Trophopathic Diseases or Systemic Nutritional Disturbances as Reflected in the Mouth

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Trophopathic Diseases or Systemic Nutritional Disturbances as Reflected in the Mouth*

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[EDITOR'S NOTE: *At first glance this article may not attract the reader's interest; the subject matter appears to be completely foreign to dentistry. However, we assure our readers that if they will but read it, they will be fascinated by it.*]

Trophopathic diseases is a term which I suggest as a classification of a group of systemic clinical entities due primarily to nutritional disturbances, which you, as dentists, see reflected in the oral cavity.

I believe there is a common denominator as an etiologic basis in pellagra, sprue, pernicious anemia, and certain degenerative diseases of the central nervous system, even though, pathologically, different anatomical systems are predominantly involved. This common denominator is fundamentally a disturbance of nutrition based on a failure of certain enzyme systems to function normally. The purpose of this paper is to attempt to correlate some of these facts in the light of our present knowledge.

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The concept of the electrical constitution of matter is hardly more than three decades old, but the resulting impact on man's thinking has been staggering to the imagination. When anyone mentions the atomic bomb or the splitting of the atom, most of us visualize first an appalling loss of life as part of a war tragedy. On second thought, our minds turn to some peaceful application of atomic power, such as, the driving of a large ship across the Atlantic Ocean by means of a pound of atomic fuel. Since it is natural for us to think in medical terms, the third idea that might occur to us is the use of radioactive isotopes in tracer studies of the metabolism of the body, and the better utilization of radioactive substances as tools in modern medical therapy.

Dr. Laing

ATOMIC AND NUCLEAR FORCES

This morning I should like to discuss with you an atomic relationship quite different from those already mentioned; namely, the concept that atomic and

nuclear forces dominate all the metabolic processes of the human body. Also, that only as we understand the fundamentals of atomic structure, how the electrons, protons and neutrons control the relationships of atoms, how the atoms and their charges determine the activity of molecules, and how the molecules in turn direct the course of all systemic reactions, can we intelligently diagnose human diseases and plan logically for adequate remedy. In other words, and in the last analysis, all the millions of changes which are constantly in progress in every human organism are either normal or abnormal, depending upon the balancing of the positive and negative electrical forces of the reacting components. In fact, all the activities of the body, mental and physical, may be looked upon as being activated by differences in electrical potential, between the atoms and the molecules, inside and outside the billions of cells of which our bodies are made. Of course, the aggregates of molecules are ordinarily called "chemical compounds," and it is of these simplified entities that we usually think when we discuss body reactions. We say, for instance, that magnesium combines with chlorine to form magnesium chloride. What we generally fail to reveal is that magnesium chloride does not act in the body as such, in the bound state as part of a salt. Only in the dissociated form, wherein aqueous solution magnesium acts independently of chlorine, is the body benefited or harmed by the intake of this salt. Here it is important to note that this is true also of the activity of all other salts, as well as of combinations of other chemical groups to form substances that are known as enzymes, which are organic catalysts produced by living organisms.

In fact, it is this particular form of combination—called the enzyme form—which controls the activities of all other substances and reactions in the body. It is this type of product, made up as it is in great variety of positive and negative radicals, especially balanced for specific purposes, which directs the course of the metabolic processes of the human organism. Whatever function of the body you may consider, whether it is tooth growth, gastric digestion, muscular movement, mental concentration, or the mere process of blushing, many enzymes play a role in their initiation and control. They are the prime movers of all body activity; the catalyzers, the directors, the governors, the controls.

ENZYMES

Essentially, enzymes may be viewed as a three-way combination of a metal, a specific protein complex, and one or more vitamins.[1] Until recently it was thought that only one vitamin was to be found in any one enzyme, but with the discovery that folic acid is a vitamin composed in part of another vitamin known as para-amino-benzoic acid, it is conceived that two (or even more) vitamins may combine to form one of the three links in the enzyme chain. The nature of the activities of the enzymes depends obviously upon the kinds of metals, vitamins and proteins involved. It is logical when any one of these three components is altered, either as to type or quantity, that the resulting activity may be changed in character and degree. These enzymes are the tools which the body uses to direct its mental and physical activities. They are the things which first get out of gear when the processes of the body become abnormal. The prevention or remedy of disease must, therefore, come through proper use or manipulation of these systems. We know that we can repress some of them by drug administration, but what we have yet to learn is still more important; namely, how we can stimulate the activity of those that are functioning subnormally, or perhaps hardly at all, even though working in the proper direction.

As dentists, you may logically ask what these enzymes have to do with the problems associated with the diagnosis and treatment of abnormalities of the oral cavity. The answer is that many enzyme systems are involved in the growth of the tooth, its normal nutrition, and its repair processes. Among these I will mention only one; namely, alkaline phosphatase.

This enzyme is activated by magnesium and has to do with the deposition of calcium and phosphorus in tooth structures and bone in general. It is also concerned in the metabolism of phospholipids of the nervous system, carbohydrates, and neucleotides.

As for the saliva, the principal enzyme in the human saliva is ptyalin, which is an amylase. There are also present urease, protease, lipase, maltase, and catalase. There is some evidence that urease aids in protecting tooth structure from caries decomposition by forming ammonia from the urea present in the saliva, thus producing alkalinity which tends to offset the damaging effects of the acid-producing bacteria.

VITAMIN C DEFICIENCY

You are all familiar with gingivitis and the relationship of Vitamin C deficiency as one of the factors producing pathological changes in the endothelial walls of the capillaries, because of a reduction in the amount of intercellular substance. When this deficiency is marked, the gingiva are swollen, spongy and hemorrhagic; bone is absorbed in the alveolar processes, and the teeth become loosened. All fibrous tissue in the body is involved in the extreme condition of scurvy, but the dentin, cartilage, bone and vascular endothelium are especially involved.

The tongue is an organ which may reflect in vivid fashion many pathological states resulting from the imbalance of various enzymatic systems. Very striking among these are the disease entities known as sprue, pellagra and pernicious anemia. For example, Bicknell and Prescott[2] say:

"These are three separate disease entities, but there is good reason for believing that they are allied nutritional diseases. There are many symptoms common to all of them—gastro-intestinal symptoms, neurological manifestations and a macrocytic anemia. A patient with achlorhydria, stomatitis, glossitis, diarrhea, mental depression, involvement of the lateral and posterior columns of the spinal cord, and severe anemia, but no cutaneous lesions, may be suffering from any one of them. If, in addition, there is a characteristic symmetrical, bilateral, exfoliative dermatitis of the hands and feet, a diagnosis of pellagra may be made; if the anemia responds to injections of liver and returns on withdrawing the latter, pernicious anemia is diagnosed; while the passage of large, fatty, fermenting and pasty stools confirms the diagnosis of sprue."

These authors have very aptly expressed the close relationship of these diseases, but I should like to emphasize further some of the various aspects. In any one of the three, we may have a highly variable picture that ranges from the symptoms and signs of anemia on the one hand, to those of marked involvement of the nervous system on the other. As, for example, in pernicious anemia, when the neurological symptoms are marked, the disease is classified as subacute combined degeneration of the cord. However, if the anemia picture is predominant, then the patient is classified as a macrocytic anemic and treated as such. The tingling and numbness, which are often present, are due to peripheral neuritis and may occur many months before the hematologic findings are evident.

PELLAGRA

The classical picture of pellagra as taught with the three "Ds"—diarrhea, dementia and dermatitis—is rather misleading. Clinically, the triad is seldom seen except in advanced cases. The early symptoms are bizarre and ill defined. There may be abdominal pain, muscular weakness, and nervous manifestations, ranging from numbness of the extremities to morbid features and mental confusion, so that we may have peripheral neuritis, encephalopathy, and subacute combined degeneration of the cord occurring in any combination—together or singly—in a patient. The tongue early in the disease is red and swollen at the tip and lateral margins, and there is often a burning sensation which may extend down into

the esophagus and stomach. In my experience, glossitis and the neurological symptoms are the commonest findings, and they occur in individuals with bad food habits which may or may not be associated with alcoholism. They are also found in the so-called "conditioned pellagra," secondary to organic disease, especially of the gastro-intestinal tract. The symptomatology[3] is most marked in the spring and summer months, so in the endemic cases it is definitely seasonal in its incidence.

The consensus in recent years has been that tropical sprue, non-tropical sprue and celiac disease are fundamentally the same condition. But here again there may be involvement of several systems. If certain nutritional defects are dominant, the disease is classified as macrocytic hyperchromic anemia. Yet, as stated above, one of the major complaints is diarrhea. Glossitis may precede such diarrhea by many months, the tongue and mouth become sensitive, and a stomatitis develops. Later it becomes beefy red with atrophy of the filiform papillae, and finally, in long-continued cases, smooth and shiny. Paresthesias (or numbness) of the hands and feet, denoting peripheral neuritis, are common, but the subacute combined degeneration of the spinal cord is rare as compared with its manifestations in pernicious anemia. However, depression, memory loss, irritability and emotional instability may occur. The diet in these individuals has been excessive in carbohydrates and low in proteins, as in pellagra.

DEMYELINATION

The neurological findings in the nutritional diseases of sprue, pernicious anemia and pellagra are due, as you may be anticipating, to the partial loss of the nerve coverings or sheaths—a process called "demyelination." Such demyelination may occur in slight or marked degree in the peripheral nerves, or in the spinal cord, or in the brain. The myelin sheath[4] of the nerve fibers is a semi-fluid, fatty substance, almost white in color. One of its functions is to protect the nerves against irritation or damage. Another, as will be noted later, is to aid in the transmission of nerve impulses. This sheath, which is part of the neuron (a structural unit of the nervous system), is ectodermal in origin, and is the most vulnerable of all nerve cells in the central nervous system, according to Cobb.[5] It is said to be damaged before the axon in such diseases as measles, chicken pox and avitaminosis. A general rule is that the larger, more swiftly conducting axons—which are those with the highest specialization of function—have the thickest myelin sheaths. Incidentally, thiamine[6] is essential in maintaining the energy supply of the myelin sheath, and in metabolizing galactose with the formation of galactolipids which constitute about one-third of the lipids of the white matter of brain tissue. Thiamine is the coenzyme of the enzyme carboxylase, which catalyzes one of the steps in the oxidative metabolism of carbohydrates, such as glucose. Disturbance of this mechanism at this stage leads to an accumulation of pyruvic acid which aggravates the breaking down of the myelin sheath.

E. Weston Hurst,[7] using repeated small doses of carbon monoxide (CO), potassium cyanide (KCN) or sodium azide (NaN_3), produced experimental demyelination in animals. Similar changes followed the administration of barbiturates to monkeys. Larger doses of KCN produced in monkeys a necrosis of the white matter which occurred suddenly and simultaneously over considerable areas of the cerebral hemispheres—a condition not unlike the lesions of Schilder's encephalitis in man and the monkey. According to Hurst, demyelination is a biochemical process involving the metabolism of some enzyme system which is essential to myelin nutrition.

Another observation of great importance is the possible correlation of copper deficiency in soils with myelin degeneration in sheep and in their offspring. The disease is known as "swayback," or "pining," or as "enzootic ataxia." Its symptoms are similar to those of Schilder's disease in man.[8]

Follis[9] presents a very intriguing hypo-

thesis, based on experimental work with swine, in which he states that pyridoxine is intimately connected with the metabolism of myelin, and that pantothenic acid affects the integrity of the cell body itself. He further states that in myelinoclastic diseases, such as multiple sclerosis, the myelin sheath is primarily affected, while in polioclastic diseases, such as epidemic encephalitis, the cell body is first injured and myelin degeneration follows.

RELATED DISEASES

Three disease entities have been reviewed in considerable detail for the purpose of demonstrating the fact to you that they all have a common denominator as far as the nervous system is concerned; namely, demyelination. They share this pathological process with several other diseases which, on first thought, seem not to be at all related. Among these are the following: (1) multiple sclerosis, (2) amyotrophic lateral sclerosis, (3) Friedreich's disease, (4) Schilder's disease, (5) Devic's disease, and (6) certain types of neuritis.

Reference will be made to multiple sclerosis as an example. It is often called "disseminated sclerosis," and is at present one of the commonest chronic diseases of the central nervous system. It appears to be on the increase in the United States, but the incidence here is much less than in certain parts of Europe. The cause of the disease is unknown, and the older theories have been disproved. Among the numerous new theories that have been advanced is that of Morrison,[10] who has succeeded experimentally in producing lesions which resemble those of multiple sclerosis by injection of autoantigens. This suggests a possible relationship with sensitization.[11]

But, before further attempting to explain a possible correlation of these related diseases to specific causative factors, I feel that I must emphasize another common denominator influence; namely, that nervous tissue exhibits a marked preference for carbohydrates as a source of metabolic energy. In other words, glucose and its equivalents are constantly utilized in the maintenance of nerve form and stability, as well as in the energizing of nerve activities. Obviously, when and if there is any interference with the processes of conversion of carbohydrates to their ultimate breakdown products of carbon dioxide and water, there is apt to be nerve irritation, or some degree of dysfunction.

However, this is a very simple statement of a very complex picture. As Dr. Carl F. Cori[12] explains, glucose is converted by step-wise addition of phosphates to simple organic acids, such as pyruvic, lactic, acetic and carbonic, and there are eleven distinct steps in the transition pathway. Each of these steps liberates an additional amount of energy and each is activated by a different enzyme. These added phosphates, through enzyme systems of their own, act as energy carriers by operating what might be called a "shuttle service" between the end products of one reaction and the starting components of the next.

STRATEGIC FACTORS

And this again brings us face to face with a concept that enzyme systems are strategic factors in all these problems. Whatever aids the functioning of the enzymes involved in the nutrition and health of the body's nerves, muscles, and other tissues, helps to prevent or to remedy these myelin deficiency diseases. Conversely, whatever damages these enzyme systems becomes a possible causative factor in the precipitation of these baffling ailments. It is important, therefore, to note some of the substances which commonly inactivate such enzyme systems. Some examples are as follows:

1. *Bacteriotoxins*—Pneumonia, Scarlet fever, Diphtheria, Erysipelas.
2. *Viruses* — Poliomyelitis, Chicken pox, Measles, Herpes Zoster.
3. *Chemicals and Drugs*—Arsenic, Alcohol, Barbiturates, Carbon monoxide, Cyanides, Gold, Lead, Mercury. The list of these dangerous substances is growing

because of the rapid development of our chemical industries.

4. *Mineral Deficiencies*—Iodine deficiency, as commonly found through the so-called goiter belt of the United States, is a typical example. Similar deficiencies are those of manganese, cobalt, and magnesium in the North Central States.

5. *Mineral Excesses*—Too much potassium, iron and fluorine are common examples.

6. *Vitamin and Essential Amino Acid Deficiencies*—As dentists, you can appreciate the fact that any one or several vitamins can be deficient under certain conditions, which is also true of the essential amino acids. An interesting illustration of the profound effect of system involvement on oral manifestations is the transverse ridging of the teeth. It may be found in several acute infections, like scarlet fever, in a poorly controlled diabetic child, or a rachitic child. The explanation for it is a marked disturbance in metabolism, resulting in a temporary interference with tooth growth.

Further experimental work in animals which is highly significant is that of Warkany,[13] who states:

"There exists a widespread belief among the laymen, as well as among physicians, that systemic and multiple congenital malformations are always the result of changes in the "germ plasm," that is, genetically determined and hereditary. This belief is not correct; in fact, it has been shown repeatedly that developmental processes can be altered by environmental disturbances in the same way as by abnormal genes. It will be of great interest to the geneticist that types of congenital malformations, which are sometimes genetically determined, such as microthalmos, cleft palate, brachygnathia, and the like, can be produced in the offspring by maternal deficiencies of well defined chemical substances like Vitamin A or riboflavin. Since it has been suggested that genes act as enzymes, it may be worth while to point out that riboflavin is known to be an essential constituent of a number of enzyme systems which perform specific functions."

7. *Vitamin Excesses*—Syndenstricker[14] has reported that when niacin was given alone to patients with pellagra, certain signs of their disease, presumably due to deficiency in other factors, are intensified. Hopkins[15] mentioned that excess of cod-liver oil was injurious to rats. It has long been known that rich sources of Vitamins A and D may be toxic when given in great excess.

8. *Antivitamins*—This is a subject which has received but little attention, yet is of vast importance. I can do no better than to quote Wooley through Green[16] on this fascinating subject.

"Wooley[17] has pioneered in providing a framework for a rational pharmacology based on the antivitamin concept. He showed that certain antivitamins can produce a state of avitaminosis, in some cases in a matter of hours, merely by displacing the vitamins competitively from their catalytic complexes. Since profound pharmacological effects attend the syndrome of avitaminosis, antivitamins have to be regarded as potential pharmacological agents. Thus, pyrithiamine rapidly induces the disorders of the central nervous system which are characteristic of thiamine deficiency. The lesion is, of course, righted at once by addition of large enough amounts of thiamine. Since the quantitative importance of the catalytic reaction in which vitamins participate varies, depending upon the organ or part of organ, it does not follow that all antivitamins will exhibit similar pharmocological effects. On the contrary, it would appear that each antivitamin would selectively poison only a particular portion of the nervous system, as well as only particular organs. A complete series of antivitamins should provide a wide range of specific pharmacological agents, all of which are reversible by addition of the vitamins which they imitate. The beginnings in this new field of exploration are still modest, but the horizons seem immense."

It is significant that the action of sul-

fonamide is through its interference with the growth of bacteria by its competitive displacements of para-aminobenzoic acid in the nutrient medium.

MINERAL ELEMENTS

In what has gone before I have mentioned a number of mineral elements, but have not stressed them particularly. Now, I wish to remind you that in just the few enzyme systems involved in nerve, brain and muscle tissue, at least the following mineral elements participate: sulphur, magnesium, manganese, calcium, phosphorus, zinc, cobalt, iron, and copper. I am quite sure that there are others, but this is enough to support the concept that the diseases which involve primarily the bone marrow, the blood stream, the lungs, the stomach, the teeth, the muscles, and nerves—and, secondarily, all the organs and parts of the body—are intimately related to the problem of the mineralization of the nation's soils.

If these and the other minerals required by our bodies are plentifully supplied to the plants on which we, or our food-supply animals live, then we can be fairly sure that our own foods will be fully enriched and adequate. But, if our farm soils are not thus adequately mineralized, it is equally certain that we as a people are going to suffer increasingly from the many diseases that are caused directly and indirectly by food-factor deficiencies.

According to a well known authority, Dr. Jacob G. Lipman[18] of the New Jersey Agricultural Experiment Station, the annual loss of mineral elements from the agricultural soils of the nation is little short of alarming. For instance, in one year for which suitable figures were assembled, the gross losses, fertilizer gains, and net losses of minerals were for arable soils and pastures as given in this chart. The "losses" include removal of minerals by cropping and by erosion through wind and water. The "gains" comprise additions of fertilizers, manures, bedding, rainfall, irrigation, seeds and fixed nitrogen.

Probably no worth-while estimate is to be found of the losses from soils of all the other minerals which are utilized by plant and animal life, but it is only reasonable to assume that the depletion of other minerals is very much in proportion to those enumerated in the chart. It is, therefore, equally serious from the standpoints both of crop quantity and food quality.

Obviously, excessive growth of a plant is not a measure of plant health, or a criterion of its nutritive value for human beings, any more than is excessive size of the body a measure of a person's health status. Nitrogen, potash, phosphates and lime—which constitute the principal

Annual Balance of Plant Nutrients in Soils of the United States, 1930

TONS

	LOSSES (Harvested Crops, Grazing, Erosion, Leaching)	ADDITIONS (Fertilizers and Liming Materials, Manures and Bedding, Rainfall, Irrigation Waters, Seeds Nitrogen Fixed)	NET ANNUAL LOSS
NITROGEN	22,899,046	16,253,862	6,645,184
PHOSPHORUS	4,221,302	1,447,835	2,773,467
POTASSIUM	50,108,560	5,151,076	44,957,484
CALCIUM	68,185,730	12,561,673	55,624,057
MAGNESIUM	24,557,881	4,040,813	20,517,068
SULPHUR	12,043,901	9,029,690	3,014,221

(All figures subject to change and correction.)

mineral elements in commercial fertilizer —can produce increasing crop yields when supplied liberally to run-down soils. But these do not assure crops of greatest nutritive value. In fact, the opposite result may often be obtained. For an excess of lime will render iron, manganese, boron and other essential elements relatively unavailable to the plant.

IMBALANCE OF MINERALS

This explains to some extent why an imbalance of minerals increases the susceptibility of plants—both fruits and vegetables—to blight and to rotting, and also why it is important for humans to use as foods only those plants (or the animals living on such plants) that are known to be internally sound and healthy, rather than those that are good merely in outward appearance. For it is not only the pick-up of minerals obtained from well nourished plants that counts—it is still more important that such plants contain the complex organic substances which plants synthesize through the mediation of the complete soil mineral assortment. This further explains also how the mineral composition of the soil influences the vitamin content of the plant. For instance, boron in the soil increases the Vitamin A content of apples, and manganese enhances the vitamin content of tomatoes, strawberries, and other fruits. "Mottle leaf" of citrus, and "rosette" of fruit trees are common diseases known to be due to a deficiency of zinc. Mentioning only a few of the minerals which play a strategic role in animal nutrition, I remind you that copper, as has long been known, is an important factor in the formation of hemoglobin. It also is a component of the ascorbic oxidase enzyme, and of the enzyme tyrosinase, which has to do with the metabolism of tyrosine, one of the vital amino acids. As in plants, however, so in animals, there is such a thing as an excess of copper. It can become a body poison.

Cobalt, too, is related to hemoglobin synthesis, and its biological importance is revealed by the fact that it is a component of the recently discovered Vitamin B 12. This vitamin is being heralded as of value in the treatment of the neurologic and hematologic phases of pernicious and other types of macrocytic anemias. While results are yet to be proved, it is significant that a metal such as cobalt is apparently a catalyzer of this vitamin activity. A material excess of cobalt produces an abnormal increase in red blood cells, or a condition known as polycythemia. The most recently discovered member of the Vitamin B complex is B 14. It is possible

Amino Acid Content of Alfalfa Hay According to Soil Treatments with Trace Elements

(PERCENTAGE OF DRY LEAVES)

Plot No.	1.	2.	3.	4.
Treatment	Calcium	Calcium & Manganese	Calcium & Boron	Calcium & Mixture*
Valine	2.19	2.40	2.13	2.59
Lucine	4.37	4.89	5.55	5.24
Arginine	0.380	0.434	0.418	0.415
Histidine	0.654	0.807	0.726	0.835
Threonine	0.862	0.954	1.071	1.014
Tryptophane	0.546	0.640	0.856	0.670
Lycine	1.57	2.12	2.13	1.87
Isoleucine	2.64	3.63	4.09	3.44
Methionine	0.100	0.242	0.173	0.229

* Mixture of cobalt, copper, zinc, manganese, and boron.

that it will prove to have a bearing on the formation of some part of the hemoglobin molecule.[19]

ZINC

Zinc is another mineral element which plays a role in many metabolic processes of the human body. It is associated with the production of insulin, with the release of carbon dioxide from the blood into the lung spaces, and possibly with the formation of gastric juice by the stomach mucosa. Strange as it may seem, the concentration of zinc in the dentin is many times greater than in the blood stream, yet apparently none of it is found in the tooth enamel. As a component of the enzyme, carbonic anhydrase, zinc is concerned with the speed of impulse transmission in the nervous system.

As for phosphorus and potassium, all plants need them for growth and both are required in liberal quantities by animals and man. However, an excess of potassium can be toxic to man, for in such quantities it suppresses nerve impulse transmission and causes paralysis. Likewise, in the soil, an excess of potassium interferes with proper plant growth and retards the synthesis of some of the B complex vitamins. Also a lack of phosphate reduces the synthesis of riboflavin by plants and in animals has several deleterious effects, e.g., the excessive excretion of calcium. As one authority, Dr. H. H. Mitchell[20], University of Illinois, says: "Regardless of huge stores of phosphorus in the skeleton, the animal lives on a hand to mouth phosphorus supply for anabolic uses."

Now considering that an important factor in the enzyme systems of the body is the protein content, it is well to note experiments by Sheldon, Blue and Albrecht,[21] Missouri Agriculture Station, who, along with other prominent researchers, have shown conclusively that even minor deficiencies of the so-called trace minerals in soil greatly alter the character of the protein content of animal and human foods. For example, this chart shows that as we vary the calcium content of soils, the ratios of the amino acids of hay, alfalfa, and lespedeza are materially altered. The same is obtained by changing the soil content of copper, boron, cobalt, manganese, and zinc. These are only a few examples of the damaging effects resulting from soil deficiencies of these items. In other words, it is easy enough to understand from these figures that the composition of the hay or wheat or corn, or of any other crop grown in a particular part of the United States 50 or 100 years ago was quite different from the composition of the same plants grown in the same soil today.

It thus becomes apparent that there is a balance in nature which cannot safely be ignored, and this applies first to soil, then to plants, animals, and man,—since man acquires all the elements that constitute his makeup from these sources.

SUMMARY AND CONCLUSIONS

We have discussed the obvious pathology and, I fear at times, the end point or the irreversible. However, the lesions which are not so obvious should be the ones to command our attention.

If we accept the concept of the electrical constitution of matter, we cannot escape the conclusion that all change is organic, and thus it becomes evident that the psyche and soma, or the mind and body, cannot be separated. Differentiation between functional and[22] organic disease is purely arbitrary. What is functional today will be organic tomorrow when the technical advances will allow us to interpret the biochemical lesions which up until now have not been appreciated.

The diseases which we have discussed have all been associated with positive etiologic factors, at one time or another, such as bacteria, fungi, and viruses. In the light of our present knowledge it would seem more logical to ascribe negative factors as the primary causative agents in many of them. The lack of these substances or the failure to utilize them, producing disturbances in the enzyme systems, and thus an unbalanced state in the organism resulting in what we term a morbid state or disease. I

would like again to emphasize that these "Trophopathic Diseases" are primarily caused by disturbances of nutrition, and, secondarily, at times by some of the above positive factors when some of the defense mechanisms have been interfered with.

Let us hope that we are cognizant of the tremendous role that emotions can play in producing pathology in the organism, but let us not ignore such fundamental considerations as the part played by the basic mechanisms that control the irritability and metabolism of the cell itself.

In conclusion, may I reiterate that what you see as dentists, and what we see as physicians is but part and parcel of the same morbid processes. We must view these trophopathic diseases with a broad understanding, bearing in mind, if we are to do the best for our patients, that we must consider some of these processes to be less irreversible than has commonly been thought in the past. We must approach our work with the optimism that is warranted by the research advances in the sciences of which we are a part.

BIBLIOGRAPHY

1. GREEN, D. E.: *Advances in Enzymology, Interscience, New York, 1941, Vol. 1, p. 177.*
2. BICKNELL, F. and PRESCOTT, F.: *The Vitamins in Medicine, 1947, p. 352.*
3. SPIES, TOM D.: *Rehabilitation Through Better Nutrition, 1947.*
4. ELLIOTT, H. C.: *Textbook of the Nervous System, 1947, p. 113.*
5. COBB, S.: *Foundations of Neuropsychiatry, 1948, p. 142.*
6. WEIL, A.: *Textbook of Neuropathology, 1945, p. 204.*
7. HURST, E. W.: *Experimental Demyelination of the Central Nervous System, Australian Journal of Experimental Biology, 1942, Vol. 20, pp. 297-312.*
8. FOLLIS, R. H.: *Pathology of Nutritional Disease, 1948, p. 52.*
9. FOLLIS, R. H.: *Pathology of Nutritional Disease, 1948, p. 233.*
10. MORRISON, L. R.: *Disseminated Encephalomyelitis Experimentally Produced by the Use of Homologous Antigen. Archives of Neurology and Psychiatry, 1947, Vol. 58, pp. 391-416.*
11. COBB, S.: *Foundations of Neuropsychiatry, 1948, p. 176.*
12. CORI, C. F.: *Northwestern University, Lecture in Biochemical Chemistry, Dec. 1948.*
13. WARKANY, J.: *Vitamins and Hormones, Edited by Harris, R. S. and Thimann, K. V., 1945, p. 97.*
14. SYNDENSTRICKER, V. P.: *Annals Internal Medicine, 1941, Vol. 15, p. 45.*
15. HOPKINS, F. G.: *British Medical Journal, 1923, Vol. 11, p. 693.*
16. GREEN, D. E.: *Currents in Biochemical Research, p. 160.*
17. WOOLEY, D. W.: *Science, 1945, Vol. 100, p. 579.*
18. LIPMAN, J. G.: *New Jersey Agricultural Experiment Station Bulletins, 1930.*
19. NORRIS, EARL R. and MAJNARICH, JOHN J.: *Action of Enzymes on Vitamin B_{12} and Pteridines. Science, 1949, Vol. 109, pp. 33-35.*
20. MITCHELL, H. H.: *Journal of Animal Science, 1947, Vol. 6, p. 365.*
21. SHELDON, V. L., BLUE, W. G., and ALBRECHT, W. A.: *Diversity of Amino Acids in Legumes According to the Soil Fertility, Science, Vol. 108, pp. 426-428.*
22. COBB, S.: *Foundations of Neuropsychiatry, 1948, p. 100.*

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