
Allergies (histamine)	Asthma
A.L.S.	A.I.D.S.
Hypertension	Anorexia
Hyperthyroid	Fungus
Hyperadrenia	Hypotension
Hodgkins	Hypothyroid
Leukemia	Hypoadrenia
Infections (bacterial)	Infections (viral)
Myasthenia Gravis	Lupus
Multiple Sclerosis	P.M.S.
Ulcers	Yeast

(peptic or duodenal) Ulcers (gastric)
Diabetes Diabetes
(juvenile) (adult onset)

Nutritionally Induced Deficiencies

Nutritionally induced deficiencies (relative or absolute), are not uncommon and have often been brought about by nutritional megadosing. Megadosing, especially of single nutrients, which may occasionally be called for, will produce a pharmacological reaction. The response to mega therapy's high nutrient intake (vitamin or mineral) can be interference with the utilization of another nutrient, thus becoming an antivitamin or antimineral. The results may be favourable but, if continued for long periods, could eventually produce an induced deficiency of another nutrient. As an example, excessive vitamin E intake will produce signs and symptoms similar to a vitamin A deficiency. Supplementation of vitamin A will counteract the effects of vitamin E and will eventually produce a vitamin D deficiency. These side effects could be prevented simply by reducing the intake of vitamin E. As another example, if a patient is experiencing calcium deficiency symptoms and is not responding to 800, or 1000 milligrams of calcium supplementation per day, the clinician's first inclination is to increase the dosage, perhaps two or three times this amount. This may improve the patient's symptoms but, even after several months, reduction in calcium intake will result in an almost immediate return of symptoms. In order to maintain the patient in an asymptomatic state, the dosage requirements will usually increase with time rather than decrease. If the synergists and antagonists of calcium are considered, such as the addition of vitamin D, magnesium, or copper, and the reduction of vitamin E, vitamin A, potassium, phytic and oxalic acid foods, the patient may respond to only 400 milligrams of calcium supplementation per day.

Conclusion

* The understanding of nutrition and its important role in health is continually developing and becoming more accepted as an intricate part of health care, particularly among today's progressive health care providers. In the book *Nutrition*

Immunity and Infection, Mechanisms of Interactions, R. K. Chandra states that "... the function of many cell types have been found to be altered in nutritional deficiency states." Chandra reported his observations that not only undernutrition, but overnutrition can alter immune responsiveness. This is especially true of trace element nutrition, in that too much of an element can be as detrimental as too little.

Absolute mineral deficiencies are rare today, however relative deficiency states are common. With a better understanding and application of these concepts, a more comprehensive eclectic approach to health care can be realized, thus avoiding the examples of nutritional roulette described previously. Specific application of the known stimulatory and sedative substances to individual treatment may then lead to improved responses with fewer undesirable side effects.

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