THE PLACE OF NUTRITION IN THE RELATIONSHIP BETWEEN ENVIRONMENT AND HEALTH

H. D. KRUSE, M.D.

IN THE relationship of environment to health and welfare, nutrition occupies a key position. For, many environmental factors, inside as well as outside the body, exert influences upon nutrition which it in turn reflects in health and welfare. As an intermediary, it is at once a clearing house and relay system. To show its strategic position, as well as its complex and intricate nature, let us first take an inventory of its known relationships demonstrated from data on man. For with full acknowledgement of underlying animal studies for their vast accumulation of knowledge upon which the science of nutrition was erected, its ultimate acceptance and application depended upon demonstration in man.

In many minds diet is so closely associated with nutrition that often the terms are used interchangeably with complete confusion from lack of distinction between them. Nutrition is a bodily process; diet refers to a regimen of food which supports nutrition. Over the past decade particularly, computations on food production and imports have yielded data on per capita consumption of foods (1). Numerous diet surveys in their various forms and determination of levels of nutrients in blood have revealed dietary patterns in terms of foodstuffs or their component nutrients (2, 3). From the results of these inquiries, valuable generalizations have been drawn. Even with standards set so low that few would dispute their decisiveness, a substantial prevalence of unsatisfactory diets has been recorded. Furthermore, interesting regional differences appear both in the prevalence of deficient diets and in the nature of the inadequacies. That economic forces influence the diet is well-known. For one thing, in general the nutritive quality of the diet varies with the income level. The poorest diets and greatest percentage of poor diets are found in lowest income groups. Then too, when low incomes remain stationary with

increase in cost of obligatory items in the budget, such as rent, the allotment for food suffers. Contrariwise, when low incomes are raised, families reflect the favorable change in their fortunes by an upward shift in the character of their diet. In some instances it has been shown that within the family, food was not distributed among its members according to their needs; the mother spared others and fared worst.

Data with an even closer bearing upon the problem have come from surveys of nutritional status with identification of malnourished persons. After physical measurements had been abandoned because they were not sufficiently sensitive, accurate, or comprehensive, and biochemical determinations of the concentration of nutrients in the blood had likewise been rejected because they reflected, not nutritional status, but dietary intake, appraisal from clinical signs was adopted (4). While controversy has raged over the association of these signs with specific nutrients, most observers agree at least that they are related to nutrition. Surveys have revealed an appreciable proportion of malnourished persons: exactly how many has depended on where the scale was set (2). As in dietary pattern, the worst nutritional status and the highest percentage of poor status are found in the lowest income groups. What at first was surprising but upon reflection became understandable, the proportionate prevalence and severity of the signs of malnutrition increased with age (4).

After the collection of data on dietary intake and clinical signs of deficiency states, the second stage in the epidemiological approach to malnutrition in its natural setting was the attempt to demonstrate association between the two sets of data. One successful example is noteworthy because it comprised a disease that had not yet been established as having a deficiency origin. Within a limited radius Goldberger, Wheeler, and Edgar Sydenstricker demonstrated differences in food supply and incidence of pellagra that were related (5). But the method of correlations has its limitations in proof of etiology. If a positive association is found between two sets of data, it does not necessarily

indicate a causal relationship; if the association is suggestive of a causal nexus, it does not point out which member is cause and which is effect; if one element is identifiable as the cause, it is not necessarily the only cause. Appreciating these points Goldberger turned to the experimental production of pellagra and its cure for demonstration of its nutritional character. But this example is not typical of the data or kind of correlation applied to it today. For one thing it comprised extremes in diet and deficiency disease. Particularly, it should be noted that pellagra represented a somewhat fully-developed, florid deficiency state. Then too, correlation was sought between pellagra and diet, not a particular component of the diet.

Present-day attempts start with the assumption that prevalence of dietary deficiency in a particular nutrient and clinical signs attributed to it should show positive correlation. With some exceptions, this expectation has proved disappointing. Evidence indicates that under certain limited circumstances, it is obtained. But for the most part, there is no association. Two possibilities appear. Shortcomings in the collection of data and use of equivocal standards in the dietary survey; and subjective differences in observation and standards in clinical appraisal may have vitiated the results. Or, secondly, rather than reject the results of attempted correlation because they do not substantiate a preconceived notion, it might be better to accept them and scrutinize the basis of the conflicting assumption. Comment here will be restricted to this latter approach because its range of influence not only covers much of the first, but goes far beyond it.

It is indeed helpful to note the particular procedure of inducing deficiency states and the type of resulting diseases which helped to mold the traditional prevailing concepts of their cause and nature; for quite understandably they led to the erroneous assumption that short-term dietary data and nutritional status should of necessity exhibit a positive correlation. The view on etiology was derived from experiments in which deficiency diseases were induced in animals by subjecting them unremittingly

to a diet nearly totally deficient in a nutrient. Animals were plunged into a deficiency state. The only variable studied and allowed to differ between groups was diet. All other environmental variables were minimized or equalized and therefore ignored. When this procedure with animals is compared with the free operation of many factors on man in his environment, there are more points of difference than similarity. The deficiency disease produced in animals by this procedure was analogous to the florid type traditional in clinical medicine, but not to other forms beginning to be recognized. Could these concepts of the character of a deficiency disease and its production be inadequate?

By integrating observations on their pathology, signs, and response to therapy, it has been possible to create a broader concept of the character and course of deficiency states that takes in all the facts (6). In its essentials it points out that deficiency states are characterized by three quantities: speed, intensity, and stage. In speed the deficiency process may be acute or chronic. Although finer divisions are recognizable, according to the simplest classification, it may be mild, moderate, or marked in degree; and it may be early, intermediate, or advanced in stage. Time which appears in both the speed and duration of a deficiency state is an important element in this concept. Actually, the acute form in man is an exacerbation. It is a transitory episode arising out of the chronic and subsiding into it. It does not persist since it either leads to death or most frequently disappears. Its dramatic character imparts to it an importance out of all proportion to its prevalence. In contrast, the chronic is persistent and basic since it underlies the exacerbation. The chronic, furthermore, is the most prevalent type. It should be emphasized that the tissue changes in the acute and chronic forms of a deficiency state occur in the same sites but are different in pathology. Significantly, many signs of the chronic type have been regarded in the past as signs of aging. This concept of deficiency states, particularly its element of time, explains in large part why

positive correlation between diet intake and clinical signs is obtained only under narrowly limited circumstances. Time is required for the effects of poor diet to be manifested in tissue pathology. As a corollary, diet may change quickly either improving or worsening without absolute concurrent change in tissue pathology. Most importantly, on the other hand, tissue manifests cumulative as well as contemporaneous pathology. Naturally the cumulative pathology bears no necessary comparable relation to the dietary record during a particular limited period. Further, the concept explains the recorded differences in diagnosis, prevalence, and therapeutic response. Most important, it opens new vistas of investigations in medicine.

The prevalent view of etiology has been simple: faulty diet causes deficiency disease. But this doctrine, reflecting mostly one source of data, has never been sufficient to cover all instances; and upon closer scrutiny it becomes apparent that it does not embrace all the components in any instance. It has long been known that other factors than diet affect nutrition. In 1866, long before the nutritional character of pellagra was recognized, Roussel pointed out that the efficient cause had to be in conjunction with a set of conditions for production of that disease (7). McCarrison, in 1921, in his book STUDIES IN DEFICIENCY DISEASES devotes a chapter to Factors Influencing the Onset of Morbid States Due to Food Deficiency (8). As the list of these items has meanwhile been extended, they have been variously designated but today most commonly as conditioning factors (9). But, because it has been difficult to relate many of them to diet, it has been equally difficult to place them in the existing etiological scheme; consequently, they have been treated as something separate and apart. The result has been a narrow, disjointed view of etiology, never an inclusive, integrated system.

I should like to present briefly a new concept of the etiology of deficiency states (10) that accommodates all the seemingly divergent aspects. (Fig. 1.) Tissue nutrition in respect to the biologically active form of any nutrient depends upon the ratio

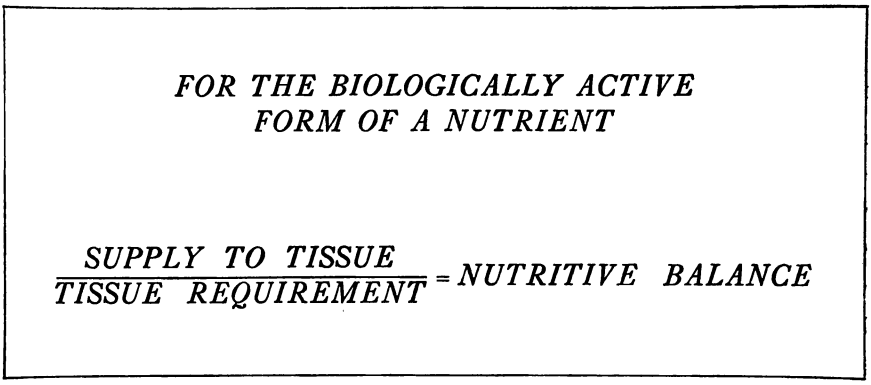

Fig. 1. Ratio determining nutritive balance of a tissue in respect to the biologically active form of a nutrient.

of $\frac{\text{tissue supply}}{\text{tissue requirement}}$. At any given time, the just previous tissue status $\times$ the ratio = current tissue status. All the external and internal environmental factors that influence either or both members of the ratio in whatever direction are conditions, a precise yet shorter term for conditioning factors. (Fig. 2.) These exceedingly numerous conditions may be conveniently classified according to their natural location and character which have, however, no necessary bearing on the manner in which they act upon the ratio. (Fig. 3.)

Conditions that increase the numerator or decrease the denominator tend toward making the ratio favorable; those that operate oppositely conduce to an adverse ratio. (Fig. 2.)[1] In a broad, loose sense, an adverse ratio and the combination of conditions responsible for it comprising a complex can be regarded as the cause of the resulting deficiency state in the tissue and its ensuing pathology. But in the interest of clarity and precision in delving into the etiological system, a distinction should be drawn between the ratio and the conditions. The adverse ratio is the primary, direct, immediate cause of the tissue deficiency process; while the combination of conditions influencing the ratio to that end are secondary, indirect, mediate causes. Most

[1] Parenthetically, it should be noted that for some nutrients the ratio has an optimum zone above which as well as below which it is adverse. For example, a supply of lipogenic nutrients in excess of requirements would be conducive to obesity.

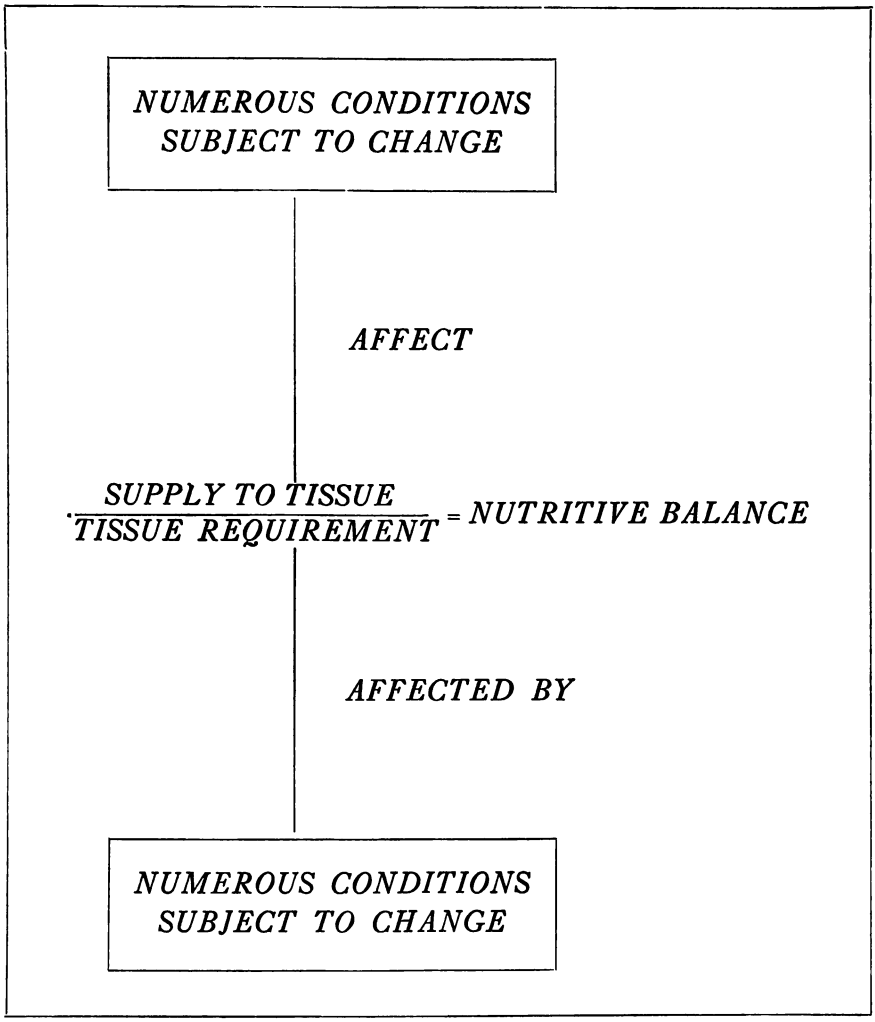

Fig. 2. Action of conditions on members of ratio determining nutritive balance.

simply and accurately designated, the adverse ratio expressing deficiency is the cause; factors responsible for its unfavorable level are adverse conditions. These conditions are a prerequisite to its existence and continuation as well as a qualification determining its alteration or cessation.

Several features of this etiological system merit comment. One is the dynamic behavior of the ratio. Conditions capable of change are constantly exerting influence on it. Another charac-

CLASSIFICATION OF CONDITIONS

1. *External Environment*

a. *Socio-Economic*
- Living conditions
- Working conditions
- Available foods
- Ability to seek them
- Income
- Education

b. *Physical and Chemical*
- Radiant energy
  - Light, infra-red
  - Ultra-violet, x-ray
  - Radioactive
- Temperature
- Mechanical
  - Trauma
  - Physical movement
  - Pressure; irritation; friction
  - Occlusion
  - Dentures
- Toxicants

c. *Dietary*
1) Form of nutrient
   - Provitamin: analogue
   - Potential or intrinsic biological activity
2) Level
3) Imbalance—
   - Disproportion
4) Interrelations
   - a. Protein-Carbohydrate-Fat
   - b. Vitamin-Vitamin
   - c. Vitamin { Protein / Carbohydrate / Fat }

2. *Bodily Environment*

a. *Digestive and Metabolic Channels*
- Functional form of nutrient
- Appetite
- Ingestion
- Digestion
- Absorption
- Transport
- Formation of enzyme
- Breakdown of enzyme
- Elaboration } Metabolism
- Utilization } Metabolism
- Storage
- Metabolic level
- Excretion
- Biosynthesis
  - Intestinal synthesis
- Biodegradation
  - Intestinal destruction

b. *Functions and Reactions*
- Disease { Degenerative / Neoplastic / Organic / Toxic / Infectious }
- Chemotherapy
- Endocrine relationship
- Nutritional status
  - Morphology and physiology of tissue
- Growth
- Pregnancy
- Lactation
- Work
- Psychobiology
  - Food habits
  - Psychosomatic reactions

5) Inhibitors—Antagonists
   - Anti-vitamins
6) Enzymatic destruction
7) Autoxidation-rancidity
   - Oxidants-autoxidants
8) Processing of foods
9) Availability of nutrients
   - Precipitation
     - Phytic acid—Iron
     - Oxalic acid—Ca
10) Acceptability—
    - Palatability

Fig. 3. Classification of conditions affecting the ratio according to their natural location and character. The list is not exhaustive.

teristic is the multiplicity of conditions in action at any one time. Some are continually in operation; others are occasional. It is the net effect of the aggregate that determines the quotient. Never is one solely responsible for an adverse ratio. Thirdly, since not only the cast of conditions but also the degree of influence of any condition may change from time to time, the etiological complex exhibits relativity. At any one time, the influence of each adverse condition is relative; at another time the relative influence of each adverse condition in the composite may have changed. Fourthly, expressing a dynamic process, the ratio is characterized by velocity, intensity, and duration, which it derives from the resultant of many conditions and imparts to the tissue. Here again, time through its inherence in velocity and duration is an element in etiology as it is in the resulting pathological process in the tissue.

To clarify what is meant by conditions and how they influence the ratio, it might be helpful to cite a few familiar examples of them and their effect on the development or accentuation as well as on the subsidence of deficiency states. (Fig. 3.) A gastro-intestinal disorder may impede absorption and transport of nutrients and thereby interfere with supply to the tissues. Decrease in supply diminishing the quotient of the ratio tends to a deficiency state. With abatement or disappearance of the adverse condition, supply and the resulting quotient would increase unless other unfavorable conditions intervened with counteraction.

Acting on the other member of the ratio, growth, pregnancy, and physical labor are conditions conducing to deficiency states by raising the level of requirements. It is a byword that young animals subjected to an incomplete diet must grow if they are to develop acute deficiency states. Growth makes exacting and unyielding nutrient demands which reduce the quotient and accentuate the deficiency state. Arrest of growth with consequent lowering of requirements changes the denominator in the opposite direction. As another example, signs of deficiency states may flare up during pregnancy. That an increase in nu-

trient requirements is associated with pregnancy is generally accepted; this increase in the divisor of the ratio, operates adversely towards reducing the quotient. With the termination of pregnancy, its effect on the ratio ceases; its particular aliquot of the divisor drops out.

In historical accounts it is recorded that among sailors with scurvy, hard work often precipitated collapse. Conversely, a pellagrin put to bed, even though continuing to eat a pellagra-conducive diet, shows remission for a time. Here the lowering of requirements from reduced activity is tantamount to nutrient therapy; for reducing the denominator has the same mathematical result as increasing the numerator. It should be noted too that conditions differ in their efficiency of exercising influence on the ratio. Although it may seem odd, it is nevertheless true that bed-rest is nutrient therapy in highly effective form.

In all three examples, growth, pregnancy, and work, the recognition of increased requirements associated with them is evidenced by larger recommended dietary allowances. The attempt is to increase supply to counterbalance the increased requirements. But to repeat, although each of the three conditions may precipitate an aggravation of deficiency states, it should not be concluded that any of them alone can bring it about. Unless other adverse conditions, such as inferior diet, disease or pre-existing poor nutritional status prevail, growth, pregnancy, or physical exertion does not set off deficiency signs. Of the aggregate of adverse conditions contributing to an unfavorable ratio, one is usually decisive in the sense that it adds enough to tip the scale. It is, however, not necessarily the major adverse force; rather its timing attracts disproportionate attention to it.

At the risk of seeming to minimize diet, whereas the intent is to bring the ensemble of conditions in proper perspective in which neglected members are elevated to their rightful place, it should be pointed out that poor diet is not the cause of a deficiency state but a condition conducive to it. Poor diet alone

cannot produce a deficiency state; for it is never the sole condition in operation—other conditions intrinsically participate. Deficiency states may even occur when diet is satisfactory and therefore operating favorably on the ratio. True, in many, if not most, instances of deficiency disease, poor diet is the major adverse condition; but in other instances, it is a minor condition. Sometimes deficiency disease occurs when diet is not an adverse condition.

Besides these more familiar examples, the list includes several conditions less commonly recognized as related to nutrition. Mechanical stress, a general term covering many specific situations, is a condition affecting the nutrition of tissues. It may be recalled that one of the usual signs of scurvy in the infant is subperiosteal hemorrhage in the thigh, a site of considerable movement. Contrariwise, when the hind leg of a guinea pig on a scurvy-conducive diet is immobilized, acute changes do not occur (11). Similarly, it is probable that movement of the tongue, one of the most active organs in the body, contributes to the acute glossitis of pellagra. In a kindred category is pressure, such as occurs in dental occlusion. In its more severe form of malocclusion even greater pressure is applied on fewer points of contact. It then becomes understandable why the severest changes in gingivitis of avitaminosis C are often located at these sites. Ill-fitting dentures in their effect on the gums and angles of the mouth fall in the same category. Another type of condition apt to be overlooked is radiant energy. Intense light or glare aggravates or elicits photophobia and lacrimation in persons affected with ariboflavinosis. Conversely, confinement to a dark room or use of dark glasses is a temporary expedient minimizing an aggravating condition. It should be repeated that they are conditions, not causes; that they affect the nutrition of tissues; and that each may contribute to a deficiency state but alone is not responsible for it.

Two of the most influential adverse conditions are infection and existing poor nutritional status. Twenty-five years ago it was vigorously debated whether xerophthalmia was an infection

or a deficiency disease. Careful histopathological studies settled the issue: xerophthalmia was shown to be a deficiency disease in which infection usually supervened (12). Other deficiency states have now been observed to conform to the same pattern. At a certain stage in their development, secondary infection of the tissue is almost invariable. As a condition, not a cause, infection aggravates and accentuates existing pathology. Also especially noteworthy among the list of conditions is existing nutritional status. If the tissue is already the site of deficiency pathology, usually chronic, its requirements obviously are raised. One of the outstanding reasons that an acute deficiency sign may be induced in one study but not in another is the initial difference in the nutritional status of the subjects.

Far-reaching as are the implications of this concept, they do not exceed the facts. At the least, this concept with its multiplicity of conditions and its element of time helps to clarify why a positive correlation between diet intake and prevalence of deficiency states is usually not obtained. What is more important, it brings out the relationship of the many environmental conditions, both external and internal, to nutrition. It also explains the character and course of deficiency processes and their prevalence. It bears directly upon the assignment of cause in diagnosis and influences views on dietary requirements. But its greatest import comes from the realization that the possibility that a disease of unknown cause may be nutritional in nature is not to be forthwith dismissed because it apparently is not the effect of dietary deficiency alone; rather this contingency can be examined on broader etiological grounds.

It has been demonstrated that many conditions, among them growth, pregnancy, and health, affect nutrition. But whether there is a reverse relationship, a reciprocity of nature, in which nutrition influences these functions of life has been a transcendent question. Studies with animals on these relationships have yielded a decisive and convincing affirmation; but before acceptance of this applicability to man the prerequisite of evidence from human studies has properly been interposed.

From surveys of university students in Boston and Toronto (13) it was found that cohorts with average age of 18 years had gained nearly 2 inches in height over 15 years during a period which started with the beginning application of the newer nutritional knowledge. It has been shown repeatedly—Mann, Orr, and McCollum were among the first to bring forth evidence—that children eating a poor diet and already retarded in growth gain in height and weight upon receiving supplementary food of high nutritive value (14). As for nutrition and childbearing, results from studies in four localities, Philadelphia (15), Toronto (16), Boston (17), and England (18) have led to substantially the same conclusion: the nutrition of a gravid woman influences the course of her pregnancy and parturition; and the status of the newborn. If this condensed statement seems to underrate the importance of its message, it is no exaggeration to declare that it points to the single greatest new measure for prenatal care.

On a vaster scale intimations have come from England on the influence of nutrition on health. One source was a controlled study of mass migration in which part of a population moved from slum dwellings in Stockton-on-Tees to a modern housing estate, while a second comparable group remained (19). For the five years subsequent to moving, the transferred population had an increase of 46 per cent over its previous mortality rate; while the group remaining in the slum dwellings showed a reduction. When the expenditures of the two groups were compared, it was found that the transferred population allotted a lower percentage of its budget for food because of its higher rentals. The report states: "It is difficult to come to any other conclusion than that the increased mortality was associated with the dietary deficiencies."

Using data of national magnitude, Magee accredits nutrition with the improvement in the public's state of health in the United Kingdom during wartime (20). He writes: "A diet more than ever before in conformity with physiological requirements became available to everyone, irrespective of income.

The other environmental factors which might influence the public health had, on the whole, deteriorated under the stress of war. The public health, so far from deteriorating, was maintained and even in many respects improved. The rates of infantile, neonatal, and maternal mortality and the stillbirth rate reached the lowest level ever."

Valuable as is the existing body of knowledge for immediate application, it is equally worthy for opening new avenues of exploration which may bring further rewards to public health. It is becoming increasingly clear that nutrition is a much more complex, far-reaching, and influential force than has generally been admitted. More conditions are now recognized as affecting it; while its many, wide spheres of influence are coming to be appreciated. With it all, promising lines of investigation beckon.

For one thing, the effect of conditions on nutrition might well be more intensively studied. For example, more knowledge about the influence of hormones on nutrition might be expected to bring benefits to man. Then too, certainly high on the agenda for investigation is the important set of postulated relationships: nutrition in its effect on physical performance, fatigue, psychological functions, congenital deformities, immunity and resistance to infectious diseases, aging, and longevity. In some instances preliminary evidence holds forth promising prospects (21, 22, 23, 14). It need scarcely be mentioned that the plan and execution of studies on such questions are beset with pitfalls. Here concepts of deficiency states and their etiology are helpful guides. It is no accident that many of the studies on man thus far yielding positive results were conducted for a somewhat longer period than has been the custom in the past, though still not long enough.

Equally stimulating is the virtually virgin field of study on the possible relation between nutrition and diseases of unknown cause. One lead is at hand for exploring this labyrinth. Consider that the fully-developed deficiency diseases affect many bodily tissues, systems, and sites; and that the pathology of the chronic form is different from that of the acute, although

the sites are the same. Thus far study of the chronic form of each deficiency state has only reached the sites of early change. Certainly it is reasonable to expect that the sites of later change in the acute process have their chronic counterpart. But they are now unstudied. Even this list might well be found to be in need of amplification. In truth, there should be further study directed towards a complete catalogue of tissues, systems, and sites affected in deficiency states. It should be borne in mind, moreover, that the so-called typical sequence in the procession of signs simply reflects the influence of that combination of conditions most frequently prevailing. A shift in emphasis among this combination of conditions may bring about accentuation of a late, out of all proportion to that of an earlier, sign. Furthermore, a less usual condition may aggravate an unusual site producing an atypical sign. For example, a chronic deficiency state and a supervening impairment of cerebral circulation together with contributory conditions may be conducive to encephalopathy, without acute signs of pellagra elsewhere, yet with response to niacin. Or an existing chronic deficiency state and an added endocrine disorder, together with other adverse conditions, may bring about an abdominal hemorrhage actually on the basis of a vitamin C deficiency. A table of systems and sites affected in deficiency diseases would show many open spaces for the chronic form which continued study might be expected to fill.

On the other hand, consider that medicine abounds in chronic disorders of unknown etiology. Their essentially chronic nature is especially significant. It should also be noted that the new concept of integrated conditions influencing the ratio in nutrition covers wide latitude. Hence, neither in nature nor cause would it be incompatable for chronic diseases now of unknown etiology to be nutritional. Clues on possible relations might be obtained by referring the systems and particular sites affected in these chronic disorders to the table showing the expected distribution of lesions in chronic deficiency states. Here again, because of the chronic nature of the diseases, only prolonged

studies will provide valid information. But for each identification, nutrition would gain an expected syndrome; chronic disease, a known etiology; and social medicine, a triumph.

In conclusion, both in retrospect and prospect, nutrition is seen to signalize the influence of environment on health and, as the crucial medium between them, to occupy a paramount position in that system.

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