Introduction

When the term allergy was coined in the early 1900’s, it was used to apply to observable cause and effect maladaptive reactions between the evoked emergence of symptoms on exposure to environmental substances. In the late 1920’s, the antibody mechanism of some acute allergic reactions was discovered and after this, the specialty of allergy rapidly became immunologically oriented. In doing so, other environmentally evoked reactions were ignored or discounted as not so and even sometimes attributed to placebo effect resulting from over enthusiastic expectations from either patient, doctor or both. Arthur Coca, founder and longtime editor of The Journal of Immunology, described as significant in his writings nonimmunologic reactions which he called nonreaginic allergy (1956, 1953). He characterized these nonimmunologic reactions as occurring in degenerative diseases and specifically named hypertension, cardiac dysrhythmia and diabetes mellitus as sometimes being of this order. Nonreaginic allergy has never been

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a universally popular term or concept but has been used to explain nonimmunologic reactions observed by those allergists and non-allergists who collectively have called themselves clinical ecologists (Dickey, 1976). Clinical ecologists initially and largely have come from the specialty of allergy and have continued to use the immunologic model in their work, even in relationship to the nonimmunologic reactions. In doing so, they developed serial dilution intradermal testing and neutralization, serial dilution sublingual testing and neutralization, sniff testing, provocative food testing, provocative chemical testing and cytotoxic testing. These tests are based on the evidence of evoked inflammatory reactions, either locally as in the skin or blood cells or systemically in symptom production. Furthermore, bio-ecology using a nonimmunologic medical model has combined laboratory assessment measuring varied biological shifts occurring when maladaptive reactions occur. A differential diagnosis between evidence of immunologic reactions compared to nonimmunologic metabolic reactions reveals that a majority of mental, physical and degenerative diseases are largely nonimmunologic in origin. Furthermore, if and when immunologic reactions do emerge
in the degenerative disease process, they usually are secondary to a more primary metabolic disorder.

To understand the degenerative disease process, there is a need to contrast the law of parsimony with the General Adaptation Syndrome (GAS) as outlined by Hans Selye (1956). The law of parsimony proposes a single cause of each specific disease. The GAS proposes multiple stressors disordering multiple metabolic functions coalescing into a disease syndrome named according to the organ system affected. From my observations, I have concluded that infections such as causing epidemics, specific toxins and so forth can have single causes for the disordered state but that by and large mental and physical degenerative diseases occur according to the postulated GAS. More progress is made in understanding the disease process by the process of examining for multiple stress factors than by being satisfied with trying to find a single factor. It has been a deterrent to progress to assume a necessity of finding a single cause for each disease symptom complex.

In the mid 1960s, I began to question, as many others have done, the assumed psychological origin of schizophrenia. With the help of Martin Rubin, Ph.D., Biochemist, I began to use laboratory assays to examine for metabolic disorders, nutritional deficiencies, metabolic errors and so forth. This search led me to be a consultant to a boarding school for youth who had disorders in the areas of learning, emotional and social. On these youth, I was using a chemical survey. At the same time, Sol Klotz, M.D., Internist-Allergist, was doing a traditional skin testing allergy survey. He proposed to me that some of their behavior disorders may relate to maladaptive reactions to environmental substances, especially food. We both considered that the first question to be answered related to the validity of symptom provocative testing. To answer this question, two double-blind studies were done (Klotz, 1976). A comparison between distilled water and food extracts was made. These turned out to be highly significant positive studies. This gave me the courage to proceed with provocative testing, using the method of a four to six day period of avoidance followed by exposure to single test food meals which revealed a high percentage of cases in which major mental and physical symptoms diminished or disappeared within the five days of avoidance and reemerged in response to the test meals of single foods. Even in the diagnosed emotionally ill cases, percentage wise physical symptoms were more frequent than mental symptoms. What had heretofore been considered somatization in schizophrenia was now observed to usually be caused by maladaptive reactions to foods, chemicals and inhalants. I have not been satisfied with a model patterned after the symptom reaction immunologic model. My goal has been to search out the potential multiple metabolic factors emerging during these maladaptive nonimmunologic reactions to foods, chemicals and inhalants. Monitoring body chemistry in a non-reactive state compared with a symptom reactive state give evidence of:

1. multiple causes rather than single causes,
2. a central, progressive disease process with the characteristics of initial disordered acid base balance progressing to a carbohydrate metabolic disorder, disordered lipid metabolism and disordered amino acid metabolism,
3. an adaptation to the chronic stress of frequent contact with specific foods and chemicals resulting in addiction with the characteristics of an initial relief phase on contact with the addictive substance and a later emergence of symptoms on withdrawal,
4. monitoring the chemistry of addiction reveals the chemistry of the basic degenerative disease process of disorders of acid base balance, carbohydrate metabolism, lipid metabolism, amino acid metabolism and oxidation reduction metabolism.

**DISCUSSION The Role of General and Specific Indicators of Disease**

General indicators of nonimmunologic metabolic disorders before differentiation into specific disease entities should be sought. These are such as observed as occurring during acute maladaptive reactions precipitated
by provocative test exposure such as acute brief metabolic acidosis, acute brief drop in peripheral temperature, acute brief episode of muscle weakness, drop in ascorbic acid and increase in dehydroascorbic acid, etc. The laboratory evidence stemming from the inflammatory process, endogenous evoked general toxicity and oxidation-reduction (reduction) should be tapped as providing general indicators of the basic generalized undifferentiated disease process. This area deserves in-depth study.

As the disease progresses, it differentiates into specific organ system disorders with the emergence of specific indicators indicative of each disease process added to the general indicators. These specific indicators should be sought out in each case to determine the degree of disease progression and provide optimum therapeutic options. Examples of specific indicators of differentiating progression of the disease process are such as nutritional deficiencies or disorders, metabolic errors, progressive metabolic involvement disordering carbohydrate metabolism, lipid metabolism, amino acid metabolism, etc.

Specific indicators for schizophrenia have not yet been conclusively worked out, and it is as yet uncertain if they exist. A symptom complex has diagnostically been assigned the name schizophrenia; however it appears to be a heterogeneous organic disease with also common denominators to a more central disease process. As far as possible, both general and specific indicators of disease should be incorporated in the examination. As these primary nonimmunologic disease processes progress, there develops increasing evidence of secondary developing immunologic disorders (non-IgE) such as complement disorders, decreased B and T lymphocytes, C reactive protein, latex fixation, non-IgE immunoglobulin disorders, etc. When present, the reversal of these immunologic factors can be useful as evidence of correction of the disease process by such immunological treatments as reversal of the addictive state by (1) avoidance, spacing and rotation of foods or reduced contact with symptom incriminated chemicals, and (2) detection of nutritional disorders secondary addiction or otherwise chronic symptom evoking exposures, etc.

Primary immunologic reactions are seldom involved in central nervous system disorders. A wide assortment of non-immunologic metabolic disorders are demonstrated to be the cause of the acute inflammatory allergic-like reactions evoking symptoms. Hans Selye’s General Adaptation Syndrome is demonstrated to be appropriate for these nonimmunologic reactions, and this involves the stages of the disease process of: (1) an acute nonadaptive reaction, (2) adaptive reaction, and (3) chronic nonadaptive reaction. Occasionally, placebo effects are seen in specific neurotic patients. Fortunately, these are sufficiently infrequent as to not interfere with diagnosis in the majority of patients. Adaptive addiction emerges as a major mechanism of symptom formation. Adaptive addiction is a state of stress that disorders metabolism in many ways. Central to this disorder is the production of endorphins such as methionine enkephalin, leucine enkephalin and opiate alkaloids which are addicting and maintain this state of addiction.

The Role of Ammonia Metabolism
(Pangborn, 1981)

There is emerging evidence from an amino acid profile of food addicted patients that both the urea cycle and lysine metabolism are interfered with, producing bouts of hyperammonemia. Indeed, a wide assortment of mental and physical symptoms are produced on provocative test exposure to ammonia, revealing a hypersensitivity to ammonia that has undoubtedly been created by the disordered ammonia metabolism.

The Role of Disordered Citric Acid Cycle Metabolism

The amino acid profile reveals evidence of deficient alpha-ketoglutaric acid. Alpha-ketoglutaric acid is associated with B6 as a co-factor in several functions. It now appears that this is likely the greatest culprit producing a B6 utilization disorder, even in the presence of adequate B6.

The Role of Metabolic Acidosis
(Boyd, 1973; Chatterjee et al., 1975; De Wied, 1978; Hughes, 1956; Randolph, 210
Metabolic acidosis is observed to emerge during addictive withdrawal, acute maladaptive reactions (to foods, chemicals and inhalants), diabetes and infections. Many body enzyme functions are dependent on a narrow pH range. Metabolic acidosis (1) reduces enzyme function of the urea cycle with the consequences of emerging blood ammonia, (2) produces opiate alkaloids, (3) activates kinin and prostaglandin inflammatory reactions and (4) likely is one of the metabolic disordered conditions necessary for the pathological production of ascorbic acid change to dehydroascorbic acid in the blood.

Disordered acid-base balance is a likely cause of the obsessive-compulsiveness observed as running through a wide spectrum of mental disorders. This likely stems from an imbalance between α-endorphin and β-endorphin produced by the state of acidosis.

The Role of Amino Acids in Neurotransmission
(Christie et al., 1979; Cohen et al., 1980, 1976; Davis et al., 1976, 1980; Etienne et al., 1979; Ferstrom et al., 1972; Gelenberg et al., 1980, 1979; Gibson et al., 1978; Growdon, 1980, 1979; Growdon et al., 1977; Hartmann, 1978; Hirsch et al., 1978; Peters et al., 1979; Scally et al., 1977; Tam-minga et al., 1977; van Praag, 1980; Wurt-man, 1980)

Increasing or decreasing specific amino acids can have values as well as dire consequences in specific cases. Increasing dietary amino acid precursors to neurotransmitters increases the brain level of the neurotransmitters themselves.

Gelenberg postulates the possibility of fine tuning brain function by a combination of food substances known to evoke specific responses as well as eliminating substances evoking maladaptive responses. This research postulation is compatible with our clinical experience in which we observe even now an emerging healthy growing edge of a new scientific Bio-ecologic Psychiatry, obviously worthy of in-depth definitive study for which exciting profitable value can be predicted.

The Role of Phenolic Food Compounds

It is likely that our high level of petrochemical hydrocarbon contaminants, and specifically including phenol, is such a stress on the enzymes which handle phenol-ring food compounds that an inhibition of the production of these enzymes occur interfering with the metabolic handling of these foods. When a period of avoidance of the contaminants and of phenolic foods evoking symptoms does not occur, then desensitization of these phenolic food compounds is in order.

The Role of Maladaptive Reactions to Specific Sugars
(Hsia, 1969; Isselbacher, 1966)

Glucose intolerance is an inherent aspect of addiction, and indeed the chemistry of addiction is observed to be the chemistry of chemical diabetes and eventually leading to maturity-onset diabetes if and when the adaptive addiction cannot be maintained. Fortunately the percentage proceeding from chemical to maturity-onset diabetes is small; however it should be understood that the same complications occur in the chemical diabetes stage as occur in the overt clinical stage of diabetes. Of the other known maladaptive reactions to sugars, the two most important are lactose intolerance and galactose intolerance. These are sufficiently frequent as to warrant a routine examination with a lactose tolerance test and a galactose tolerance test. When the galactose tolerance test is positive, there should be a further differentiation of the genetic disorder vs. the nongenetic reversible disorder of galactosemia. This can be achieved by a galactosemia enzyme screening test.

The Role of Essential Fatty Acids
Prostaglandins are made from essential fatty acids. There are both anti-inflammatory and inflammatory prostaglandins. It appears evident that deficiency in prostaglandin production produces a state of imbalance between inflammatory and anti-inflammatory
factors with inflammation in the ascendency. The necessary nutritional fatty acids can be obtained in such as cold pressed vegetable oils (as linseed oil, safflower oil, sunflower oil, soy oil), fish oils, raw fish or primrose oil. Many substances, likely including petrochemical contaminants, block linoleic acid from progressing to gamma-linolenic acid. Providing extra linoleic acid may override this block. Using primrose oil, which contains gamma-linolenic acid, bypasses this step. It is important to have prostaglandin nutritional precursors available so that adequate PGE1 is available to control inflammation.

The Role of Celiac Disease
A high percentage of physically and mentally degenerative disease subjects react maladaptively to cereal grains containing gluten. The majority of these can be returned to these cereal grains after three months of avoidance. In order to determine the probability as to whether it would be safe to return a subject to the cereal grains, it is well to do a celiac test in which the subject eats cereal grains containing gluten all day long. Prior to this test day, a serum alkaline phosphatase is taken and the next morning after this all-day test, another alkaline phosphatase is run. A drop of 20 percent is presumptive evidence of celiac disease.

The Role of Infection
Seldom are infections the initial cause of physical and mental degenerative diseases, but frequently they become a part of the disease process once it has been established. The two most serious culprits are the opportunists, Staphylococcus invading the nose, sinuses and pimples and Candida albicans infecting the throat, colon and vagina. These should all be examined for, and when present, vigorously treated. Staphylococcus can often successfully be treated with an autogenous vaccine. Candida albicans requires appropriate antibiotic treatment which should include throat, colon and vagina. It is to be understood that maladaptive reactions, including addiction to foods, chemicals and inhalants, create a state of acidosis which encourages the invasion of Candida albicans.
A part of the treatment of a chronic Candida albicans infection should be the correction of this state of acidosis.

The Role of Quantity
Clinical ecology has tended to use the allergy model of reactivity which basically disregards quantity. The assumption has been that any amount ranging from small to large was maladaptive. However, it is being observed that there are many cases in which quantity does make a difference, since varying enzyme capacity to handle a food is also dependent on quantity. Thus, a person with enzymatically disordered urea cycle metabolism, carnosine or anserine intolerance would have symptoms with a large protein meal (with meats containing carnosine and anserine in carnosinase disorder) but may be symptom free with a 10 percent protein meal. Also, a high protein meal can be such as to over stress the enzymatic digestion capacity of this protein to be reduced to its respective amino acids thus leaving long-chained polypeptides (exorphins) for absorption.

CONCLUSIONS
Immunologic inflammatory reactions are well substantiated by specific test techniques. Nonimmunologic allergic-like maladaptive inflammatory reactions have been logically questioned because of the usual subjective techniques used in their diagnosis. The fact these reactions are readily reversible rather than relatively fixed as IgE mediated inflammatory reactions adds further difficulty to diagnosis. Nonimmunologic allergic-like inflammatory reactions can be substantiated by double-blind testing and especially by laboratory demonstrated biochemical monitoring of such as acid-base balance, lipid metabolism, carbohydrate metabolism, amino acid metabolism, oxidation-reduction metabolism and ascorbic acid-dehydro-ascorbic acid ratios. Adaptive addiction as the second stage of the General Adaptation Syndrome emerges as central in a basic degenerative disease process in a large number of both physical and mental degenerative diseases. Biochemical monitoring reveals this to be varied stages of the diabetes mellitus disease process and if and when the
adaptive addiction fails, emerges as maturity-onset diabetes mellitus. If and when immunologic reactions emerge in this primary degenerative disease process, they are secondary to and not primarily the cause of the basic degenerative disease process. Likely causes of the emergence of maturity-onset diabetes as an end result of this basic degenerative disease process is on the order of:

1. endorphins and exorphins disordering pancreatic function
2. reduced production of cystine needed for the insulin molecule
3. pancreatic damage from high blood dehydroascorbic acid
4. as well as possibly superimposed viral infections on unhealthy pancreatic tissue created by 1 to 3 above.

The specific tissues that will react first to this basic degenerative disease process are likely determined by such as:

1. genetic predispositions
2. specific nutritional deficiencies
3. prior injury
4. prior or current infections. Rational therapy embodies a lifestyle system of:
   1. reversal to a non-addictive state by avoidance and spacing of contact with foods and chemicals below symptom formation and or the emergence of laboratory demonstrable abnormal chemistry
   2. optimum nutrition, especially as determined by laboratory assessment
   3. a noninfected state
   4. optimum exercise.

Our observations reveal that bio-ecology is specific for reversal of the chemical diabetes phase of the disease process. Potts (1980, 1977) has documented bio-ecology as providing a high degree of reversibility for the disease process, even after it has progressed to the maturity-onset diabetes stage.

In emotional degenerative cases, the specific application of an array of psychotherapeutics for retaining, problem solving, development of social skills, unlearning of phobias, inhibitions of obsessions and compulsions and in a few cases that do not recover by avoidance and spacing, nutritional and psychotherapeutic application of a stimulation to normalization of biochemical function through such as electrical stimulation (nonconvulsive and convulsive types). The hair test biopsy for essential minerals and heavy metals has inherent weaknesses to be considered, such as environmental contamination and leaching during washing, in spite of which it provides a limited but considered to be useful perspective when correlated with serum studies and, when indicated, urine studies. The usefulness of the cytotoxic test is limited to reactions occurring to the blood cells. It does not differentiate immunologic from nonimmunologic reactions nor indicate that these reactions are symptomatic. It reveals only a small but useful portion of the inflammatory potential of the disease process and is considered as an ancillary test to more definitive tests. The quantitative 24 hour amino acid study is judged to be the most revealing and likely most definitive of the tests used. It reveals deficiencies, excesses, metabolic disorders (genetic and developed) and enzyme disorders and is indicative of enzyme cofactor disorders or deficiencies. It serves as the window through which the metabolic process is observed. Provocative stress testing serves the useful role of disordering chemistry for objective laboratory monitoring and disordering body function evoking symptoms for objective and subjective observations. The most useful clinical potential comes from correlating the limited values of the several tests. Useful would be an in depth study determining the qualitative values contributed by each test.

References


