"In biology as in physics it is a truism that the deeper one goes in exploring elementary questions, the more one encounters paradoxical and puzzling phenomena." (1) This is particularly true in the study of the body's immune system. In fact, this statement was made by researchers investigating the immune response.

The human defense mechanism operates through a complicated maze of reactions. It becomes even more complicated when one realizes that it is integrated into the psychological, neurological and endocrine systems. It is also closely related to and dependent upon proper nutrition. To better understand this complicated system we will look at its components or responses, rather than viewing it as one large complex system.

The Immune System

The function of the immune system is to distinguish self from non-self and to eliminate non-self. It is also involved in preventing attack by internal (auto immune disorders) and external factors (invading organisms, i.e., viruses, bacteria, and xenobiotics).

Primary Organs

Bone Marrow - Stem cells are produced in the marrow that differentiate into lymphocytes (other cells such as erythrocytes, granulocytes, etc., are also produced but this discussion is limited to the lymphocytes).

Thymus - Involved in hormone production (thymosin) and the development of immunocompetent T-cells from migrating lymphocytes.

Secondary Organs

Lymph Nodes, Tonsils, Adenoids, Spleen and Gut (pyres patches of the small intestine).- Their purpose is to localize and prevent the spread of infections. As lymphocytes migrate through these organs, immunocompetent T-cells and B-cells emerge by way of the medullary, or cortical tissues of these organs.
Cells of the Immune System

**B-lymphocytes** - Involved in antibody or humoral immunity.

**T lymphocytes** (T-helper, T-suppressor, T-Killer Cells) - Involved in cell mediated immunity.

**Phagocytes** - PMN's, eosinophils, and macrophages.

**Basophils, and Mast Cells** - Mediate acute hypersensitivity and inflammation through histamine release. Basophils are found in circulation while mast cells are in tissues.(13)

There are of course other components of the immune system, but for simplicity and space they will not be discussed. There are many compendiums on the subject for those who would like to explore further.

**Classification of The Immune System Response**

From the following information, we can gain a greater understanding of the immune system and its responses after it has been categorized. The immune system can be divided into two categories, the humoral-mediated response and the cell-mediated response, each having a specific function.

<table>
<thead>
<tr>
<th>Humoral-Mediated Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody Mediated</td>
</tr>
<tr>
<td>B-Cells</td>
</tr>
<tr>
<td>Serum Immunity Transfer</td>
</tr>
<tr>
<td>Primary defense against Bacterial Infection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cell-Mediated Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell Mediated</td>
</tr>
<tr>
<td>T-Lymphocytes and Factors Responsible For Transfer of Immunity</td>
</tr>
<tr>
<td>Host Defense against Virus, Fungi, Intracellular Organisms, Tumor Antigens, Allograft Rejection</td>
</tr>
</tbody>
</table>

**How The Immune System Can Be Harmful**

There is mounting suspicion that the immune response can actually be harmful to cells. On the basis of research into the immune system, Notkins and colleagues made the following statement, "...there is growing evidence that cells are damaged not directly by replicating viruses but by a specific immune response that produces the symptoms of the disease."(2) The authors site Clemens von Pirquet, an Austrian pediatrician who more that 60 years previously, speculated that the immune response may be responsible for injury to tissues. Wallace P. Rowe, a virus researcher at the National Institutes of Health, later confirmed von Pirquet's suspicions. His experiments involved the study of the lymphocyte choriomeningitis (LCM) virus. When introduced into lab animals the virus spread rapidly throughout the body. In six days the animals began to show an immune response to the virus, developed meningitis and died. To determine the immune systems involvement, Dr. Rowe performed another experiment, in which he exposed one group of animals to radiation, as radiation is known to suppress the immune response. Whereas, in the control group, the immune system was not suppressed. After the
LCM virus was introduced into the animals, the virus spread throughout the bodies of both groups. The control animals developed meningitis and died, as in previous experiments. However the immune suppressed group did not develop meningitis. Rowe, therefore found that the meningitis was caused not by the virus itself, but by the body's immune response to the virus.

**Free Radicals and the Immune Response**

Maeda, and colleagues published studies that indicate that superoxide radicals were generated by an influenza virus in infected animals. They suspected that the immune response was responsible for generating the oxygen free radicals that injure normal tissues and not the replicating virus itself. (3) Maeda, and other researchers suggest that this mechanism of increased free radical formation may account for the symptoms produced in response to other types of viruses. They include those associated with influenza, viral hepatitis(4,5), measles (6), herpes virus((7,8) and human acquired immune deficiency syndrome.(9,10)

Free radical formation is a result of normal metabolism (oxidative-reduction reactions). It is estimated that each cell takes more than a thousand oxidative hits per day. The body is capable of handling 99% of the normally generated radicals. However, when nutritional status is compromised due to infections, malabsorption, and chronic disease, the bodies free radical quenching capabilities may be reduced considerably, even during a normal immune response.(11,12) The immune response can be affected not only by individual nutritional deficiency, but by nutritional imbalances as well.

**Metabolic Types and the Immune Response - Cellular - Humoral**

In viewing the immune response through hair tissue mineral analysis (HTMA) patterns, we must first recognize the difference in Fast and Slow Metabolic Types. In the Slow Metabolic Type 1, there is usually found an adrenal insufficiency. Calcium and magnesium levels are markedly elevated in relation to phosphorus, sodium and potassium. The opposite HTMA pattern is found in Fast Metabolic Type 1’s. Calcium and magnesium levels are low relative to phosphorus, sodium and potassium, and increased thyroid and adrenal activity exists.

The cellular immune response is parasympathetic or thymus mediated, and is indicated by the Slow Metabolic HTMA pattern. The humoral immune response can be classified as sympathetic or adrenal mediated, and is indicated by a Fast Metabolic HTMA pattern.

**Antagonism's Within The Immune System**

When observing the immune response in relation to metabolic types, several things become evident. For example, the sympathetic and parasympathetic neuroendocrine system is known to function together in the normal healthy individual. However, one group can become dominant and actually antagonize the other. Therefore, the immune system may also lose its synergistic relationship and become unbalanced. The cellular response can become over active and eventually suppress the humoral response. Conversely, the humoral response can become dominate and decrease the body's ability to initiate a cellular immune reaction.

In the Fast Metabolic Type 1, there is an elevation of sodium and potassium, which represents an increase in adrenal activity, or humoral immune response. As hormones from the adrenal cortex increase, thymus and lymphatic function decrease, due to involution or shrinkage. This is a well-known phenomenon.(14,15,16)
The Slow Metabolic Type 1 pattern (elevated calcium, magnesium relative to phosphorus, sodium and potassium) is indicative of an increase in thymic response with a corresponding decrease in adrenal activity. This eventually results in the inability to initiate a humoral immune response.

Other researchers have found this to be the case. Harrison, found an inverse relationship between humoral and cellular mediated immunity in subjects at risk of insulin-dependent diabetes.(17) It is speculated that in an autoimmune disease, such as insulin dependent diabetes, the pancreatic beta cells are destroyed or impaired by the T-cells, which is associated with cell-mediated immunity. It is interesting that HTMA patterns of patients with adult onset diabetes, are commonly associated with the slow metabolic pattern, or increased cellular immunity. Other studies have reported finding an imbalance between the cellular and humoral response in conditions such as lupus, rheumatoid arthritis, Sjogren's syndrome, Chron's disease, and celiac disease.(18) In other words, it is very evident that the cellular immune response can over-power the humoral immune response and vice-versa. The following statement by Katz illustrates this point very well, "...it is becoming increasingly well documented that, in some animal models and in humans, the humoral immune system can act to the detriment of the host and indeed, block the activity of the cellular immune system in its attempt to destroy neoplastic cells." (19)

**Acquired Immune Deficiency Syndromes (AIDS) and HTMA Patterns**

The hypothesis that an imbalance could occur in the immune system was made in the early 1980's after testing a number of AIDS patients. Their HTMA typically showed a pattern very similar to the Slow Metabolic Type 1, in conjunction with markedly elevated copper levels and low tissue zinc. I should emphasize that these tests were from male homosexuals who were in the ARC (Aids Related Complex) stage or who had developed full-blown AIDS. From their HTMA patterns, I suspected not an immune deficiency, but an over-active cellular immune response. These patients were surely immuno-compromised, but not due to thymus insufficiency. Their HTMA profiles indicated that their thymic (cellular) response was actually over-powering their adrenal (humoral) response. This would result in the inability to activate the adrenal mediated alarm response to ward off other invading organisms. This would eventually lead to the susceptibility toward opportunistic infections, particularly bacteria, and parasites. However, the cellular immune system would eventually wear out allowing other organisms to proliferate, such as viruses, fungi, yeast, etc. The lymphatic tissues of AIDS patients have been reported to show evidence of destruction when viewed microscopically. Many of the opportunistic diseases that develop are similar to zinc deficiency, copper toxicity, or low Zn/Cu related conditions.(20) Herpes, pneumonia, anorexia, hepatitis and retinitis are common in ARC and AIDS patients. The main goal in treating these patients would therefore not be to support or enhance the immune (thymus) response, but to suppress it. This has been suggested by other investigators, who demonstrated that activation of the thymus response in patients with AIDS and ARC produced deleterious results while the use of immunosuppressive agents, such as steroids, and even cyclosporin produced favorable results. (21,22) Cyclosporin is a drug used to prevent organ or tissue rejection following transplants, and acts as a cellular immuno-suppressant.

Of course other minerals also affect and regulate the immune response. As mentioned previously, we typically see elevated calcium with an increased thymus response. Remember that the thymus is responsible for fighting viruses. Excess calcium has been found to increase viral proliferation. Studies have been done where dormant viruses were introduced into lymphatic tissue. When the concentration of calcium was increased in the medium, the dormant viruses became active and spread rapidly. This was prevented when calcium was blocked.(23)
Zinc deficiency is also associated with increased viral susceptibility, and zinc has been shown to kill some viruses upon contact. Copper on the other hand, is a powerful zinc antagonist, and in excess can be considered a viral-inducing agent. It is very typical to find elevated levels in AIDS and ARC patients, as well as in individuals suffering from mononucleosis and viral hepatitis. One agent sodium diethylthio-carbamate, or ditiocarb, has been reported to be very helpful in treating AIDS patients. It is interesting to note that this chemical inhibits a number of copper dependent enzymes.(24)

We also see this slow metabolic or parasympathetic pattern in patients suffering with chronic fatigue syndrome. Recent studies suggest that an increased cellular immune reaction is associated with this condition.(25) Preliminary results of an ongoing HTMA study of fibromyalgia patients are showing a common pattern of increased thymus or parasympathetic immune response in this condition as well.

The humoral immune response is associated with resistance to bacteria. Copper deficiency increases host susceptibility to bacteria infections, such as E. Coli and Staph aureus, as does magnesium deficiency.(26,27) Low HTMA copper, calcium and magnesium relative to elevated sodium and potassium is typically found in the Fast Metabolic Type 1. To reiterate, the Fast Metabolic Type 1 pattern may be viewed as a humoral dominant immune response with a corresponding thymus suppression.

Over the years, we have classified diseases into sympathetic and parasympathetic categories. We find that the Fast Metabolic Type is susceptible to certain conditions not commonly seen in the Slow Metabolic Type and vise-versa. When correlating metabolic types with specific immune responses, we can see the possibility of immune reactions being associated with various health conditions.

Nutrition and Immune Competence

A competent immune system is extremely dependent upon the nutritional status of the host. Numerous studies show the importance of nutrition and the ability to resist infectious processes. Infants born malnourished are much more susceptible to infections compared to normal infants. Chandra, has reported the effects of single nutrient deficiency upon the ability to resist infections. The mortality from Listeria infection was improved by almost 50% when zinc was supplemented, and even the response to vaccines was improved greatly in elderly patients receiving a nutritional supplement compared to those receiving a placebo. These are just two of the many examples that have been reported.(33) Vitamin and mineral supplementation have proven to enhance the resistance to infections in the elderly, and thereby reduce morbidity and improve mortality and productivity in this age group.(34) Interestingly, improvements were noted in elderly individuals who showed no sign of nutritional deficiency.

This illustrates the inadequacy of the RDA currently established for the older age groups, and casts doubts about nutritional RDA's established for other age groups as well.

<table>
<thead>
<tr>
<th>Disease Manifestations and Immune Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sympathetic</strong> (Increased Humoral Response)</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>Allergies (Histamine)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Cushing's Disease</td>
</tr>
<tr>
<td>Juvenile Diabetes</td>
</tr>
<tr>
<td>Bacterial Infections</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Hyoparathyroidism</td>
</tr>
<tr>
<td>Multiple Sclerosis (true)</td>
</tr>
<tr>
<td>Parkinson's Disease</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis</td>
</tr>
<tr>
<td>Anxiety</td>
</tr>
<tr>
<td>Malignancies (fast growing, metastatic)</td>
</tr>
</tbody>
</table>

**Psychoneuroimmunology (PNI)**

PNI is a developing field, involved in exploring the mind-body relationship. Researchers have found a link between the emotions and how the body responds to disease through the immune system. Strong emotions such as grief, hostility, and frustration can affect the immune system through neuroendocrine pathways. Individuals suffering from severe depression such as widowers are found to be more susceptible to disease due to altered immune responses, compared to those who have not stayed in a chronic state of grief.(28,29)

Even though the mind can predispose the body to illness, it may also help overcome illness. Reports have shown that modification of attitudes and behavior can be helpful in treating conditions as diverse as skin conditions, heart disease, neurological conditions, cancer, arthritis, burns, viruses, etc.(30)

Stress, or more appropriately distress is one of the major factors that can contribute to physical deterioration, disability, and a compromised immune system. This can be said another way, in that it may be our response to stressors that can lead to adverse changes in our immune response. There are times when we all have experienced a very stressful situation. Our response to the stress can take two directions. One is that we have an immediate and perhaps strong reaction, appropriate to the stressor. Afterwards, as our body and mind stops reeling from the experience we get on with our normal routines. Yet at other times, the effects of the stress can become long-lasting, affecting us for days, weeks, months, and even years afterwards. Even though the mind can set off a series of responses that will affect us physically (psychosomatic), we should also be aware of the reverse. Our chemistry can also contribute to a series of events that will affect us mentally (somatopsychic).

**Personality Traits and PNI**

Dr. George F. Solomon, a professor at UCLA, is a pioneer in the field of PNI, and is considered the foremost authority on the subject. He has described his findings of the personality traits, or characteristics of the immunologically healthy individual.(31) They include;

1. Being in touch with psychological and bodily needs.
2. Being able to meet those needs by assertive action.
3. Possess coping skills that include a sense of control, which enables one to ward off depression.
4. Express emotions, such as sadness and anger.
5. Willing to ask for and accept support from loved ones.
6. Have a sense of purpose in work, daily activities and relationships.
7. Have a capacity for pleasure and play.
I would like to discuss these characteristics or rather changes in the characteristics in relationship to the stress response, commonly known as the general adaptation syndrome (G.A.S.). (32)

Ideally, all things being equal, i.e., a healthy mind and body, all the above traits would be present. Of course ideal is something that we are always aiming for, and is difficult to maintain. Therefore, perhaps the term optimum would be more appropriate.

**Alarm Stage of Stress**

The first stage of stress is the alarm stage. This stage produces a powerful sympathetic neuroendocrine response. The hypothalamus stimulates the pituitary, which releases thyroid stimulating hormone (TSH), anti-diuretic hormone (ADH), adrenocorticotropic hormone (ACTH), and growth hormone (GH). This neuroendocrine reaction results in an increase in cellular metabolic activity throughout the body. Other reactions include peripheral protein breakdown, increased cellular amino acid uptake, decreased peripheral response to insulin, etc. Many senses become heightened, along with the musculature becoming tense, body temperature elevates, the adrenal glands enlarge, blood pressure goes up and the pulse elevates. The body is certainly ready for flight or fight at this stage. Normally there is a progression from this stage to the resistance stage. However, as I have explained in the past, some individuals do not progress readily to the next stage, if they do not have the necessary requirements to do so. If this is the case, eventually physical and emotional changes will be noted. Inflammation, hypertension, arthritis, anxiety, fear, and depression are just a few of the symptoms associated with this stage of stress. We can surmise that the immune-competent personality traits affected would include numbers 1, 2, 5, 6, and 7.

**Resistance Stage**

The resistance stage of stress is associated with continued sympathetic stimulation. There is an outpouring of anti-inflammatory hormones, glucose levels increase, protein catabolism occurs, the thymus and lymphatic tissue shrink, blood pressure, cholesterol, pulse, body temperature and metabolic activity increase further. Normally, the sympathetic neuroendocrine discharge abates, tissue repair occurs, the stress is handled successfully and the body returns to the normal mode, or recovery stage. If again, progression to the recovery phase cannot take place, physical and emotional changes will eventually develop. They include, diabetes, cardiovascular disease, immune deficiency, predisposition to bacterial infections, anxiety, paranoia, hostility, repression, frustration, phobias, mania, etc. All the immunological personality traits would most likely be affected.

**Exhaustion Stage**

If the exhaustion stage of stress is eventually encountered, there is a major shift in neuroendocrine dominance. The cellular immune system over-responds, thereby suppressing the important alarm stress glands such as the adrenals and thyroid and the metabolic rate decreases. Physical and emotional symptoms eventually develop such as low blood pressure, fatigue, poor circulation, blood sugar disturbances, osteoarthritis, depression, suppression, predisposition to viruses, fungus, yeast and feelings of inferiority or lack of self worth. Here again, all the immunological personality traits would probably be affected.

Each stage of the stress response requires essential nutritional factors. A lack of these essential nutrients can adversely affect the physical response as well as the emotions of an individual.
Conversely, being aware of the emotional factors can help in dealing with physical changes. As mentioned previously, being aware of and addressing a person's emotions have helped in the treatment of many physical conditions. (30)

Conclusion

As can be seen from this data, a competent immune system depends upon balance. This balance is achieved largely through optimum nutrition. HTMA when properly performed and interpreted can substantially contribute to the assessment and maintenance of optimum nutritional status of the individual. HTMA may also contribute to the determination of metabolic typing, thereby, providing an easily obtained and economic test for determining individual susceptibility to disease, reaction to xenobiotics, and immune regulation.