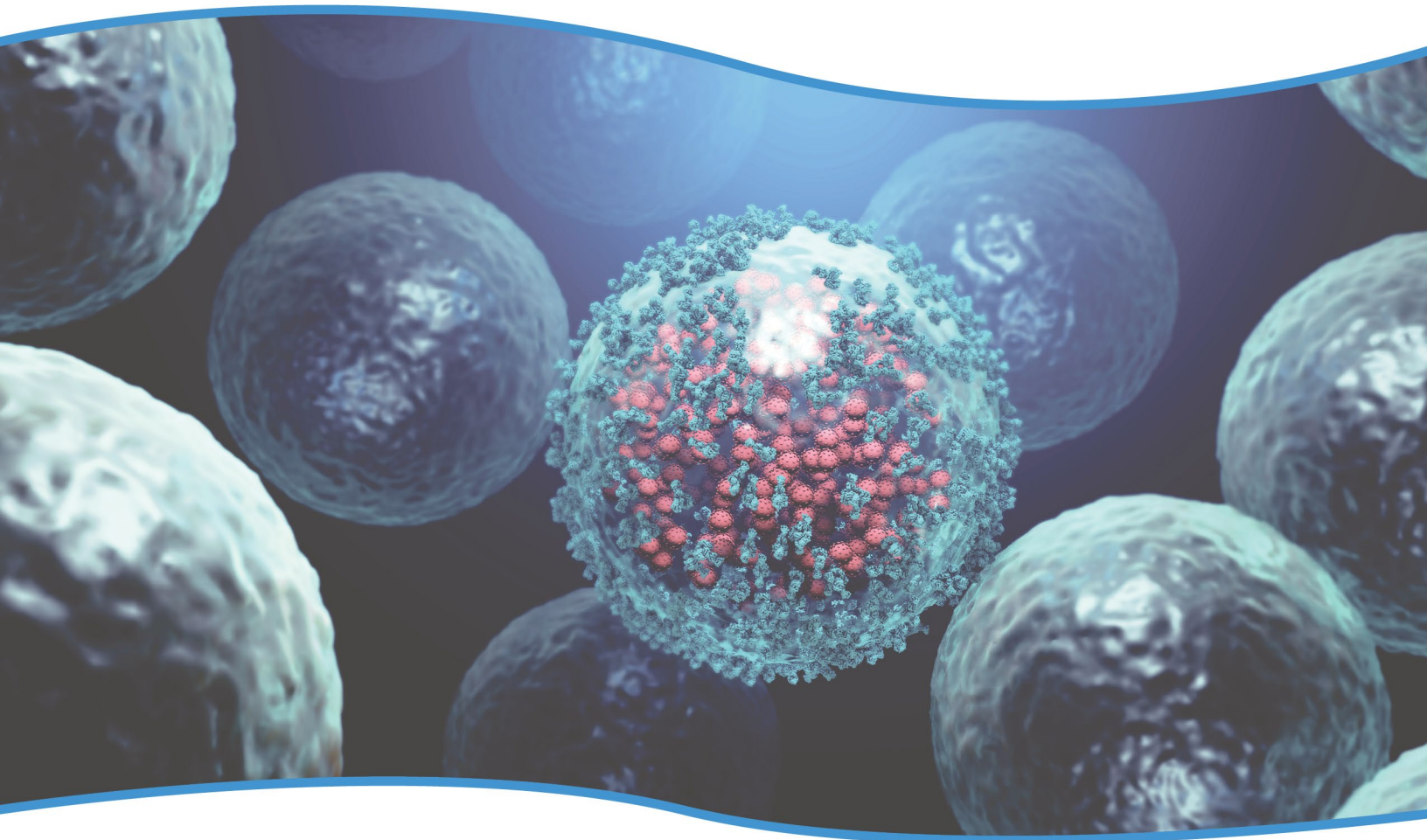


The Lymphocyte MAP[™]

Advanced Immune Mapping



Patient Educational Guide

Aristo Vojdani, PhD

HOW IMMUNE ARE YOU?

Why do different people, exposed to the same virus or antigen, get different degrees of illness ranging from no symptoms to critically ill?

What are the underlying immune imbalances which may trigger disease conditions?

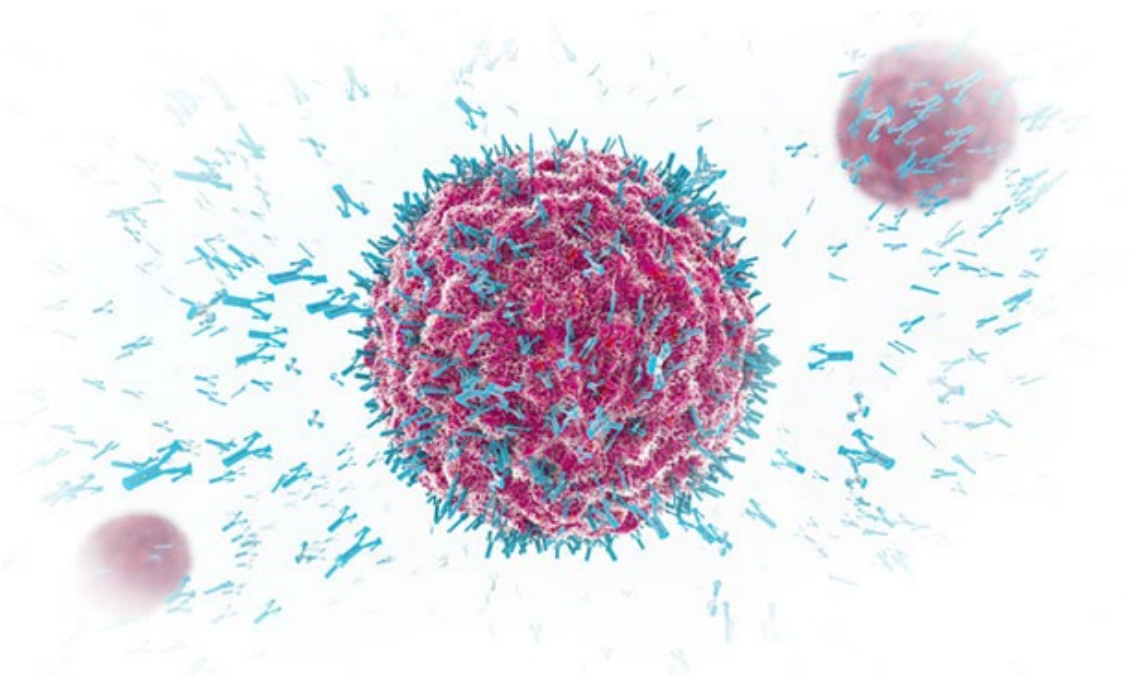
The recent pandemic of COVID-19 has brought to everyone's attention how critical our immune system is to sustaining life. It is the **first and last** line of defense against an antagonistic environment.

To increase our chances of staying healthy, we must address these critical factors:

1. exposure to harmful antigens,
2. malfunctions, or deficiencies in our immune system,
3. dysfunction, or permeability of our internal barrier systems

The most important of these is the functioning of our immune system. It is the state of our immune system that determines how efficiently we respond to the viruses, bacteria and other antigens that get through our barriers.

To keep our immune system balanced and strong, we must effectively evaluate its key components, and their performance.



THE LYMPHOCYTE MAP™

The Lymphocyte MAP is an advanced and in-depth test panel, which establishes a new industry standard in screening the immune system. It can give your healthcare practitioner:

- an invaluable picture of underlying immune imbalances that may trigger complex diseases.
- information about how environmental triggers could affect your immune system, potentially resulting in disease conditions.
- the ability to better identify immune conditions at an earlier stage, which if not addressed, may cause over-reaction (autoimmunity), or under-reaction (immune deficiencies) of the immune system, thus, allowing you to gauge existing susceptibilities.
- a more precise immune picture to help plan a treatment regimen or monitor its success.
- very useful surrogate markers for the diagnosis of autoimmune diseases, immune deficiencies, allergies and hypersensitivities.

MAPPING THE IMMUNE SYSTEM AND ITS PERFORMANCE

The immune system is a network of complex cells, and it is their numbers, percentages, and ratios or proportions to one another that determine how well the immune system will perform when all the cells are called upon to act together. These cells are the foundation of our body's defense strategy. They include:

Leukocytes – WBC – POLICE PATROL

One of the most important cells of our immune system is the leukocyte or white blood cell (WBC), which circulates throughout the body. Like a policeman or soldier, this cell continuously patrols the body for the presence of harmful enemies. When white blood cells encounter a virus, such as SARS-CoV-2, they start to multiply, and also send out communicative signals to other types of defensive cells to multiply as well so that they can all join forces to fight together to stop the virus from establishing itself in the body.

However, in a small percentage of cases, due to a low level of WBCs and coordination of the body's defense system, the virus can win the battle, resulting in the takeover of the body by the dreaded disease. The white blood cells that protect the body against pathogens consist primarily of macrophages, T lymphocytes and B lymphocytes.

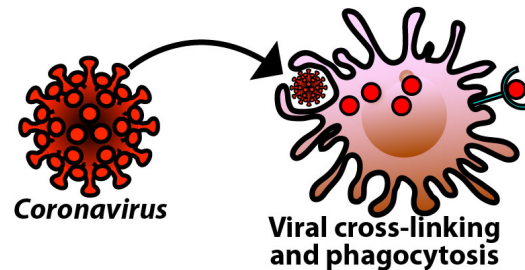
Lymphocyte



Macrophages – PACMAN CELLS

Macrophages are white blood cells that swallow up and digest germs, plus dead and dying cells, and act as the first line of the body's defenses. The macrophages leave behind parts of the invading germs called antigens. The body identifies antigens as dangerous and stimulates antibodies to attack them.

Macrophage in the process of taking up coronavirus. After digesting the virus, the macrophage will present a small leftover part called an antigen to a T cell in order to start the process of antibody production.

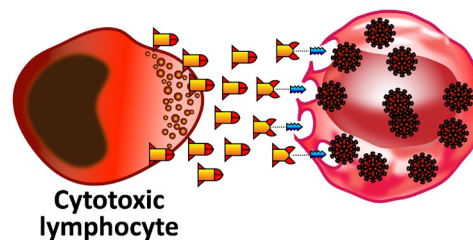


T lymphocytes or T cells – MISSILE LAUNCHERS

T lymphocytes, or T cells, are another type of defensive white blood cells; they are messengers to initiate the process of protective antibody production.

T lymphocytes also attack cells in the body that have already been infected by a virus. They do this by releasing missile-like materials that penetrate the membranes of cells infected with a virus, or even cancer cells, then completely destroy them from within. This is why these T cells are called cytotoxic T lymphocytes or killer lymphocytes.

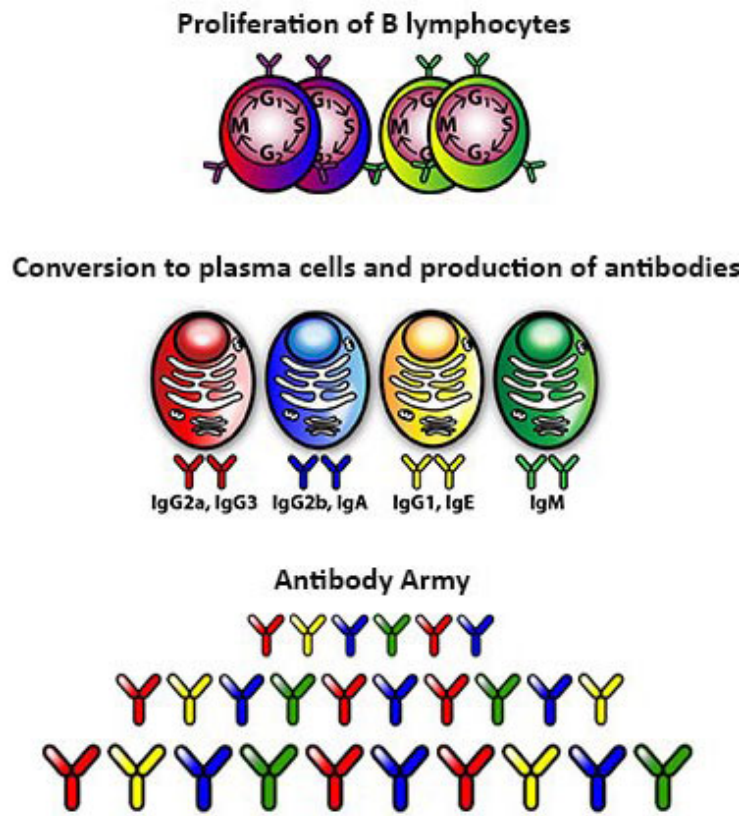
Cytotoxic T lymphocyte in the process of killing a viral-infected cell or cancer cell.



B lymphocytes or B cells – ANTIBODY ARMY

B lymphocytes, or B cells, are white blood cells whose job is to produce the antibodies that attack the antigens of the virus that have been left behind by the macrophages. This process of antibody production is brought about by collaboration between macrophages, T and B lymphocytes.

This converts the B cells into plasma cells, the cell factories that produce antibodies.



B cells collaborate with T cells and macrophages and convert into plasma cells, which produce Y-shaped neutralizing antibodies that can neutralize viruses.

WHAT FACTORS HAVE A NEGATIVE IMPACT ON THE IMMUNE SYSTEM?

Scientists have discovered that our immune response is largely controlled by our lifestyle factors such as stress, lack of physical activity, exposure to toxins and nutrition, as well as genetics.

These factors can weaken the immune system, hyper-activate it, or cause communication issues between the immune cells. These can affect the balance of the immune cells and compromise an optimum response.

For a comprehensive evaluation, your doctor can do a lab test evaluation of your body's defenses which will not be limited to the macrophages, T cells and B cells previously mentioned.

THE LYMPHOCYTE MAP™ - NUMBERS, RATIOS, PERCENTAGES AND ACTIVITY - NRPA

Lymphocytes and their subpopulations are the key elements of the immune system. In adults, they account for about 20-49% of the total number of white blood cells. It would be vitally important to measure decrease or increase in the percentage and number of these important lymphocytes. It is the numbers, ratios, percentages and activity level of these lymphocytes, and their subpopulations which are responsible for protection against various environmental factors, including viruses.

When healthy, these NRPA's are in a precise and pre-determined relationship to one another. It is the disruption of these finely balanced relationships which can compromise the immune function.

These are NOT measured by a CBC test, which is just part of a yearly checkup. There is a significant difference between lymphocyte immunophenotyping and the complete blood count (CBC), which is used for checking the overall health of a patient.

A CBC could be absolutely normal, but the patient could actually be suffering from immune dysfunction, which includes immune deficiencies, hidden inflammation, autoimmunities, hypersensitivities and allergies induced by environmental triggers. These immune disorders can be detected by the advanced immunophenotyping of lymphocytes done by Cyrex Labs.

Our genetics and lifestyle choices form what we call our "immunotype" (also known as immune fingerprint or immune signature). Specific parts of our immune system can be tested to discover our immunotype. Once we know our immunotype, it becomes easier to understand our immune response.

The Lymphocyte MAP test panel identifies 13 different immunotypes and their resulting immune characteristics. It was developed by one of the world's top immunologists, Aristo Vojdani Ph.D.

It starts with a simple blood draw that can be ordered by your healthcare practitioner. Upon review of the test results and the proper identification of your immunotype, your healthcare practitioner may recommend some of the following steps:

1. Medication to down-regulate or up-regulate your immune system.
2. Reduce or eliminate exposure to certain antigens (additional tests may be necessary).
3. Dietary and nutritional immune response modifiers appropriate for your immunotype.
4. Steps for management of your stress.
5. Physical activity and exercise for the improvement of your immune function.
6. Other lifestyle changes to improve your immune function.
7. A follow up test in a few months, or annually as part of a regular check up to optimize your immune system.

Please consult your healthcare practitioner to evaluate your immune system, or to identify your particular immunotype.

EXPLANATION OF TEST RESULTS

The Lymphocyte MAP evaluates 28 biomarkers and determinants, which include the following:

Total Lymphocyte and Percent Lymphocytes

One of the most important soldiers of the white blood cell army is the lymphocyte, so-called because they are the main type of cells found in lymph. Lymphocytes include T cells, B cells, and natural killer (NK) cells.

Each one of these lymphocytes plays a different role in protecting the body against foreign invaders. Each lymphocyte also has different subtypes or subpopulations that act together in concert to protect the body against its enemies. The optimal number for lymphocytes is around 2,200. Too high or too low numbers could reflect the general health of the patients, which is why this is usually part of a general yearly checkup.

Percentage and Total T Cell

Lymphocytes that migrate from their birthplace in bone marrow to the thymus gland for maturation are called T (for thymus) cells. T cells actively participate in the immune response against foreign materials. They can be easily distinguished from other lymphocytes by the presence of specific T-cell surface materials and by staining with colorful reagents.

Your test results may show too many or too few T cells in your blood. The total number of T cells ranges from 440 to 1,600, with the optimal number being around 1,020.

If your test results show a much lower or much higher number than 1,020, this may be a sign that your immune system isn't working properly.

- High T cell count may mean that you don't have enough B cells, which are responsible for producing the antibodies that are designed to protect you against infections.
- Low T cells may mean you have too many B cells in your blood, and thus may be producing too many antibodies.
- Low T cells have been observed in patients with viral infections and other environmental factors that destroy T cells.

Percentage and Total B Cell

Special white blood cells that develop from stem cells in the bone marrow are called B (for bone) cells. With help from the T cells, B cells become activated and produce the antibodies that fight infections and stop the enemy from damaging our body's cells. The total number of B cells ranges from 90 to 400, with the optimal number being around 245.

- Low B cells may lead to a weak immune system that can't fight off a viral or bacterial infection.
- High B cells could result in too many antibodies, which could lead to autoimmunity.

T Cell and B Cell Ratio

This number represents the relationship or proportion between the numbers of your T cells and the numbers of your B cells. The optimal T and B cell ratio would be around 7.5.

- A ratio much greater than 7.5 means you might have too many T cells in your blood.
- A ratio much lower than 7.5 means you may have too many B cells.
- Too high or too low a ratio indicates that your immune system is not working at its best.

Percentage and Total T-Helper (CD4+) Cell

T cells are further divided by function into cytotoxic T cells and T-helper (Th) cells. Th cells in turn are also divided into different subtypes, some of which are covered in this report. The Th cells are also called CD4-positive T lymphocytes. As their name indicates, T-helper cells help the body's killer cells to kill pathogens and help the B cells to produce the body's antibody weapons. They act like liaisons between the different parts of the immune system, serving as key mediators of immune response.

The measurement of Th cells is done with colorful reagents that make it possible to count these cells with a high degree of accuracy. The total number of CD4 cells can range from 500 to 1,100, with the optimal number around 800. The CD4+ Th cells are at the core of cellular immunity.

- The lower the number of Th cells, the greater the damage to the immune system and the greater the risk of illness due to immunodeficiency.
- High CD4+ cells can lead to an over-active immune system, inflammation and autoimmunity.

Percentage and Total Cytotoxic (CD8+) Cell

Cytotoxic T cells (also known as CD8+ or suppressor cells) are a subtype of T cells that kills cancer cells, cells infected by viruses, or cells damaged by environmental toxins. When activated, they release missile-like particles called granules. These granules contain materials called perforin and granzymes, which can penetrate and destroy enemy cells.

The accurate counting of CD8 T cells is also made possible with special colorful reagents. The total number of CD8 cells is between 200 to 500, with the optimal number around 350.

- Low or high CD8 numbers automatically affect the number of CD4 cells, thus also affecting the CD4/CD8 ratio. This is why the examination of the CD4/CD8 ratio after T cell/B cell ratio is helpful in the interpretation of the results of The Lymphocyte MAP™.

T-Helper (CD4) Cell/Cytotoxic (CD8) Cell Ratio

The CD4/CD8 ratio measures the proportion of CD4 T-helper cells to CD8 cytotoxic T cells. The resulting value can help predict the likely course of a disease. The most optimal ratio of CD4/CD8 is around 2.5.

- The greater the numbers go higher than 2.5, i.e., a CD4/CD8 ratio of 4.0 or 6.0, the greater the probability of immune activation and autoimmunity.

When the CD4/CD8 ratio moves in the other direction, e.g., a ratio of 1.2 or 0.5, then the probability of immunodeficiency caused by viruses and other environmental factors proportionately increases.

Percentage and Total T-Helper-1 (Th1) Cell

The T-helper-1 or Th1 cell is the first baby of the mother T cell. The Th1 cell's job is to stimulate our cell-mediated immune response by giving the right ammunition to the cytotoxic CD8 soldiers, so that they can fight and even prevent cancer and viral/bacterial infections. The total number for Th1 cells is between 150-550, while the optimal number is around 350. Lower or higher than this may mean that your immune system isn't working properly.

- Low Th1 cells may mean you have a problem with the hormones in the immune system responsible for producing Th1 cells.
- High Th1 cells may lead to an over-active immune system, inflammation and autoimmunity.

Percentage and Total T-Helper-2 (Th2) Cell

The T-helper-2 or Th2 cell is the second baby of the mother T cell. The Th2 cell primarily assists and stimulates the B cells into producing protective antibodies. The total number for Th2 cells is between 70-150, while the optimal number is around 110.

- High Th2 cells can result in the production of too many antibodies, which has been associated with asthma, allergies, hypersensitivity, and some types of autoimmunities.
- Low Th2 cells will automatically result in an increase in the number of Th1 cells, which may lead to an over-active immune system, inflammation and autoimmunity.

T-Helper-1 (Th1)/T-Helper-2 (Th2) Ratio

Any changes in the numbers or percentages of Th1 and Th2 cells and their relationship with each other can easily be observed by checking this in your test results. The optimal ratio for Th1/Th2 is around 3.

- Anything significantly below or above 3 may be an indication of over- or under-activation of your immune system, which has been associated with asthma, allergies, hypersensitivity, atopy, hyper-inflammation, autoimmunity and immunodeficiencies.

Percentage and Total T-Helper-17 (Th17) Cell

The Th17 cell gets its name from the hormone-like material called IL-17 that it produces. This lymphocyte's main job is the clearing of extracellular bacteria and fungi. The total number for Th17 cells is between 30-90, while the optimal number for Th17 is around 60.

- Therefore, low Th17 cells may result in bacterial or fungal infection.
- On the other hand, due to the inflammatory nature of this cell, high Th17 cells could lead to a variety of hyper-inflammatory and autoimmune disorders.

Percentage and Total Regulatory T (Treg or Th3) Cell

The Th3 or regulatory T cell (Treg) is a particularly important member of our immune defense force. Tregs are known to be involved in the induction of mucosal, peripheral and central tolerance, which is highly important in immune homeostasis and the prevention of autoimmunity. These Th3 cells act like the conductor of the immune system's orchestra, making sure that both Th1 and Th2 cells work in perfect harmony and balance with each other. Any disruption of this balance may result in bias towards either Th1 or Th2, leading to autoimmunities, allergies, and hypersensitivities. The total number for Treg cells is between 10-50, while the optimal number for Tregs in the blood is around 30.

- Numbers significantly above 40 may result in suppression of immune response, immune deficiency, and increased infections.
- Numbers way below 30 may lead to allergies, hypersensitivity, some inflammatory diseases, and autoimmune disorders.

T-Helper-17 (Th17)/Regulatory T cell (Treg) Ratio

Another way to examine the immune system for any imbalances is by looking at the ratio between Th17 and Treg cells. The optimal Th17/Treg ratio is around 2. Greater numbers of Th17 cells in proportion to Tregs results in a higher Th17/Treg ratio, while, obviously, more Tregs in proportion to Th17 cells would lower the ratio.

- A Th17/Treg ratio significantly above 2 may result in tissue inflammation, systemic and organ-specific autoimmune disease.
- A ratio way below 2 may result in bacterial and fungal infections.

Percentage and Total Natural Killer (NK) Cell, Cytotoxic Natural Killer Cell, and Natural Killer T Cell

Natural killer (NK) cells are major components of the innate immune system. They kill viral-infected and tumor cells without pre-stimulation. Some NK cells also act as the interface between the innate and adaptive immune systems.

Among the ranks of the NK soldiers, there is a subset of super-soldiers that are like master ninja assassins, which we can call cytotoxic NK cells (CNK). These cells are naturally more cytotoxic than their lesser-performing brothers. There are also T cells that act like NK cells, and are called natural killer T cells or NKT cells.

The total number for NK cells is 60-220, while the optimal number is around 140. The total number for CNK cells is 30-200, while their optimal number is around 115. The total number for NKT cells is 10-120, while their optimal number is around 65.

- A low percentage of NK cells in the results below the optimal range means that enemies (environmental factors) have invaded and have managed to kill many defensive cells, leaving the body with too few soldiers to fight infections and tumor cells.
- A high percentage and high absolute numbers of NK cells above the optimal range means that in response to an invasion, the commander-in-chief has called for additional troops to fight infections and tumor cells.
- Low NKT cells may lead to enhanced infection, induction of autoimmune diseases, and higher tumor burden. High NKT cells may lead to neurological autoimmunities, COPD, and phospholipid syndrome.

CYREX LYMPHOCYTE IMMUNOPHENOTYPING

Cyrex Immunity classifications are based solely on, and refer solely to, absolute lymphocyte counts and their subsets. Immunity types are identifiable patterns that show the immune system is responding to circumstances or environmental factors. While cell counts and immunity types may provide valuable insights, they are not indicative of any specific condition or disease and should not be used alone to interpret the results. The Lymphocyte MAP™ provides two important categories of information: (1) each parameter/determinant provides important information on its own, and (2) the relationship between parameters provides another set of invaluable information categorized in multiple immunity types (immunophenotype patterns).

- Immunity type 1. Immune balance or harmony** at the time of testing, due to one of the following: Total Cell Counts are all within the reference range; some determinants (percentages or ratios) may be out-of-range.
- Immunity type 2. T cell Dominance** at the time of testing, due to one of the following: high T cell with normal or low B cell, or normal T cell with low B cell results.
- Immunity type 3. B cell Dominance** at the time of testing, due to one of the following: high B cell with normal or low T cell, or normal B cell with low T cell results.
- Immunity type 4. Immune Hyperactivity/CD4 Dominance** at the time of testing, due to one of the following: high CD4 with normal or low CD8, or normal CD4 with low CD8 results.
- Immunity type 5. Immune Deficiency/CD8 Dominance** at the time of testing, due to one of the following: high CD8 with normal or low CD4, or normal CD8 with low CD4 results.
- Immunity type 6. Th1 Dominance** at the time of testing, due to one of the following: high Th1 with normal or low Th2, or normal Th1 with low Th2 results.
- Immunity type 7. Th2 Dominance** at the time of testing, due to one of the following: high Th2 with normal or low Th1, or normal Th2 with low Th1 results.
- Immunity type 8. Regulatory T cell Imbalance** at the time of testing, due to one of the following: high or low regulatory T cell results.
- Immunity type 9. Th17 Dominance** at the time of testing, due to one of the following: high Th17 with normal or low Treg, or normal Th17 with low Treg results.
- Immunity type 10. Th1+Th17 Dominance** at the time of testing, due to one of the following: high Th1+Th17 with normal or low Treg.
- Immunity type 11. Th2+Th17 Dominance** at the time of testing, due to one of the following: high Th2+Th17 with normal or low Treg.
- Immunity type 12. NK Cell Imbalance** at the time of testing, due to one of the following: high or low NK or Cytotoxic NK cell results.
- Immunity type 13. NKT Cell Imbalance** at the time of testing, due to one of the following: high or low NKT cell results.

Low numbers of lymphocytes and their subsets may result in one or more absolute counts being out of range, while other absolute counts might even be over the high limits of the given range, but in certain cases the results would not fit within the Cyrex-defined criteria for Immunotypes 1-13. Under such circumstances the results would be labeled as **No Immunotypes Apply** at time of testing.

THE LYMPHOCYTE MAP™ AS PART OF YOUR YEARLY CHECKUP

We are all unique individuals, with our own personal histories, lifestyles and environments, and unique genes, which all combine to give us unique immune fingerprints or immunotypes. Our immunotype is the state of our immune system at the time of testing, yet it can change with time, based on its influencing factors.

Differing Immunotypes in individuals may be partially the reason why we may not all react to a pathogen or disease in exactly the same way. Some of us may have immune systems that are more sensitive or more resistant to particular immune disorders. This may explain why a cold can be just barely a quick annoyance to one person and a long, work-stopping, miserable torment to another. It also explains how one person can catch COVID-19 and get no symptoms at all, another can get sick for three days, yet another for two weeks, and another can actually die from it. However, the value of a comprehensive immune evaluation goes beyond susceptibility factors.

It is important for your doctor to know what your immune status, or immunotype is, so that you can identify the areas of your immune system that may need attention.

Therefore, an annual checkup of your immunotype is essential to help optimize your immune system.

To your Health!



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