

Functional Medicine University's Functional Diagnostic Medicine Training Program

INSIDER'S GUIDE

Special topic: the fdm approach to auto-immune conditions

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Contents

Contents.....	2
Autoimmunity: A Functional Medicine Approach	5
Some of the possible contributing factors include:.....	5
Environmental exposures.	5
Antigen Overload	5
Oxidative stress.....	5
The Auto-Immune Investigation Challenge Notes from the Medical Literature.....	6
Investigating Rheumatoid Arthritis.....	8
How is RA diagnosed?	8
The following labs make up the basics of ruling in or out RA.	8
Citruinated Peptide (anti-CCP) Antibodies in RA.....	8
Allopathic Approach for Rheumatoid Arthritis	8
The Logical Approach to Rheumatoid Arthritis The Patient Specific Approach	9
Cortisol/Inflammation Connection	11
Effects of Divergence from Normal Levels of Cortisol and DHEA	12
Physiology Cortisol is the precursor of cortisone and acts as an anti-inflammatory; and it is the primary hormone directing immune function.	13
Recommended Treatment for Depressed Cortisol	14
Recommended Treatment for Depressed Cortisol	15
Recommended Treatment for Depressed DHEA	15
Calculating the DHEA/Cortisol Ratio	15
If low DHEA/cortisol ratio:	15
If high DHEA/cortisol ratio:	15
The Gut Connection to Rheumatoid Arthritis	16
To review, the inflamed leaky gut.....	17
Causes of Leaky Gut.....	17
Test for Leaky Gut.....	18
Intestinal Barrier Function Test Explained.....	19
How is mucosal barrier function evaluated?.....	21
If a hyper elevated or shut down mucosal barrier and/or leaky gut is confirmed, it is extremely important to identify the cause.....	21
Possible causes.....	21
Consider the following actions: Consider "4 R" approach to GI health:	22

If depressed mannitol with an elevated or normal lactulose/mannitol ratio	23
Possible causes:.....	23
Consider the following actions: Consider "4 R" approach to GI health:	23
Depressed Secretory IgA.....	23
Overview	23
Recommended Treatment to Increase Secretory IgA	24
Mycoplasma and Rheumatoid Arthritis	25
Minocycline in rheumatoid arthritis	25
Rheumatoid Arthritis and Oxidative Stress	27
Treatment Protocols.....	28
If high catechol and/or 2,3 DHB:.....	28
If high lipid peroxides:.....	28
If low reduced glutathione:.....	29
If low superoxide dismutase (SOD) and/or glutathione peroxidase (GSH-Px):...	30
The role of Vitamin D Deficiency in Pain, Inflammation, and Inflammatory Diseases	31
Testing for Serum Vitamin D	31
Replacing Vitamin D.....	32
Contraindications for Vitamin D Supplementation	32
Rheumatoid Arthritis and Sex Hormones.....	33
Rheumatoid Arthritis and Fatty Acids.....	34
The Role of Essential Fatty Acids in Health and Disease	37
Low Delta-6 Desaturase Activity.....	37
Insulin Dysregulation	37
Clinical Applications	38
Autoimmune Diseases.....	38
Interpretation of the Fatty Acid Profile	38
If analysis shows: Low alpha-linolenic acid (ALA)	38
If analysis shows: Low eicosapentaenoic acid (EPA) or Low docosapentaenoic acid (DHA)	38
If analysis shows: Elevated linoleic acid (LA) and/or arachidonic acid (omega 6 fatty acids)	38
Delta-6 desaturase deficiency:	38
If analysis shows: High linoleic acid (LA) AND Low di-homo-gamma linolenic acid (DGLA) If AA is also low, the problem is more severe.....	39
If analysis shows: Low EPA.....	39
If analysis shows: High or normal EPA and low DHA	39

Dysglycemia and Hyperinsulinemia:	39
If analysis shows: Low DGLA AND High AA	39
If analysis shows: Low oleic acid (18:2n-9) and high stearic acid (18:0)	39
If analysis shows: High trans fats Elaidic acid (18:1n9t) [Indicates increased oxidative stress levels and a need for additional anti-oxidant protection.]	39
If analysis shows: Elevated levels of saturated fats	39
Rheumatoid Arthritis and Digestive Function	41
Rheumatoid Arthritis and Amino Acids	43
Interpretation of Amino Acid Profile:	44
Gastrointestinal	44
Cardiovascular	45
Oxidative Stress	45
Detoxification	45
Musculoskeletal	46
Nutrient Adequacy	46
Endocrine	47
Neurological	48
Rheumatoid Arthritis and Element Imbalance	49
Rheumatoid Arthritis and Bacterial/Parasitic Infection	50
Recommended Treatments:	53
Acknowledgements	56

Autoimmunity: A Functional Medicine Approach

Of the many diseases afflicting the general public, a large number fall under the heading of **autoimmune diseases**.

The list of diseases associated with autoimmunity includes but is not limited to the following conditions:

- Rheumatoid Arthritis,
- Ankylosing spondylitis,
- Sjorgen's syndrome,
- Lupus,
- Fibromyalgia,

It is commonly accepted that autoimmune diseases represent an over-active immune system that attacks itself by mistake.

There are more than 80 types of autoimmune diseases, and some have similar symptoms. Getting diagnosed can be frustrating and stressful. In many people, the first symptoms are being tired, muscle aches and low fever.

Some of the possible contributing factors include:

Environmental exposures.

Continued exposure to heavy metals and environmental pollution can result in overloading the immune system. Our air, water, and food in particular are full of toxic substances.

Antigen Overload

An antigen is a substance that when introduced into the body stimulates the production of an antibody. Antigens include toxins, bacteria, foreign blood cells, and the cells of transplanted organs.

Oxidative stress

Oxidative Stress plays a role in autoimmune diseases.

Chronic systemic inflammation is related to several autoimmune disorders, such as lupus, rheumatoid arthritis, Sjogren's syndrome, and fibromyalgia. Inflammation can be traced to destructive cell-signaling chemicals known as **cytokines** that contribute to many degenerative diseases.

The Auto-Immune Investigation Challenge

Notes from the Medical Literature

Autoimmunity, in which the immune system recognizes and attacks the self's own tissue, is not as simple as it seems. Self-recognition appears to be at the heart of health as well as of certain diseases.

One of the paths to this insight has been provided by the autoimmune disorders, in which the immune system attacks normal, healthy tissue. Autoimmune disease, which may be crippling or fatal, can strike any tissue or organ.

Research work on a form of autoimmune arthritis shows that the basis of autoimmunity may be a resemblance between a specific foreign molecule and a molecule of the self.

This finding is consistent with a model of the immune system in which the immune system receptors that perform the work of recognition can themselves be recognized by other receptors. Such "self-recognition," which was strictly outlawed by older models of the immune system, may form the basis of a network whose equilibrium keeps the body healthy. When it is disrupted, as it is in autoimmunity, disease results.

The list of autoimmune diseases is both long and disturbing. It includes multiple sclerosis, in which the tissue attacked is myelin (a sub-stance that sheathes nerves in the central nervous system); myasthenia gravis, in which the target is a receptor molecule for the important neurotransmitter acetylcholine; rheumatoid arthritis, whose target is the peripheral joint; type I (juvenile) diabetes mellitus, in which the cells producing insulin are destroyed, and systemic lupus erythematosus, in which DNA, blood vessels, skin and kidneys are attacked. These immunological attacks are detected in clinical laboratory by the measurement of **tissue-specific and tissue non-specific antibodies**.

Autoimmune diseases can be separated broadly into two categories. One group is characterized by the presence of auto antibodies which are broadly reactive with **nuclear or cytoplasmic antigens** and do not demonstrate any tissue specificity. Included in this group are diseases such as rheumatoid arthritis, SLE, mixed connective tissue disease, scleroderma, Sjogren's syndrome, and dermatomyositis/polymyositis.

A second group of autoimmune diseases is characterized by autoantibodies which demonstrate **tissue specificity**. These diseases include thyroiditis, chronic liver diseases (including primary biliary cirrhosis and chronic active Hepatitis), certain cases of pernicious anemia, and myasthenia gravis.

An assault on the self through molecular mimicry or antigenic similarity between foreign antigens (virus, bacteria) and human tissue antigens which may end with an autoimmune disease. This process which may strike many target tissues is shown in Table 1.

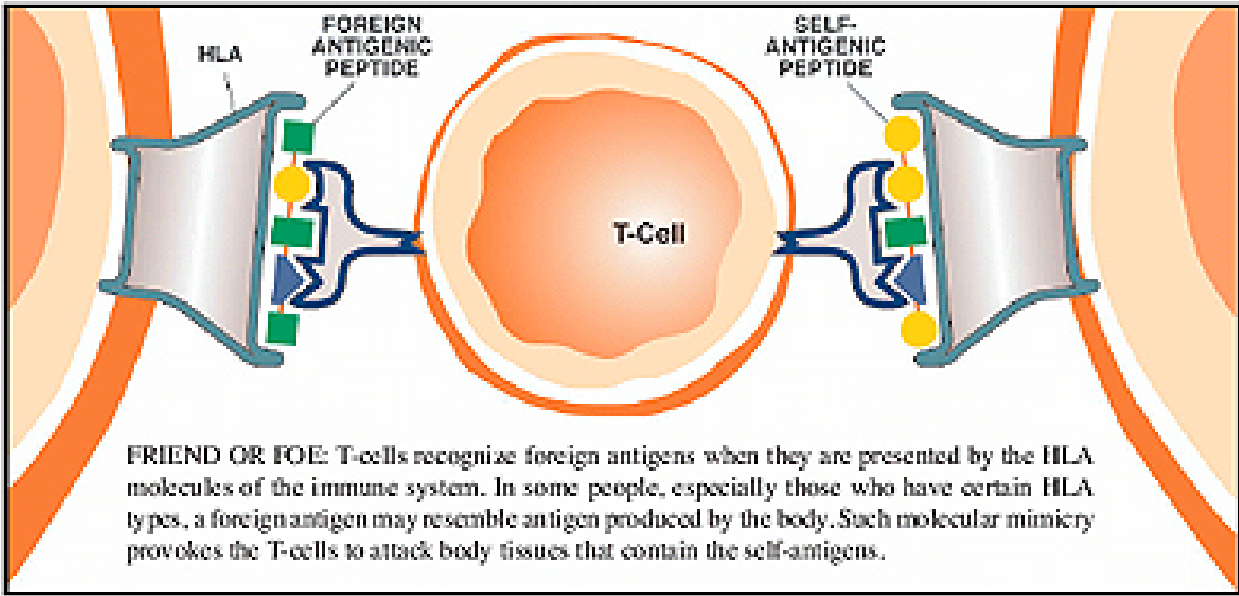


Table 1: Where Autoimmunity May Strike

<u>DISEASE</u>	<u>TARGET</u>
Addison's disease	Adrenal gland
Autism	Gut and brain
Autoimmune hemolytic anemia	Red blood cell membrane proteins
Crohn's disease	Gut
Goodpasture's syndrome	Kidney and lungs
Graves' disease	Thyroid
Hashimoto's thyroiditis	Thyroid
Idiopathic thrombocytopenic purpura	Platelets
Insulin-dependent diabetes mellitus	Pancreatic beta cells
Multiple sclerosis	Brain and spinal cord
Myasthenia gravis	Nerve/muscle synapses
Pemphigus vulgaris	Skin
Pernicious anemia	Gastric parietal cells
PostStreptococcal glomerulonephritis	Kidney
Psoriasis	Skin
Rheumatoid arthritis	Connective tissue
Scleroderma	Heart, lungs, gut, kidney
Sjogren's syndrome	Liver, kidney, brain, thyroid, salivary gland
Spontaneous infertility	Sperm
Systemic lupus erythematosus	DNA, platelets, other tissues

Investigating Rheumatoid Arthritis

How is RA diagnosed?

Allopathic and functional medicine practitioners will commonly use a variety of tools to diagnose RA and to rule out other conditions. **These include a good medical history, physical examination and standard laboratory tests.**

The following labs make up the basics of ruling in or out RA.

- Citrullinated Peptide (anti-CCP) Antibodies
- **Rheumatoid** factor
- Erythrocyte sedimentation rate
- C-reactive protein
- White blood cell count
- Blood tests for anemia.

X-rays can be used to determine the degree of joint destruction but are not useful in the early stages of RA before bone damage is evident. They can be used later to monitor the progression of the disease.

Citrullinated Peptide (anti-CCP) Antibodies in RA

Anti-CCP antibodies are potentially important markers for diagnosis and prognosis in rheumatoid arthritis (RA), because they:

- are as sensitive as, and more specific than, IgM rheumatoid factors (RF) in early and fully established disease
- may predict the eventual development into RA when found in undifferentiated arthritis
- are a marker of erosive disease in RA
- may be detected in healthy individuals years before onset of clinical RA

Allopathic Approach for Rheumatoid Arthritis

The primary objective of traditional medicine is temporary relief of pain and dysfunction via pharmaceutical agents.

The most common pharmacologic therapy includes a combination of DMARDs (disease modifying antirheumatic drugs) also known as SAARDs, or slow acting antirheumatic drugs and nonsteroidal anti-inflammatory drugs. DMARDs include methotrexate, gold,

hydroxychloroquine, sulfasalazine, azathioprine, and penicillamine with methotrexate the most popular among rheumatologists

Corticosteroids are also used for their anti-inflammatory and immunosuppressive properties. Given early in the course of the disease, they appear to reduce the progression of erosive joint changes. However, because of adverse effects of corticosteroids they should be used in the lowest possible dose for the shortest possible treatment interval.

The Logical Approach to Rheumatoid Arthritis ***The Patient Specific Approach***

It is not uncommon to have two arthritis patients with perhaps identical symptoms, yet their arthritis is associated with causative factors that require not only different but in fact exact opposite treatments.

The trial and error, shot-in-the-dark approaches to arthritis are a never-ending source of frustration to both you and your patients.

Case in point: two patients are seen experiencing the same identical RA symptoms, painfully swollen knees and loss of shoulder mobility. The treatment protocol prescribed for the first patient helps immensely; yet in the second patient the arthritis stays the same or even gets worse, while at the same time causing the patient to experience painful abdominal cramps and a headache.

What do you do now? Try another arthritis remedy?

What works for one arthritis patient will not help another and may even make him worse. If you are going to offer effective treatments to your arthritis patients you need the means to determine each individual's specific biochemical glitches.

You have a choice to make.

You can either continue with a time-consuming, expensive and frustrating trial and error approach to finding what treatment “might” help any particular patient -- or -- you can eliminate the guesswork by putting a scientific assessment system on your side.

Do you begin to see why all the arthritis remedies being peddled by the nutrition supplement companies are a joke? They do not address the fundamental question of **cause**.

As a functional medicine practitioner you have the tools to identify the specific biochemical, physiological and environments cause(s) of each arthritis patient.

Based on this information you will be able to outline a logical treatment protocol focused on the objective “causes” of the disease.

There is a growing population of health professional including medical physicians who are embracing the power of functional diagnostic medicine.

As practitioner using the functional medicine approach you can compare yourself to a CSI agent. Looking for the “key” issues to crack the case is your primary objective.

In order to solve the case, there are some additional action steps that are required.

Aside from the typical entrance medical questionnaire which simply asks for main complaint and duration of symptoms, you will have the patient complete a detailed medical history which digs deep uncovering the possible biochemical, physiological issues present in that patient.

Of course your next action will commonly require ruling out or in a number of potential cause(s).

The following should be considered as potential causes of RA.

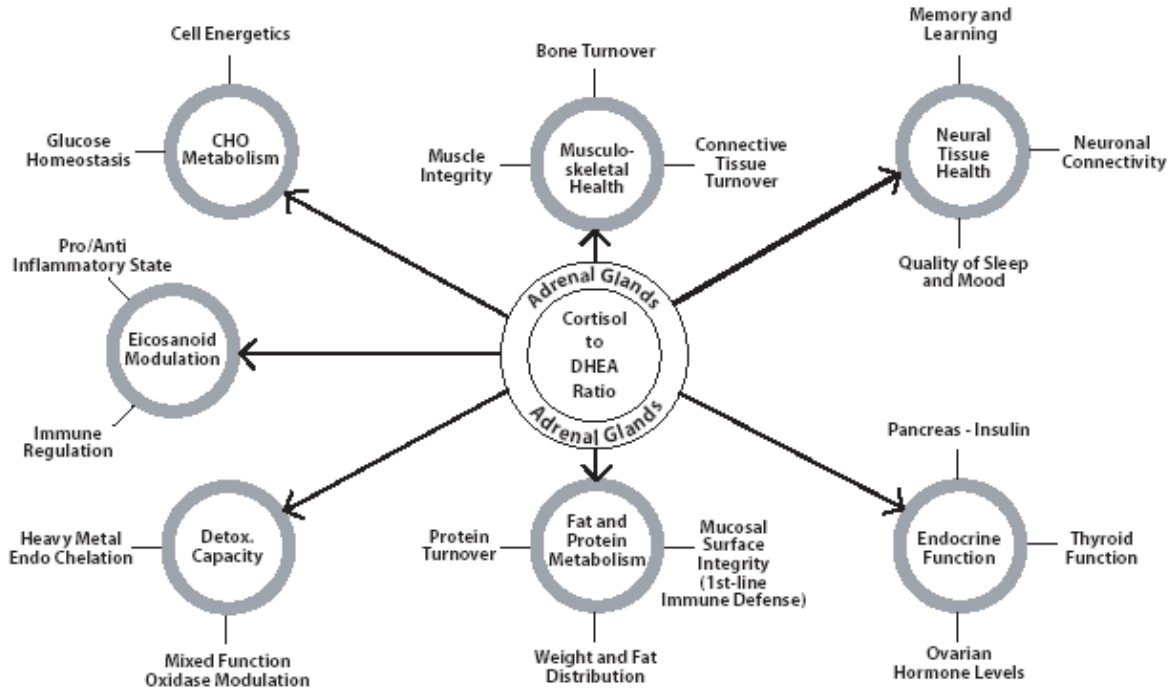
- Compromised Cortisol/DHEA/SigA
- **Increased Intestinal Permeability/Leaky Gut**
- Bacterial, Parasitic Infections (**Mycoplasma Infection**)
- Hormonal Imbalance
- Fatty Acid Imbalance
- Nutritional and Amino Acid Co-factor Deficiencies
- Oxidative Stress

Important Point: It must be understood by your patients that the degree of improvement from RA has a lot to do with how much damage has already been done by the disease itself. Functional medicine offers the RA patient the unique opportunity to uncover the potential causes. Unfortunately, if the disease has progressed to the point of causing permanent damage, then we have to be realistic in letting the patient know that their prognosis is not as good as someone who is seen in the early stages of the disease. This does not mean in any way that offering the science of functional medicine is not of value. **Far from it!**

In fact, the functional medicine practitioner may be the key to stopping further debilitation and without contradicting myself, you never know what recuperative powers a patient has until you give the body what it so desperately needs.

As was previously discussed in detailed with CFS and Fibromyalgia we once again return to Cortisol/DHEA as a central theme.

Cortisol/Inflammation Connection



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As is evidenced by review of the above diagram, cortisol and DHEA play a direct role in eicosanoid modulation in addition to other key factors to uncovering the probable issues related to RA.

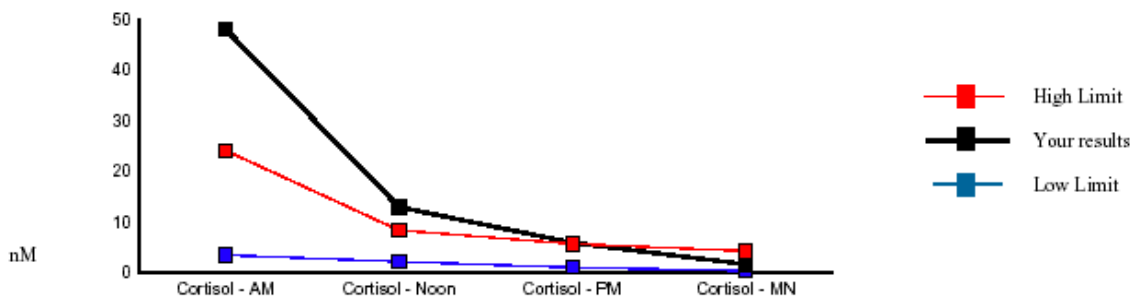
Again we return to initially investigating the cortisol/DHEA function.

43 Adrenal Stress Plus

Metho

Cortisol - Saliva

	<u>Normal Results</u>	<u>Abnormal Results</u>		<u>Reference Limits</u>
Cortisol - AM		48.1 H	nM	3.4 - 24.1
Cortisol - Noon		12.9 H		2.1 - 8.3
Cortisol - PM		5.8 H		0.9 - 5.6
Cortisol - MN	1.6			0.3 - 4.2
Total Cortisol		68.4 H		6.7 - 42.2



Effects of Divergence from Normal Levels of Cortisol and DHEA

Maintaining physiological balance is an important aspect of vibrant health, and nowhere is this more evident when it comes to cortisol. The production of too much cortisol can literally burn up the body, and insufficient cortisol production causes the body's internal machinery to malfunction, especially at the cellular level.

The adrenal glands produce both cortisol and DHEA in the adrenal cortex under the stimulation of adrenocorticotropic hormone (ACTH), which is released by the pituitary gland. ACTH acts like a whip on the adrenals. It is in many ways similar to a jockey whipping a horse to make it run faster. If the jockey ignores the clues that his horse is fatigued and keeps whipping it, the horse will keep running until it collapses in total exhaustion or death. In the case of the human body, if we allow stress levels to become chronic and out of control, we can sooner or later expect the same result.

Optimal adrenal function exists when the ratio of cortisol to DHEA is in proper balance. This is why measuring this ratio is the best way to both evaluate adrenal function and determine the effects stress is having on overall health. When cortisol levels are elevated and DHEA is low we are considered to be in a Chronic Stress Response. When this happens we are losing (or have already lost) our ability to modulate bodily functions and are on the road to further hormone, immune, and metabolic breakdown.

For example, if cortisol levels are too high at night, rather than getting the rest and recovery necessary to maintain optimal physical repair and psychic regeneration, the body will be in a catabolic state (high nighttime cortisol levels inhibit the release of growth hormone necessary to repair and rebuild body tissues).

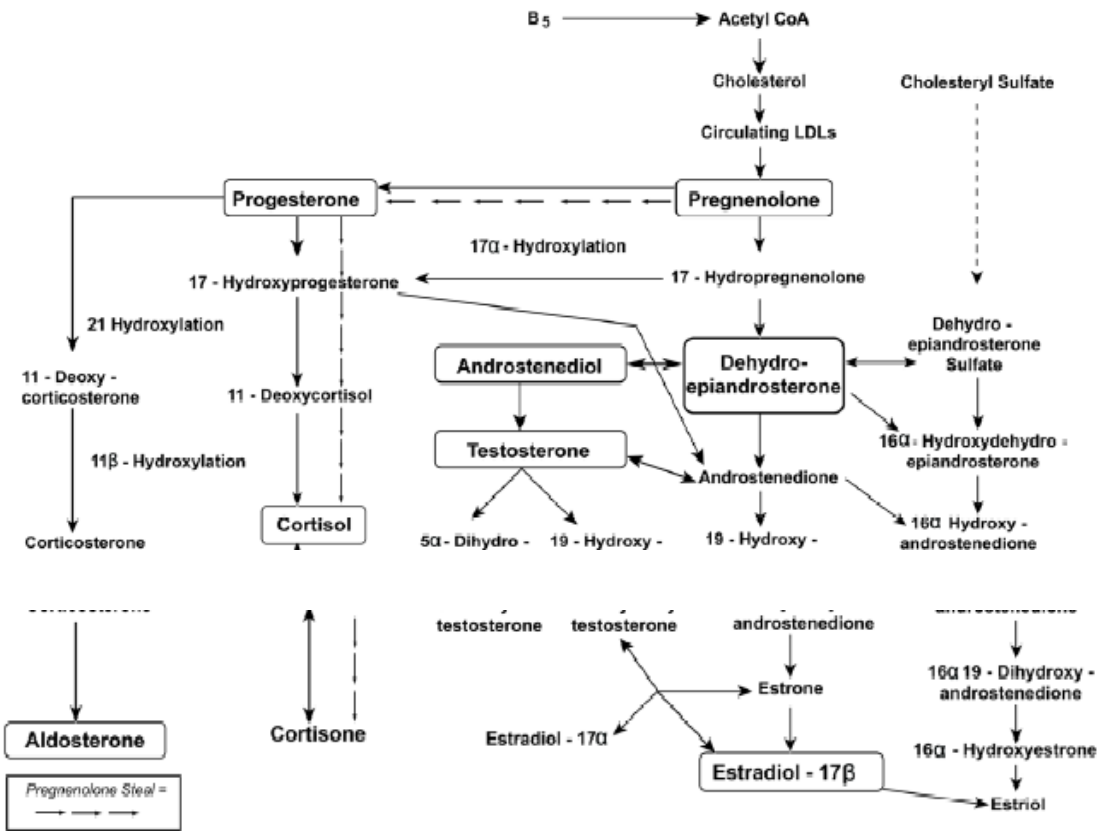
An elevated cortisol to DHEA ratio will also interfere with the **surface integrity of the body's mucosal linings** that act as its first-line immune defense. This mucosal barrier is primarily under the direction of the adrenal glands, specifically cortisol and DHEA. Cortisol and DHEA systemically modulate the production and turnover of specialized immune cells called immunocytes (also known as plasmacytes) that produce the secretory antibodies that protect us. The primary antibody of defense is **secretory IgA** (sIgA). When cortisol is elevated and DHEA is low, suppression of these mucosal immune cells occurs, compromising our first-line immune defense, resulting in low sIgA output.

The longer a person is in a state of chronic stress (high ratio of cortisol to DHEA), the more compromised his or her **first line of immune defense will be and the greater the risk for opportunistic infections and allergic reactions to foods.** This could ultimately lead to cancer, cardiovascular disease as well as autoimmune disease, a variety of degenerative diseases and accelerated aging.

In a Chronic Stress Response all body functions have become compromised due to prolonged hormone, immune and metabolic breakdown that can lead like falling dominoes to a cascade of chronic degenerative diseases from which the weakened body has a reduced chance to recover.

Physiology

Cortisol is the precursor of cortisone and acts as an anti-inflammatory; and it is the primary hormone directing immune function.



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Abnormal cortisol and/or DHEA values (either elevated or depressed) result in a decrease in the activity of the immunocytes that produce secretory IgA (sIgA). sIgA provides a mucosal first-line immune defense against virtually every pathogen, including parasites, protozoa, yeasts, fungi, bacteria, and viruses. sIgA also provides a normal immune response to regularly encountered food proteins. Dysfunctional mucosal immunity is associated with an increased risk of infections and of adverse food reactions.

Stress is a major underlying cause of many chronic illnesses, from Chronic Fatigue Syndrome to food and environmental allergy. A stressful lifestyle can lead to consistently high levels of cortisol and low levels of DHEA (dehydroepiandrosterone), which can be damaging to the brain and other tissues. Cortisol elevation also impacts immune responses, such as secretory IgA (sIgA) and antigliadin antibody (AGA) production.

The Adrenal Stress Profile is a measure of an individual's response to stress. It is also an important tool for pointing to adrenal imbalances that may be impacting a patient's health.

Total Secretory IgA (SIgA) determination from saliva is used in the clinical evaluation of the effect of stress on immunity. SIgA is a direct marker of cortisol induced immunosuppression and an indirect marker of sympathetic to parasympathetic balance. SIgA levels have additional relevance in the management of external stressors such as food intolerance, chronic parasitic, fungal and viral infections.

Various immune cells (white blood cells) cycle in and out of the spleen and bone marrow for special conditioning, and possible nourishment and instructions. This immune system trafficking follows the cortisol cycle. So, if the cycle is disrupted, especially at night, then the immune system is adversely affected.

Short and long-term stress is known to suppress the immune response on the surfaces of our body as in lungs, throat, urinary and intestinal tract. With the reduction in the surface antibody (called secretory IgA), the resistance to infection is reduced and allergic reactions are believed to increase.

Recommended Treatment for Depressed Cortisol

Lifestyle changes:

Stress reduction, rest & relaxation, prayer, meditation, regular exercise, blood sugar stabilization, sufficient sleep, elimination of food allergies and restoration of normal bowel function

Rest, exercise, prayer, meditation, relaxation exercises

Dietary changes:

Balance blood sugar with a focused low glycemic diet

Nutritional supplements: High-grade multivitamin and mineral.

Herbal Support

"Adaptogenic" herbs: American or Korean ginseng (*Panax spp.*), Siberian ginseng (*Eleutherococcus senticosus*), Withania (*Withania somnifera*)

Miscellaneous herbs:

Licorice Plus and/or Licorice Extract

Astragalus has been valued by the Chinese for centuries for its immune-enhancing and adaptogenic properties. As an adaptogen, it may modify and improve the body's response to stress through action on the adrenal cortex.

Glandular Support:

Support Adrenals from BioMatrix

Hormone replacement therapy:

Cortisol, DHEA, pregnenolone, as indicated

Never Prescribe Support Adrenal and/or Licorice Root in the evening. Last dosage should be late afternoon

Recommended Treatment for Depressed Cortisol

✚ Lifestyle changes:

✚ Support Adrenal

Recommended Treatment for Depressed DHEA

✚ DHEA or pregnenolone supplementation may be warranted

Calculating the DHEA/Cortisol Ratio

This is measurable with the Functional Adrenal Stress Profile. Simply divide the cortisol sum by the DHEA(s) average to get the ratio. A normal ratio is approximately **5:1 to 6:1**.

If low DHEA/cortisol ratio:

Suspect:

- A physiological response to stress, with shifting of the steroidogenic pathway to cortisol at the expense of DHEA

Consider the following options:

- Consider lifestyle, dietary, and herbal options outlined under high cortisol. DHEA or pregnenolone supplementation may be warranted
- Consider measuring testosterone and/or estradiol levels and intervene if necessary
- Support immune function, if indicated

If high DHEA/cortisol ratio:

Suspect:

- An abnormal physiological response to stress, with shifting of the steroidogenic pathway to DHEA at the expense of cortisol

Consider the following options:

- Consider lifestyle, dietary and herbal options as outlined under low cortisol
- Consider measuring testosterone and/or estradiol levels and intervene if necessary

The Gut Connection to Rheumatoid Arthritis

The purpose of the gastrointestinal tract (gut) is multi-fold.

1. It digests food into small easily absorbed particles,
2. absorbs small food particles to then be converted into energy,
3. attaches nutrients like vitamins and minerals to carrier proteins which then transport them across the gut lining into the bloodstream,
4. detoxifies the chemicals we daily imbibe through our air, food and water, as it contains a major part of the chemical detoxification system of the body which protects us from cancer and all other diseases, and
5. fights off infection, as it contains over half of the immune system which synthesizes immuno-globulins or antibodies that act as the first line of defense against infection, cancer and other diseases.

The leaky gut syndrome is an extremely common problem, yet is seldom tested for.

Remember this: if the gut is not totally healthy, you have no chance of healing anything else, regardless of the label on your condition. It doesn't matter what type of chronic pain you have, or if you have high blood pressure, multiple sclerosis, prostatitis, cancer, or merely accelerated aging. You are stuck until the gut is healed.

The leaky or hyperpermeable intestinal lining places a major burden on the body's ability to absorb amino acids, essential fatty acids, minerals and vitamins. It would appear that nutrients could simply slip right on into the gut. Sadly the opposite is true. For in order for the body to absorb a mineral, a **carrier protein must be attached**. This protein must hook onto the mineral that actively carries it across the gut wall into the bloodstream.

But when the bowel lining is damaged through inflammation the nutrient carrier proteins get damaged. In addition, the finger-like projections that line the gut and allow us to absorb food gets damaged. When these get destroyed, the result is malabsorption. So in addition to new food and chemical allergies and auto-immune diseases, the leaky gut victim may develop mineral and vitamin deficiencies, even in spite of taking adequate levels of them.

What can cause the inflammation that leads to the leaky gut syndrome? Examples include:

1. Abnormal gut bugs, called flora (e.g., unwanted bacteria, parasites, and protozoa from contaminated food and water, and overgrowth of yeasts like Candida from antibiotics)
2. Chemicals that irritate the gut (e.g. ingested alcohol and food additives or inhaled toluene or formaldehyde from that new carpet or paint, and of course, NSAIDs)

3. Food irritants and allergens (e.g. eating things that you know bother you and processed foods with their long list of mysterious chemical ingredients)
4. Emotions like anger and worry (which dump stress hormones into the system and cause loss of protective nutrients)

Genetic and acquired enzyme deficiencies (e.g. lactose deficiency and celiac disease), and more.

To review, the inflamed leaky gut

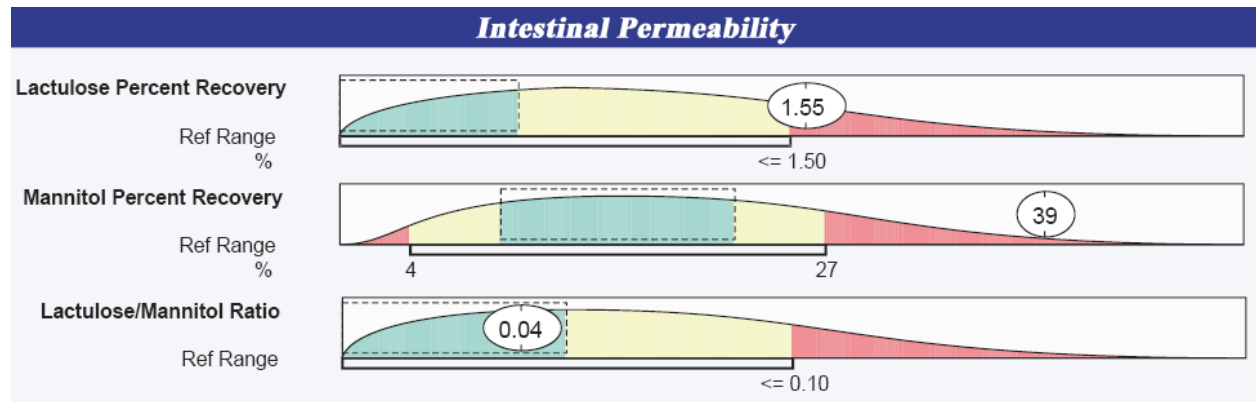
- does not absorb nutrients and foods properly, so fatigue and bloating can occur.
- allows large food antigens into the blood stream so food allergies and new symptoms are created (e.g., arthritis, fibromyalgia, etc.).
- results in damaged carrier proteins, so malabsorption and nutrient deficiencies occur. These can cause any symptom (e.g., magnesium deficiency-induced muscle spasms or body pain as in chronic back pain or angina, or copper deficiency-induced high cholesterol are just a few examples).
- overloads detoxification pathways, resulting in chemical sensitivity with brain fog, or feeling spacey, dizzy, dopey, unable to concentrate. Other times it can be other organ symptoms, including pain in places of previous injury. Undetoxified natural gas from the heating system or formaldehyde from the office carpet, for example, can back up and precipitate severe pain in old back injury sites. Furthermore, the leakage of toxins overburdens the liver so that the body is less able to detoxify all the everyday chemicals we breathe, encouraging their backlog and buildup in muscles and joints.
- damages the protective coating of your own gut antibodies, the secretory IgA. Once this is lost, the body is more vulnerable to infections in the intestines from bacteria, protozoa, viruses and yeasts (e.g., Candida). This overgrowth of unwanted bugs, called intestinal dysbiosis, further inflames the gut, creating a vicious cycle.
- allows translocation or passage of bacteria and yeast (there are hundreds of species in the intestine) from the gut cavity directly into the bloodstream where they set up infection anywhere, including muscles, joints, bones, teeth roots, coronary arteries, or even the brain.
- is responsible for auto-antibodies. Auto-immune diseases like rheumatoid arthritis, lupus arthritis, dermatomyositis,

Causes of Leaky Gut

- Intestinal dysbiosis (Candida, etc.)
- Medications (NSAIDs, antibiotics, etc.)
- Food allergy
- Chemical sensitivity

- Celiac disease, malabsorption
- Auto-immune disease
- Digestive insufficiencies
- Poor diet
- Nutritional deficiencies, and much more

Test for Leaky Gut



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Intestinal Barrier Function Test	Patient Value		Reference Range	Units
	Normal	Abnormal		
DIETARY PROTEINS ANTIBODIES				
IgG DIETARY PROTEIN	1200		400 - 2000	ng/mL
IgM DIETARY PROTEIN		8600 H	400 - 2000	ng/mL
IgA DIETARY PROTEIN		4500 H	400 - 2000	ng/mL
YEAST ANTIBODIES				
IgG YEAST	1800		400 - 2000	ng/mL
IgM YEAST		6500 H	400 - 2000	ng/mL
IgA YEAST		3100 H	400 - 2000	ng/mL

AEROBIC BACTERIA ANTIBODIES

IgG AEROBIC BACTERIA		2300 H	400 - 2000	ng/mL
IgM AEROBIC BACTERIA		5000 H	400 - 2000	ng/mL
IgA AEROBIC BACTERIA		2700 H	400 - 2000	ng/mL

ANAEROBIC BACTERIA ANTIBODIES

IgG ANAEROBIC BACTERIA		3100 H	400 - 2000	ng/mL
IgM ANAEROBIC BACTERIA		5100 H	400 - 2000	ng/mL
IgA ANAEROBIC BACTERIA		1700	400 - 2000	ng/mL

RED = Strong indication that condition exists

GREEN = Marginal indication that condition exists

Indication: Normal Levels

Possible Immunodeficiency

Food Intolerance

Yeast

Microflora Imbalance

Gut Barrier Dysfunction

© Immunosciences

Intestinal Barrier Function Test Explained

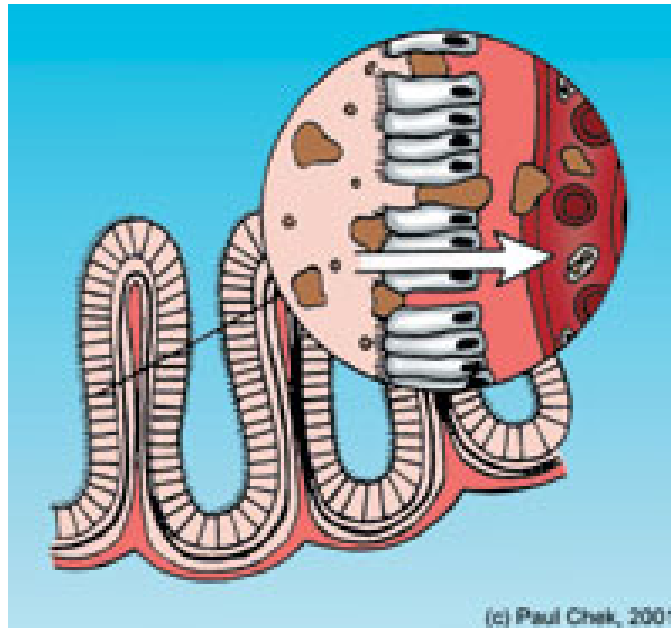
The gastrointestinal (GI) tract is the second largest body surface area and the condition of this organ and the maintenance of its uniquely balanced microflora is essential to optimal health. In addition to digesting, absorbing, and eliminating food substances and nutrients, the GI tract functions as a critical barrier between the internal and external environment. The normal intestinal epithelium is protective because it constitutes a semi-permeable (selective) barrier, which prevents toxic, antigenic or pathogenic molecules or micro-organisms from entering the bloodstream.

The importance of the intestinal microflora and more specifically its composition in physiological and pathophysiological processes in the human gastrointestinal tract is becoming more evident.

New discoveries relate to the beneficial effects of normal microflora in inhibiting metabolic events in the gut lumen, which promote colonic carcinogenesis. In addition, the intestinal epithelial barrier has substantial immunological activity, consisting primarily of secretory IgA, which binds to bacteria and other antigens preventing their attachment to epithelial cells.

Failure or abnormalities in any one of these protective functions of the intestinal barrier can result in symptoms such as Chronic Fatigue, anaphylaxis, rhinitis, and skin conditions (atopic eczema) which may be classified as food allergy.

Excess intake of alcohol, infections, NSAID use, stress, chemical contamination of food, broad spectrum antibiotics, corticosteroid hormones, and use of oral birth control pills are just a few factors that can adversely affect the intestinal barrier and permit pathogenic bacteria to produce infectious diseases either by invading into deeper tissues, or secrete antigens and / or toxins that damage local and distant tissues.



This systemic translocation of enteric bacteria and endotoxins plays a major role in the development of abnormal systemic immunity, which can result in multiple organ failure.

Damage to the mucosal barrier also occurs as a result of the overgrowth of yeast. The yeast release toxins and enzymes, and can also be translocated into peripheral organs.

Yeast proliferates in the presence of mercury, and altered pH, which accompanies abnormal composition of bacterial flora. Any of the aforementioned insults to the intestinal barrier can result in increased permeability, which can be associated with unregulated uptake of partially digested proteins with resultant symptoms of food allergy.

The key is to identify the primary cause and extent of increased GI permeability.

The Intestinal Barrier Function Test was developed because microbial flora imbalance cannot be fully understood in its diagnostic and therapeutic implications without coordination of the intestinal flora, including the dietary proteins. The Intestinal Barrier Function Test utilizes a highly sensitive and accurate ELISA test method that measures serum IgG, IgM, and IgA specific antibody titers to the purified antigens from five different dietary proteins, three aerobic, two anaerobic, and three strains of Candida.

The test only requires two milliliters of serum. False negatives for antibodies to Candida, which might be associated with a compromised immune system, can be ruled out by concomitant assessment of antibody titers for dietary proteins and GI bacterial flora. Likewise, abnormally low levels of antibodies for the array of antigens are indicative of immunodeficiency.

How is mucosal barrier function evaluated?

The BHD #344 Mucosal Barrier Function Profile measures the health of the mucosal barrier lining of the GI tract from a functional standpoint. A healthy mucosal barrier will have secretory IgA (sIgA) levels in normal range and will show normal recognition of food proteins, enteric yeasts and enteric aerobic and anaerobic bacteria. This means that IgA, IgM and IgG levels to food proteins, enteric yeasts and enteric aerobic and anaerobic bacteria are all within normal range.

What if the mucosal barrier does not recognize normally encountered antigens?

If the mucosal barrier has shut down, the results for IgA, IgM and IgG levels to food proteins, enteric yeasts and enteric aerobic and anaerobic bacteria will all be <400. A continuum of events can lead to the complete shutdown of the mucosal barrier. When a healthy mucosal barrier is first challenged by an infectious agent, sIgA rises and elevations of specific antibodies may occur. At this point the antigen load is compartmentalized within the GI tract. As the infection begins to overwhelm the mucosal barrier defenses, the humoral immune system becomes more involved.

As an infection overpowers the mucosal barrier defenses, at some point the tight junctions between the intestinal cells open up and antigen penetration into the general circulation increases resulting in an increase in allergy and inflammation. Also if any one of the three antibodies (either IgA, IgM or IgG) are elevated in each of the four compartments on the BHD #344 Mucosal Barrier Function Profile (dietary proteins, yeasts, anaerobic bacteria, and aerobic bacteria) this would indicate leaky gut (increased permeability).

If no intervention occurs, eventually the mucosal immune response begins to weaken and can eventually shut down. As time goes on it loses its ability to recognize and process antigens properly. Ever increasing antigen penetration can eventually result in overstimulation of the humoral immune system leading to hyperimmune response and eventually humoral immune system burn out.

If a hyper elevated or shut down mucosal barrier and/or leaky gut is confirmed, it is extremely important to identify the cause.

Suspect: Increased intestinal permeability/"leaky gut"

Possible causes

1. Exposure to toxic substances (drugs such as NSAIDs and alcohol, chemical exposure)
2. Food allergy/intolerance
3. Intestinal dysbiosis
4. Parasite, yeast, viral, or bacterial infection
5. Maldigestion (includes hypochlorhydria, pancreatic insufficiency, and disaccharidase insufficiencies)

6. Bacterial overgrowth of the small bowel
7. Prolonged fasting/nutrient insufficiencies
8. Inflammatory bowel disease, e.g. Crohn's disease
9. Insufficient mucosal glycocalyx and/or sIgA

Consider the following actions: Consider "6 R" approach to GI health:

- **Remove mucosal irritants** such as allergenic foods, alcohol, gluten (if sensitive), NSAIDS:
 - Consider elimination diet
 - Remove possible pathogens (bacteria, yeast, parasites)
 - Consider Comprehensive Digestive Stool Analysis or Comprehensive Parasitology
 - Reduce sugar, refined carbohydrates, saturated fat, red meat (meat can induce bacterial enzyme activity)
 - Restore proper transit time. Increase dietary fiber (esp. insoluble) and water
- **Reduce** sugar, refined carbohydrates, bad saturated fats, red meat (meat can induce bacterial enzyme activity)
- **Restore:** Proper bowel transit time (Increase dietary fiber)
- **Replace agents** for digestive support:
 - Consider pancreatic or plant enzymes, bile salts, betaine HCl, digestive herbs, or disaccharidases (e.g. lactase) where needed
 - Consider CDSA test (or other disaccharide) to rule out disaccharidase deficiency
- **Reinoculate** with friendly bacteria, if low:
 - Consider CDSA, microbiology, or Comprehensive Parasitology to rule out gut flora insufficiencies
 - Consider probiotic supplementation, including Lactobacilli and Bifidobacteria
 - Consider fructooligosaccharides and inulin to enhance growth of friendly flora
- **Repair mucosal lining:**
 - Consider L-glutamine, EFAs, zinc, pantothenic acid, vitamins C, E, and A, beta carotene, N-acetyl glucosamine, gamma oryzanol, glycerrhiza, aloe vera
 - Consider antioxidants such as vitamins C, E and A, selenium, carotenoids, glutathione, N-acetyl cysteine, pycnogenol and flavonoids
 - Consider Saccharomyces boulardii, whey globulin concentrate, or bovine colostrum to improve local immunity
 - Consider ginkgo biloba to enhance circulation to intestinal epithelium
 - Consider evaluation of overall nutritional status

If depressed mannitol with an elevated or normal lactulose/mannitol ratio

Suspect: Intestinal malabsorption often secondary to mucosal irritation and blunting of the microvilli. Increased intestinal permeability/"leaky gut"

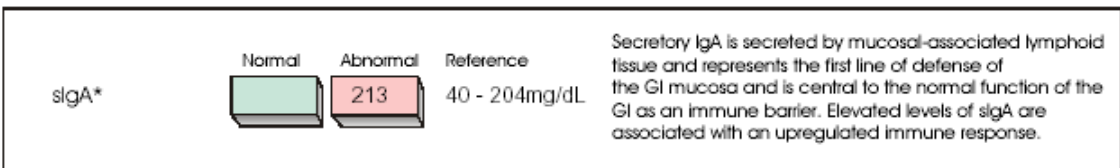
Possible causes:

- 1) Gluten sensitivity/Celiac disease
- 2) Inflammatory bowel disease
- 3) Maldigestion (includes hypochlorhydria, pancreatic insufficiency, and disaccharidase insufficiencies)
- 4) Significant parasite, yeast, viral, or bacterial infection
- 5) Bacterial overgrowth of the small bowel
- 6) Chemotherapy-induced mucosal damage
- 7) Insufficient mucosal glycocalyx and/or sIgA
- 8) Nutrient insufficiencies

Consider the following actions: Consider "4 R" approach to GI health:

Depressed Secretory IgA

Secretory IgA; stool



- Measures sIgA, the primary measurement for first line immune defense (mucosal immunity)
- Can determine possible infections, reactions to foods, and environmental toxins
- Can be correlated with the Functional Adrenal Stress Profile to compare sIgA with each cortisol level to further enhance the interpretation relative to lifestyle (clinical and subclinical sources of chronic stress), adrenal function and first-line immunity.

Overview

An overall deficiency of sIgA (low sIgA average) indicates increased risk for infections, reactions to foods and environmental toxins. An overall increase of sIgA (high sIgA

average) indicates an acute response to infection, i.e. bacteria, parasites, viral, yeasts, or fungal.

The GI tract serves a vital function by excluding the uptake of enteropathogens, which is accomplished in large part by the antigen binding activity of the immunoglobulin secretory IgA. The humoral immune status of the GI tract can be assessed by determining the fecal concentration of sIgA. The sIgA secreted by mucosal-associated lymphoid tissue, represents a pivotal and specific line of defense of the GI mucosa, along with such nonimmune factors as mucins and lactoferrin. As the principal immunoglobulin isotype present in mucosal secretions, sIgA plays an important role in controlling the intestinal milieu, which is constantly presented with potentially harmful antigens such as pathogenic microorganisms, abnormal cell antigens, and allergenic proteins.

Secretory IgA has been shown to bind to toxin A from *Clostridium difficile*, preventing its interaction with the brush border of the intestines. Other studies indicate that sIgA prevents *Vibrio cholera* from adhering to the intestinal mucosa.

Deficiencies in sIgA have been associated with increased absorption of food protein antigens as well as with lowered resistance to intestinal infection, including yeast overgrowth. In instances where sIgA is low, there is increased risk for adhesion and proliferation of pathogenic organisms, and for associated damage to the intestinal mucosa. Levels higher than reference range have been associated with atopic dermatitis, dysbiosis, increased exposure to pathogenic organisms and toxins, and increased exposure to allergens.

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Recommended Treatment to Increase Secretory IgA

- Improve Cortisol/DHEA function
- Gooseberry
- Sialex
- Vitamin E

Mycoplasma and Rheumatoid Arthritis

- The occurrence of various mycoplasma and ureaplasma species in joint tissues of patients with rheumatoid arthritis and other human arthritides can no longer be ignored.
- *M. fermentans* was suggested more than 20 years ago as a cause of rheumatoid arthritis (RA) on the basis of isolation from synovial fluids of a few patients. Recently, with PCR methodology, the *M. fermentans* genome was found in 40% of synovial biopsy specimens and in 21% of joints of patients with rheumatoid arthritis respectively. This genome was also found in 20% of patients with spondyloarthritis and psoriatic arthritis and in 13% of patients with unclassified arthritis.
- *M. fermentans* was not detected in any specimens from patients with reactive arthritis, chronic juvenile arthritis, osteoarthritis or gouty arthritis.

Minocycline in rheumatoid arthritis

In two recently-published independent randomized trials, rheumatoid arthritis patients were treated with 100 mg of oral minocycline twice daily or a placebo for a period of 26 weeks. In the minocycline group, more minocycline-treated patients than placebo showed greater than 75% improvement in swollen joint count, tender joint count and in clinical parameters such as serum C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR). In these studies, the intergroup differences were statistically significant for these findings and the mean changes over time revealed continual improvement in the minocycline-treated patients during the entire period of both studies.

This and other presently-available data on minocycline therapy in rheumatoid arthritis suggest that such treatment may be considered along with disease-modifying anti-rheumatic drugs such as methotrexate, sulfasalazine, gold salts and hydroxychloroquine. However, additional clinical research is necessary to document the long-term efficacy of minocycline in the decreased progression of joint destruction. We believe that such long-term study about the efficacy of minocycline should be conducted on patients who are positive for mycoplasma and chlamydia genome (since we detect the *Chlamydia trachomatis* genome in blood and joint fluid of 20% of patients with rheumatoid arthritis) and not by random selection of arthritis patients. Such selection or comparison between mycoplasma- and chlamydia-positive patients with mycoplasma- and chlamydia-negative individuals may further increase the clinical efficacy of minocycline or doxycycline in future double-blind placebo studies.

The eradication of the pathogenic mycoplasmas from blood and various tissue sites requires an intact functional immune system, which most patients with chronic illnesses do not possess. Therefore, immune enhancement strategies along with prolonged drug therapy may help to eliminate mycoplasma from the human body.

Drs. Baseman and Tully, in *Emerging Infectious Diseases*, Volume 3, January-March, 1997, concluded that "the available data and proposed hypotheses that correlate mycoplasmas with disease pathogenesis range from definitive, provocative and titillating

to inconclusive, confusing and heretical. Controversy seems to be a recurrent companion of mycoplasmas, yet good science and open-mindedness should overcome the legacy that has burdened them for decades."

Rheumatoid Arthritis and Oxidative Stress

The oxidative damage caused by free radicals is a pivotal mechanism implicated in the progression of rheumatoid arthritis.

Free radicals are highly reactive molecules in the body that can cause damage by destroying enzymes, protein molecules and entire cells. The oxidative damage caused by free radicals is a pivotal mechanism implicated in the progression of rheumatoid arthritis.

Because oxygen free radicals mediate tissue and joint damage in patients with rheumatoid arthritis, these patients often exhibit much higher levels of oxidation. In fact, researchers have found that low antioxidant status can actually serve as a risk factor for developing rheumatoid arthritis.

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Treatment Protocols

If high catechol and/or 2,3 DHB:

Suspect:

- Increased hydroxyl radical activity

Possible causes:

- Excess exposure to xenobiotics or gut-derived toxins/Upregulated cytochrome P450 activity
- Other sources of free radicals: Eg. Inflammation, infection, intestinal dysbiosis, trauma, radiation, ischemia
- Inadequate nutritional antioxidant reserves
- Iron overload (Can induce hydroxyl radical production)

Consider the following actions:

- Identify and reduce exposure to toxic substances and other sources of free radicals
- Consider the Detoxification Profile (if not already done)
- Consider the Intestinal Permeability test &/or CDSA/CP test to check for gut-derived toxins
- Consider Elemental Analysis to rule out heavy metal toxicity or nutrient insufficiencies
- Consider increasing intake of antioxidants
- Ascorbic acid, bioflavonoids, carotenoids, tocopherols, coenzyme Q10, melatonin, lipoic acid, N-acetylcysteine
- Consider herbal antioxidants: Milk thistle, catechin, ginkgo biloba, licorice, hawthorne, reishi, anthocyanidins, curcumin
- Consider serum ferritin test to rule out excess iron

If high lipid peroxides:

Suspect:

- Increased cellular lipid peroxidation

Possible causes:

- Excess exposure to xenobiotics or gut-derived toxins/Upregulated cytochrome P450 activity
- Other sources of free radicals: Eg. Inflammation, infection, intestinal dysbiosis, trauma, radiation, ischemia

- Inadequate nutritional antioxidant reserves

Consider the following actions:

- Identify and reduce exposure to toxic substances or other sources of free radicals
- Consider the Detoxification Profile (if not already done)
- Consider the Intestinal Permeability test &/or CDSA/CP test to check for gut-derived toxins
- Consider Elemental Analysis to rule out heavy metal toxicity or nutrient insufficiencies
- Consider increasing intake of antioxidants, especially fat-soluble nutrients: Tocopherols, ascorbic acid, carotenoids, coenzyme Q10, melatonin, lipoic acid, glutathione, N-acetylcysteine
- Consider herbal antioxidants: Milk thistle, catechin, ginkgo biloba, licorice, hawthorne, reishi, anthocyanidins, curcumin
- Consider nutritional cell membrane support Phosphatidyl choline, taurine, essential fatty acids, esp. omega 3s, reduce partially hydrogenated fats
- Consider Essential & Metabolic Fatty Acids Profile

If low reduced glutathione:

Suspect:

- Depleted glutathione reserves

Possible causes:

- Excess exposure to xenobiotics or gut-derived toxins
- Excess production of free radicals Eg. Upregulated cytochrome P450 activity, inflammation, infection, intestinal dysbiosis, trauma, radiation, ischemia
- Inadequate GSH precursors/Impaired methionine metabolism
- Insufficient nutrient cofactors for GSH production or metabolism

Consider the following actions:

- Identify and reduce exposure to toxic substances or other sources of free radicals
- Consider the Detoxification Profile (if not done)
- Consider the Intestinal Permeability test &/or CDSA/CP test to check for gut-derived toxins
- Consider Amino Acids Analysis to rule out deficiencies and methionine metabolism defects
- Consider supplementary glutathione and glutathione precursors: Reduced

glutathione, N-acetylcysteine,
L-methionine, glycine, L-glutamine

- Consider nutrient cofactors for GSH and methionine metabolism): Vitamin B6, B12, riboflavin, niacin, vitamin C, folic acid, serine, Mg

If low superoxide dismutase (SOD) and/or glutathione peroxidase (GSH-Px):

Suspect:

- Depleted endogenous antioxidant reserves

Possible causes:

- Excess exposure to xenobiotics or gut-derived toxins
- Excess free radical activity in the body
- Insufficient reduced GSH (in case of low GSH-Px)
- Insufficient nutrient cofactors for enzyme activity

Consider the following actions:

- Consider options under low reduced glutathione, in case of low GSH-Px
- Consider increasing intake of nutrient cofactors: Manganese (mitochondrial SOD), copper and zinc (cytosolic SOD), selenium (for GSH-Px)
- Consider general antioxidant support: Ascorbic acid, bioflavonoids, carotenoids, tocopherols (specifically increases GSH-Px), coenzyme Q10, vitamin D3 (specifically increases SOD), melatonin, lipoic acid
- Consider herbal antioxidant support, as in high catechol & 2,3 DHB: Milk thistle, catechin, ginkgo biloba, licorice, hawthorne, reishi, anthocyanidins, curcumin

The role of Vitamin D Deficiency in Pain, Inflammation, and Inflammatory Diseases

It is well documented that vitamin D deficiency is widespread in the general Western population. Vitamin D deficiency is due to the small amounts found in the diet and insufficient sun exposure. Vitamin D is formed from the action of sunlight on the skin that converts a prohormone called cholecalciferol into vitamin D (25 (OH) vitamin D)

Vitamin D deficiency is associated with a number of diseases and disorders not limited to:

1. Diabetes Mellitus
2. Cancer
3. Hypertension
4. Cardiovascular disease
5. Autoimmune/inflammatory disorders

Vitamin D insufficiency is prevalent in patients with chronic musculoskeletal pain. The mechanism for this is as follows:

1. Vitamin D deficiency reduces calcium absorption
2. The body increases the output of Parathyroid Hormone (PTH), which is increased to increase calcium absorption and decrease calcium excretion.
3. Increased PTH causes an increase in urinary excretion of phosphorous causing hypophosphatemia or low levels of serum phosphorous.
4. This results in a decrease in the formation of a mineral called calcium phosphate and you now have an unmineralized collagen matrix forming on the endosteal and periosteal bone.
5. Hydration of the unmineralized collagen matrix causes it to swell and put pressure on the nerve endings in the periosteum.

Testing for Serum Vitamin D

You can easily assess for vitamin D levels by measuring serum levels of 25(OH) vitamin D. The following are the reference ranges we recommend you use:

Deficient levels of vitamin D: <20 ng/ml (<50 nmol/L)

Insufficient levels: 20 – 40 ng/ml (50 – 100 nmol/L)

Optimal levels: 40 – 65 ng/ml (100 – 160 nmol/L)

Excess levels: >80 ng/ml (>200 nmol/L)

Replacing Vitamin D

If your patient is deficient or insufficient consider using up to 4,000 IU for your adult patients, 2000 IU for children and 1000 IU for infants. Higher doses of vitamin D (as high as 10,000 IU/day) are well tolerated.

It is well documented that raising serum vitamin D levels in deficient or insufficient patients will help reduce musculoskeletal pain, low-back pain and generally reduce inflammation.

Serum calcium levels should be measured regularly in patients receiving greater than 4000 IUs of vitamin D because hypercalcemia is the best indicator of excess vitamin D.

Contraindications for Vitamin D Supplementation

Vitamin D supplementation is contraindicated in patients taking thiazide diuretics.

Rheumatoid Arthritis and Sex Hormones

A review of the current medical literature shows that sex hormones can actually block some important mechanisms involved in the development of rheumatoid arthritis, including immunoregulation, inflammatory response, cytokine reactions, and cartilage damage.

In premenopausal women, most studies indicate a strong correlation between low androgen levels (DHEA, testosterone) and the progression of RA. In a study of 49 postmenopausal women with rheumatoid arthritis, DHEA levels were significantly lower than in healthy controls. [Gaby, AR. *Holistic Medicine*. Spring, 1993: p.22]

Numerous studies have shown that men with RA often present with low testosterone levels. Several studies have suggested that testosterone may play a protective role in RA, with initial deficiencies setting the stage for development of the disease.

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Rheumatoid Arthritis and Fatty Acids

Fatty acid levels can have a dramatic impact on the inflammatory responses associated with rheumatoid arthritis.

Joint pain in rheumatoid arthritis can be directly triggered by the release of inflammatory mediators like leukotrienes, whose production is dependant upon the body's balance of essential and metabolic fatty acids.

The Essential and Metabolic Fatty Acids Analysis uncovers fatty acid imbalances that may be aggravating inflammatory conditions associated with rheumatoid arthritis. It's also crucial for gauging the effectiveness of fatty acid supplementation, and can reveal inborn metabolic conversion errors that may be preventing a patient from achieving optimal levels, even with adequate dietary amounts.

References:

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Polyunsaturated Omega-3

	Results uM		
1 Alpha Linolenic (18:3n3)	3.6	3.1	2.2 - 13.0
2 Eicosapentaenoic (20:5n3)	7 L	13	6 - 118
3 Docosapentaenoic (22:5n3)	55 L	64	40 - 131
4 Docosahexaenoic (22:6n3)	112 L	117	65 - 280

Polyunsaturated Omega-6

5 Linoleic (18:2n6)	751	485 775	360 - 1,005
6 Gamma Linolenic (18:3n6)	1.3	0.6 2.2	0.4 - 3.9
7 Eicosadienoic (20:2n6)	6.6	5.0 9.4	3.7 - 11.4
8 Dihomogamma Linolenic (20:3n6)	41	34 67	24 - 86
9 Arachidonic (20:4n6)	993 H	602 985	493 - 1,108
10 Docosadienoic (22:2n6)	1.6	2.4	<= 3.2
11 Docosatetraenoic (22:4n6)	132 H	47 121	31 - 154

Polyunsaturated Omega-9

12 Mead (20:3n9)	11.3 H	8.4	<= 10.5
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Monounsaturated

	Results uM		
13 Myristoleic (14:1n5)	< 0.6	0.6	<= 1.4
14 Palmitoleic (16:1n7)	14.1 H	12.2	<= 25.0
15 Vaccenic (18:1n7)	37	27 46	24 - 53
16 Oleic (18:1n9)	846	503 876	383 - 1,103
17 11-Eicosenoic (20:1n9)	9.2 H	8.8	<= 10.9
18 Erucic (22:1n9)	8.2	4.2 11.6	3.6 - 14.0
19 Nervonic (24:1n9)	112	101 157	86 - 171

Saturated

20 Capric (10:0)	0.8	0.9	<= 1.3
21 Lauric (12:0)	1.4	2.1	<= 4.7
22 Myristic (14:0)	13.5	18.0	<= 25.0



Essential fatty acids (EFAs) exercise a powerful influence on overall health because of their pivotal role in how cell membranes function. EFAs are transformed by the body into critical local hormones, called "**eicosanoids**," that completely regulate all stages of the process of inflammation, controlling initiation, propagation, and termination of this process that is so vital to the body's ability to repair and to protect itself immunologically.

Remember the direct impact of cortisol and DHEA function on Eicosanoids

Many of the chronic inflammatory conditions that accompany an EFA imbalance are currently treated with symptom-specific pharmaceutical drugs such as steroids, Prednisone, aspirin and other NSAIDs, sulfasalazine, and colchicine. The problem with such drug therapies is that they prevent the formation of "good" anti-inflammatory eicosanoids as well as the "bad" pro-inflammatory eicosanoids, or they shift production of one type of eicosanoid to another. For effective, long-term management, eicosanoid

production should be modified through dietary changes (balancing dietary intake of specific fats, as indicated by testing) and by controlling insulin levels in the circulation.

The Role of Essential Fatty Acids in Health and Disease

The net result of this shift in the diet has been to provide ample substrate for producing arachidonic acid and very little substrate for producing eicosapentaenoic acid, since both n-6 and n-3 fats use the same enzymes for elongation and desaturation. Consequently, the body makes many more pro-inflammatory eicosanoid hormones. Chronic inflammatory diseases have reached near epidemic proportions in our society.

Low Delta-6 Desaturase Activity

Delta-6 desaturase is the rate-limiting step for transforming linoleic or linolenic acid into the longer EFA metabolites, GLA and EPA, respectively, and delta-6 is also used to make DHA out of EPA. Many people have less than optimal delta-6 activity. Infants have no appreciable delta-6 activity until about 6 months of age and must get DGLA, AA, EPA and DHA from breast milk and the diet. As we age, delta-6 activity declines progressively. Dietary factors, including alcohol, trans-fats, and saturated fats will each inhibit delta 6 and, interestingly, so too will excessive dietary linolenic acid.

Epstein Barr virus and HIV have been shown to inhibit the desaturases, and other viruses likely do the same. People experiencing post-viral fatigue syndrome have much lower levels of EFAs than controls

Low delta-6 activity can be identified by low levels of membrane DGLA, especially if the linoleic acid content is relatively higher. This scenario results in low levels of the series-1, anti-inflammatory prostaglandins, such as PGE1, made from DGLA.

Insulin Dysregulation

Too little or too much insulin in circulation can have profound effects on eicosanoid formation, contributing to chronic inflammatory processes. Insulin resistance or absolutely low levels of insulin have been shown to impair delta-6 activity, and can lead to all of the problems associated with reduced delta-6 activity above.

Insulin surges or general dysregulation, commonly found in people who eat large amounts of refined grains and simple sugars (in other words, the standard American diet), will result in greatly increased activity of both delta-6 and delta-5 desaturase. While this means that more LA will be converted into DGLA, it unfortunately also means that most of that DGLA will be quickly converted into arachidonic acid, thereby markedly increasing the body's tendency toward inflammation. Elevated membrane AA levels may indicate this scenario. People with exaggerated insulin response after eating carbohydrates (about 25% of the population) would be especially prone to overproduce AA under the influence of hyperinsulinemia. And there is a growing consensus in the research community that insulin dysregulation may be the common mediator for the cluster of conditions known as Syndrome X, including elevated cholesterol and triglycerides, hypertension, obesity, and diabetes. The mechanism of action of insulin in these pathologies may be due, in large part, to its effects on eicosanoid metabolism.

Clinical Applications

Autoimmune Diseases

Prostaglandins are known to regulate immune response and fibrous tissue formation. **Deficiency of PGE1 and/or of TXA2 and excess PGE2** appear to induce hyperactivity of B-cells, possibly due to loss of regulatory control by T-cells, and to enhance fibrosis. Drugs that induce auto-immune diseases also tend to inhibit PGE1 and/or TXA2 production, as does EBV infection and possibly other viruses. In both cases, excess auto-antibody production may result.

Using DGLA and EPA supplementation to enhance PGE1 production and reduce cytokine production may be therapeutically useful in treating vasculitis, amyloidosis, and scleroderma. Indeed, EPA/DHA supplementation has induced prolonged remission of systemic lupus erythematosus (SLE) in test subjects. Diets containing both EPA and DHA were more effective than either fatty acid alone in alleviating the severity of renal disease in an animal model for SLE. In human studies with SLE, fish oils improved inflammatory markers but did not affect either immune complex or anti-DNA antibody titer.

In rheumatoid arthritis, EPA/DHA supplementation has consistently reduced the number of painful and swollen joints and reduced neutrophil LTB4 and macrophage IL-1 beta production.

Interpretation of the Fatty Acid Profile

If analysis shows: Low alpha-linolenic acid (ALA)

Consider supplementation with: Flax seeds and oil, Walnuts and oil, Unroasted nuts and seeds, Dark leafy greens.

If analysis shows: Low eicosapentaenoic acid (EPA) or Low docosapentaenoic acid (DHA)

Consider supplementation with: Cold water fatty fish, Salmon, Sardines, Wild trout, Herring, Anchovies, Tuna, Mackerel. Fish oils (EPA/DHA) are available in a variety of supplemental forms, from bulk oil to nitrogen-sealed capsules. An algae-derived DHA is available for vegetarians and pregnant women.

If analysis shows: Elevated linoleic acid (LA) and/or arachidonic acid (omega 6 fatty acids)

Consider: Use only olive oil or high-oleic canola or high-oleic safflower oil for cooking. Avoid all other vegetable oils. Avoid all margarine and shortening.

Delta-6 desaturase deficiency:

As much as 20% of the population may have impaired delta-6 desaturase (delta-6d) activity. And delta-6d activity decreases dramatically in people as they age. This enzyme is used several times to desaturate the growing EFA chains, although the first

conversion [or desaturation] is usually the most tell-tale, when LA is converted into GLA (and subsequently into DGLA). Appropriate therapy is always to give the pre-formed oil that bypasses the action of delta-6 desaturase. **Vitamin and mineral cofactors for optimum delta-6 desaturase activity: niacin (B3), pyridoxal-5-phosphate (B6), vitamin C, zinc, and magnesium**

If analysis shows: High linoleic acid (LA) AND Low di-homo-gamma linolenic acid (DGLA) If AA is also low, the problem is more severe.

If analysis shows: Low EPA

Consider supplementation with: EPA

If analysis shows: High or normal EPA and low DHA

Consider supplementation with: DHA

Dysglycemia and Hyperinsulinemia:

One of the many effects of elevated insulin is the upregulation of the enzyme delta-5 desaturase, which converts DGLA into AA. DGLA is the most potent anti-inflammatory EFA, while AA is the most potent pro-inflammatory EFA. Thus, a major effect of high insulin levels is to put the body into a heightened pro-inflammatory state, with disastrous long-term consequences for health.

People who eat a diet high in carbohydrates, especially simple sugars, experience surges in insulin levels resulting in high levels of AA.

If analysis shows: Low DGLA AND High AA

Consider: Use only olive or high-oleic oils for cooking. Reduce the use of omega-6 vegetable oils. Supplement EPA, which slows the activity of delta-5 desaturase. Eat a diet free of simple sugars, with a relatively high percentage of protein and complex carbohydrates (beans, whole vegetables and fruits). Run a Metabolic Dysglycemia Profile to rule out diabetes, dysglycemia, insulin resistance, or hyperinsulinemia.

If analysis shows: Low oleic acid (18:2n-9) and high stearic acid (18:0)

Consider: Increase use of olive oil as dietary oil. Supplement co-factors of desaturase enzymes: niacin (B3), pyridoxal-5-phosphate (B6), vitamin C, zinc, magnesium.

If analysis shows: High trans fats Elaidic acid (18:1n9t) [Indicates increased oxidative stress levels and a need for additional anti-oxidant protection.]

Consider: Vitamin E and the carotenes are particularly indicated. Avoid all margarine, shortening and dairy products.

If analysis shows: Elevated levels of saturated fats [This results in more rigid cell membranes, especially with longer-chain saturated fats. Increased rigidity

and/or decreased fluidity decreases membrane receptor function. This can lead to hormone dysfunction or cell-cell communication difficulties.]

Consider: Reduce saturated fats in the diet (meats, chicken, dairy). Use olive oil as main cooking oil. Supplement polyunsaturated fats as indicated by report. Promote increased metabolic rates through aerobic exercise.

Interpretive Guide for Fatty Acids



Name	Potential Responses	Metabolic Association
Omega-3 Polyunsaturated		
Alpha Linolenic	L Add flax and/or fish oil	Essential fatty acid
Eicosapentaenoic	L Add fish oil	Eicosanoid substrate
Docosapentaenoic	L Add fish oil	Nerve membrane function
Docosahexaenoic	L Add fish oil	Neurological development
Omega-6 Polyunsaturated		
Linoleic	L Add corn or black currant oil	Essential fatty acid
Gamma Linolenic	L Add evening primrose oil	Eicosanoid precursor
Eicosadienoic		
Dihomogamma Linolenic	L Add black currant oil	Eicosanoid substrate
Arachidonic	H Reduce red meats	Eicosanoid substrate
Docosadienoic		
Docosatetraenoic	H Weight control	Increase in adipose tissue
Omega-9 Polyunsaturated		
Mead (plasma only)	H Add corn or black	Essential fatty acid status

Monounsaturated		
Myristoleic		
Palmitoleic		
Vaccenic		
Oleic	H See comments	Membrane fluidity
11-Eicosenoic		
Erucic	L Add peanut oils	Nerve membrane function
Nervonic	L Add fish or canola oil	Neurological development
Saturated Even-Numbered		
Capric Acid	H Assure B3 adequacy	
Lauric	H	Peroxisomal oxidation
Myristic	H	
Palmitic	H Reduce sat. fats; add niacin	Cholesterogenic
Stearic	H Reduce sat. fats; add niacin	Elevated triglycerides
Arachidic	H Check eicosanoid ratios	
Behenic	H	$\Delta 6$ desaturase inhibition
Lignoceric	H Consider rape or mustard seed oils	Nerve membrane function
Hexacosanoic	H	

<i>Saturated Odd-Numbered</i>			
Pentadecanoic	H	Add B12 and/or carnitine	
Heptadecanoic	H		
Nonadecanoic	H		Propionate accumulation
Heneicosanoic	H		Omega oxidation
Tricosanoic	H		
<i>Trans Isomers from Hydrogenated Oils</i>			
Palmitelaidic	H	Eliminate hydrogenated oils	Eicosanoid interference
Total C18 Trans Isomers	H		
<i>Calculated Ratios</i>			
LA/DGLA	H	Add black currant oil	$\Delta 6$ desaturase, Zn deficiency
EPA/DGLA	H	Add black currant oil	Eicosanoid imbalance
	L	Add fish oil	
AA/EPA (Omega-6/Omega-3)	H	Add fish oil	
Stearic/Oleic (RBC only)	L	See Comments	Cancer Marker
Triene/Tetraene Ratio (plasma only)	H	Add corn or black currant oil	Essential fatty acid status

Provided by Metametrix- www.metametrix.com

Rheumatoid Arthritis and Digestive Function

Restoring balance to the intestinal microflora has been shown to alleviate many of the symptoms of rheumatoid arthritis.

In controlled studies, researchers have found that even patients with early rheumatoid arthritis, who have not yet undergone initial treatment for the disease, exhibit crucial imbalances of bacteria flora.

A landmark Finnish study examined the effects of diet on the symptoms of rheumatoid arthritis. They found a direct association between patients who showed high improvement in symptoms and the status of specific markers for intestinal microflora. A follow-up study confirmed these results, and showed positive changes in the fecal microbial flora correlating with a marked improvement in rheumatoid arthritis conditions.

References:

1. Eerola E, Mottonen T, Hannonen P, Luukkainen R, Kantola I, Vuori K, Tuominen J, Toivanen P. Intestinal flora in early rheumatoid arthritis. *Br J Rheumatol* 1994;33(11):1030-1038.
2. Benno P, Alam M, Henriksson K, Norin E, Uribe A, Medtvedt T. Abnormal colonic microbial function in patients with rheumatoid arthritis. *Scand J Rheumatol* 1994;23(6):311-315.
3. Peltonen R, Kjeldsen-Kragh J, Haugen M, Tuominen J, Toivanen P, Forre O, Eerola E. *Br J Rheumatol* 1994;33(7):638-643. Changes of faecal flora in rheumatoid arthritis during fasting and one-year vegetarian diet. *Br J Rheumatol* 1994;33(7):638-643.
4. Peltonen R, Nenonen M, Helve T, Hanninen O, Toivanen P, Eerola E. Faecal microbial flora and disease activity in rheumatoid arthritis during vegan diet. *Br J Rheumatol* 1997;36(1):64-68.

Rheumatoid Arthritis and Amino Acids

RA therapy often focuses on two important amino acid

Many studies have confirmed a widespread deficiency of the amino acid **histidine** in patients with rheumatoid arthritis. **Histidine** can act as a chelating (purifying) agent in the body, with the ability to remove excess heavy metals in the bloodstream. One study noted that improvement in RA symptoms in patients taking the drug D-penicillamine were accompanied by a rise in serum levels of histidine, which may be the biochemical mechanism by which the drug produces its positive effect. Phenylalanine, an essential amino acid, is crucial for the synthesis of important substances in the body. DL-phenylalanine has been successfully used in pain control in diseases refractory to other treatment methods, including osteo- and rheumatoid arthritis.

References:

1. Gerber DA. Decreased concentration of free histidine in serum in rheumatoid arthritis, an isolated amino acid abnormality not associated with general hypoaminoacidemia. J Rheumatol 1975;2(4):384-392.
2. Pickup ME, Dixon JS, Lowe JF, Wright V. Serum histidine in rheumatoid arthritis: changes induced by antirheumatic drug therapy. J Rheumatol 1980;7(1):71-76.

Amino Acid Analysis (Plasma)



63 Zillicoa Street
Asheville, NC 28801
© Genova Diagnostics

Patient: **SAMPLE PATIENT** Order Number:
Age: 48 Completed:
Sex: M Received:
MRN: Collected:

SAMPLE REPORT

Plasma Representativeness Index



Nutritionally Essential and Semi-Essential Amino Acids

Amino Acid	Analytes reported in micromoles per deciliter unless stated otherwise	Reference
1 Arginine	9.5	7.5-13.0
2 Histidine	7.7	7.9-12.1
3 Isoleucine	7.70	5.40-10.50
4 Leucine	15.0	10.5-18.0
5 Lysine	19.9	15.5-27.5
6 Methionine	2.4	2.5-4.9
7 Phenylalanine	6.28	4.60-7.90
8 Taurine	4.42	5.25-9.00
9 Threonine	6.36	6.40-14.00
10 Tryptophan	3.66	3.30-6.50
11 Valine	27.6	19.0-36.0

Dietary Peptide Related markers

12 Anserine (dipeptide)	<d	<= 0.07
13 Carnosine (dipeptide)	<d	<= 0.09
14 1-Methylhistidine	0.60	<= 1.65
15 Beta-alanine	<d	<= 0.4

This test was developed and its performance characteristics determined by GSDL, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

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Credit to Genova

Interpretation of Amino Acid Profile:

Gastrointestinal

Suspect incomplete digestive proteolysis or leaky gut if: Elevated ANSERINE, CARNOSINE & low (or low normal) essential amino acids (dietary peptides) Low leucine, isoleucine, valine

Consider: Rule out pancreatic dysfunction, zinc deficiency (peptidases dependent upon zinc) Intestinal Permeability Test Comprehensive Digestive

Stool Analysis Supplement with appropriate amino acids

Suspect fat maldigestion if: **Low or elevated (urine only) taurine or glycine** (needed for bile salt production)

Consider: Comprehensive Digestive Stool Analysis Supplement with appropriate amino acids Rule out deficiency of fat-soluble nutrients

Suspect intestinal malabsorption if: **Low THREONINE** and low levels of other essential amino acids

Consider: Rule out rapid transit time Comprehensive Digestive Stool Analysis Comprehensive Antibody Assessment (food allergy may cause malabsorption)

Suspect intestinal dysbiosis if: Elevated gamma-aminobutyric acid, alpha-amino adipic acid, beta-alanine, ethanolamine or ammonia (may be produced by intestinal bacteria or yeast)

Consider: Comprehensive Digestive Stool Analysis

Cardiovascular

Suspect increased susceptibility to occlusive arterial disease if: Elevated homocystine, Low cystathionine, Elevated or low methionine, cysteine or taurine.

Consider: Supplement with magnesium, vitamin B6, B12, folic acid, serine, or betaine as needed (to facilitate methionine metabolism). Comprehensive Cardiovascular Assessment to assess specific parameters of cardiovascular status.

Oxidative Stress

Suspect oxidative stress if: Significantly elevated cystine, compared to cysteine (urine only) (cystine is the oxidized form of cysteine), Low cyst(e)ine (plasma or urine) (cysteine necessary for glutathione production), Low or elevated (urine only) taurine (taurine scavenges hypochlorite ions).

Consider: Oxidative Stress Profile (separate or included in Comprehensive Detoxification Profile), Antioxidant support as needed. Rule out magnesium deficiency.

Detoxification

Suspect impaired ammonia detoxification if: Elevated GLUTAMINE with elevated arginine or citrulline or ornithine or argininosuccinic acid and low urea (impaired urea cycle), Elevated ammonia (only if low urea), Elevated ammonia with high urea suggests protein overload, Elevated ammonia with high ammonia concentration and normal urea suggests decayed specimen.

Consider the following options: STAT blood venous ammonia measurement, to confirm ammonia excess, Reduce protein intake to less than 60 grams/day,

Alpha ketoglutarate (1500-3000 mg/day), Consider giving 3-6 gm/day if confirmed NH₃ toxicity.

Suspect impaired hepatic detoxication if: Elevated or low methionine, cysteine, cystathionine, taurine (suggestive of impaired methylation, sulfation, amino acid congugation), Elevated beta alanine (may lead to taurine deficiency), Low glycine, glutamine, aspartic acid (utilized in Phase 2 detoxication).

Consider: Supplement with amino acids, vitamin B6, B12, folic acid or betaine as needed, Comprehensive Detoxification Profile.

Musculoskeletal

Suspect increased risk of collagen or skeletal disorders if: Elevated HOMOCYSTINE with low cystathionine (impaired methionine metabolism); Homocysteine interferes with crosslinking of collagen; Elevated or low cyst(e)ine, taurine; Low methionine, lysine; Low leucine, isoleucine, valine (branched-chain amino acids); May be elevated in catabolic disorders; Elevated hydroxyproline and proline, 3-methylhistidine (suggestive of tissue catabolism); Elevated anserine, carnosine (incomplete digestion suggestive of poor tissue regeneration).

Consider: Supplement with magnesium, vitamin B6, B12, folic acid, betaine as needed. Supplement with appropriate amino acids. Comprehensive Bone Resorption Assessment to assess bone status. Ensure adequate zinc. Comprehensive Digestive Stool Analysis.

Nutrient Adequacy

Suspect increased need for magnesium if: Elevated ethanolamine, compared with phosphoethanolamine (conversion dependent upon Mg); Elevated phosphoserine, compared with serine (conversion dependent upon Mg); Low or elevated (urine only) taurine (low taurine causes body to waste Mg); Elevated citrulline or aspartic acid (conversions dependent upon Mg).

Suspect increased need for iron if: Elevated phenylalanine (unless elevated tyrosine, tryptophan) (conversion dependent upon Fe); Low histidine (iron absorption dependent on HCl)

Consider: Confirm deficiency before supplementation (e.g. ferritin, serum iron, TIBC, % saturation, transferrin)

Suspect increased need for manganese if: Elevated arginine, compared with ornithine (arginase dependent upon Mn); Elevated alanine, alpha-aminoadipic acid, tyrosine, leucine, isoleucine, or valine (all are dependent upon alpha-ketoglutarate which depends upon isocitrate dehydrogenase, a Mn-dependent enzyme); Low histidine (hypochlorhydria from deficient histamine, may lead to Mn malabsorption); Low threonine (suggests general malabsorption).

Consider: Erythrocyte or Hair Elemental Analysis; If confirmed low Mn, rule out hyperglycemia (interference with citric acid cycle, leading to poor breakdown of carbohydrates).

Suspect increased need for zinc if: Elevated ANSERINE, CARNOSINE (peptidases require zinc); Elevated phosphoethanolamine with elevated phosphoserine; Elevated leucine, isoleucine and valine (Branched-chain amino acid peptidases require zinc).

Suspect increased need for molybdenum if: Elevated taurine (with normal beta-alanine) (May suggest block in sulfoxidation); Elevated cyst(e)ine (with normal lysine and ornithine) (Sulfoxidation dependent upon Mo).

Consider: Erythrocyte or Hair Elemental Analysis Comprehensive Detoxification Profile.

Suspect increased need for vitamin B6 (P5-P`) if: Elevated CYSTATHIONINE, HOMOCYSTINE, serine, tyrosine, alpha-amino adipic acid, beta-alanine, alanine, threonine, ornithine, glycine, aspartic acid, beta-aminoisobutyric acid, leucine, isoleucine, valine Low cysteine (compared with cystathionine) or low taurine (compared to cyst(e)ine).

Consider: Mg, riboflavin, zinc (needed for B6 activation).

Suspect increased need for folic acid if: Elevated HOMOCYSTINE, SARCOSINE, glycine, serine, 1-methylhistidine, 3-methylhistidine, methionine, cystathionine or histidine.

Suspect increased need for vitamin B12 if: Elevated homocysteine, or elevated beta amino-isobutyric acid, and glycine.

Suspect increased need for fat-soluble vitamins if: Low or elevated (urine only) TAURINE; low GLYCINE (needed for bile salt production); Elevated beta-alanine (may lead to taurine deficiency); Low threonine (suggests general malabsorption).

Endocrine

Suspect adrenal insufficiency if:

Low ALANINE (increased conversion of alanine to pyruvate); Low essential amino acids (impaired digestive enzyme activity); Elevated ornithine (weakness of ornithine transaminase).

Consider:

Adrenocortex Stress Profile to assess cortisol and DHEA levels; Digestive enzyme support, as needed.

Suspect adrenal hyperactivity if:

Elevated ALANINE (increased conversion from pyruvate); Low arginine, tryptophan, tyrosine (upregulation of arginase and oxygenase enzymes).

Consider:

Adrenocortex Stress Profile to assess cortisol and DHEA levels

Suspect hyperinsulinemia if:

Low phenylalanine (upregulated conversion to tyrosine); Elevated serine, alanine, glycine (gluconeogenic amino acids)

Consider:

Measurement of fasting or 2-hour post-prandial insulin or Glucose/Insulin Tolerance Test

Suspect parathyroid dysfunction if:

Elevated phosphoserine with elevated phosphoethanolamine

Consider:

Evaluate parathyroid function with appropriate testing

Neurological

Suspect neurological / behavioral problems if: Elevated or low tryptophan, taurine, phenylalanine, tyrosine (neurotransmitter precursors)

Consider: Supplement with appropriate amino acids, vitamin B6

Elevated (or normal) homocysteine, with elevated or low methionine & low cystathionine (suggestive of low S-adenosylmethionine, low taurine, low B6)

Consider: Supplement with appropriate amino acids, magnesium, vitamin B6

Amino acid imbalances suggestive of low vitamin B6

Consider: Supplement with vitamin B6. Ensure adequacy of zinc, riboflavin, magnesium (needed for B6 activation)

Amino acid imbalances suggestive of low vitamin B12

Consider: Supplement with appropriate amino acids, vitamin B12

Rheumatoid Arthritis and Element Imbalance

Many patients with rheumatoid arthritis lack essential mineral nutrients.

Researchers have discovered that many patients with rheumatoid arthritis (RA) do not receive the recommended daily allowance of important trace minerals such as **calcium, zinc, magnesium, and selenium** from their diets. This may be one reason that controlled studies show patients with rheumatoid arthritis having plasma and red blood cell selenium levels that are much lower than those measured in healthy controls. **Selenium** plays an important role in the body's immune defense and inflammatory responses; optimal levels are critical for the function of antioxidant enzymes such as **glutathione peroxidase**, which may reduce the free radical damage associated with the progression of rheumatoid arthritis.

Zinc may also be fundamental element involved in RA mechanisms. A recent preliminary study revealed that urinary excretion of zinc was much lower in patients with RA than in healthy controls. Twenty-four hours after ingesting a 50 mg zinc tablet, zinc plasma levels for the RA patients showed no significant change, while those of controls rose significantly. These results point to abnormal zinc metabolism in RA patients, which may lead to malabsorption and chronic zinc deficiency.

Elevated levels of copper, on the other hand, have been linked with the disease severity of RA, and have also been implicated in the development of pathological lesions associated with RA.

Elemental Analysis (packed erythrocytes) measures levels of crucial toxic and mineral elements in the body using a variety of different specimen types.

References:

Stone J, Doube A, Dudson D, Wallace J. Inadequate calcium, folic acid, vitamin E, zinc, and selenium intake in rheumatoid arthritis patients: results of a dietary survey. *Semin Arthritis Rheum* 1997;23(3):180-185.

Kremer JM, Bigaouette J. Nutrient intake of patients with rheumatoid arthritis is deficient in pyridoxine, zinc, copper, and magnesium. *J Rheumatol* 1996;23(6):990-994.

Kose K, Dogan P, Kardas Y, Saraymen R. Plasma selenium levels in rheumatoid arthritis. *Biol Trace Elem Res* 1996;53(1-3):51-56.

Tarp U. Selenium and the selenium-dependent glutathione peroxidase in rheumatoid arthritis. *Can Med Bull* 1994;41(3):264-274.

Naveh Y, Schapira D, Ravel Y, Geller E, Scharf Y. Zinc metabolism in rheumatoid arthritis: plasma and urinary zinc and relationship to disease activity. *J Rheumatol* 1997;24(4):643-646.

Grennan DM, Knudson JM, Dunckley J, MacKinnon MJ, Myers DB, Palmer DG. Serum copper and zinc in rheumatoid arthritis and osteoarthritis. *N Z Med J*

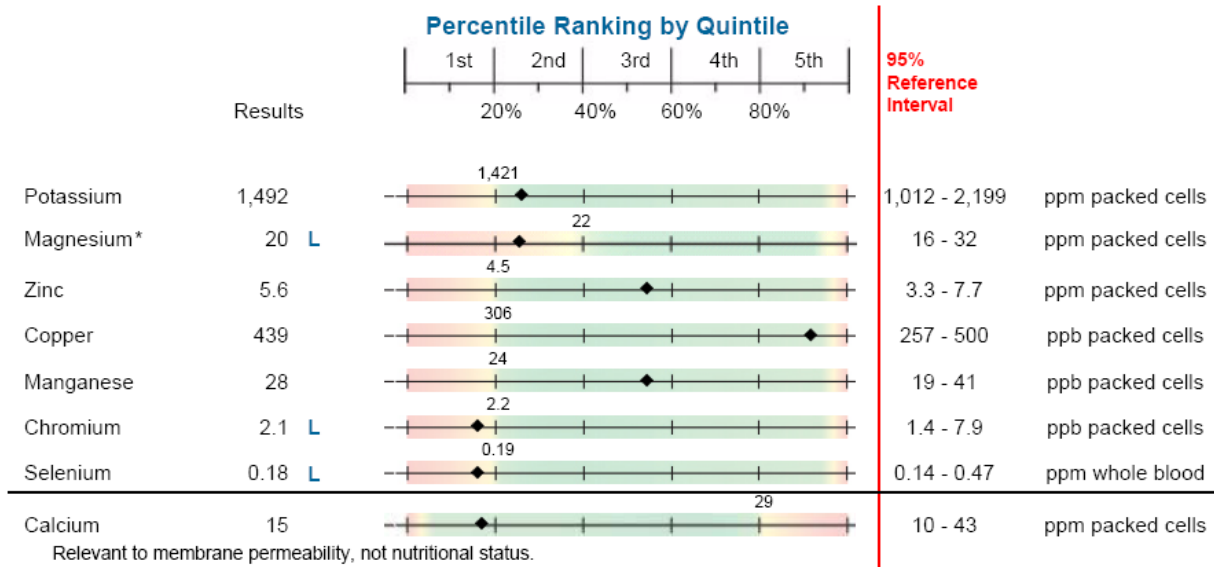
1980;91(652):47-50.

Youseff AA, Wood B, Baron DN. Serum copper: a marker of disease activity in rheumatoid arthritis. J Clin Pathol 1983;36(1):14-17.

0022 Element Analysis - Erythrocytes and Whole Blood

Methodology: Inductively Coupled Plasma/Mass Spectroscopy

Nutrient Elements



Rheumatoid Arthritis and Bacterial/Parasitic Infection

An unsuspected parasite infection can trigger symptoms of various types of joint diseases, including RA.

Because there are documented cases where arthritis has actually been triggered by parasitic infection, experts in the field of rheumatology emphasize the need to carefully consider this possibility in patients with atypical joint diseases, particularly if symptoms also include gastrointestinal upset.

The Comprehensive Microbiology/Parasitology Profile uses the most technologically advanced procedures to accurately identify bacterial/parasitic infections that could lie at the root of the symptoms seen in rheumatoid arthritis.

Reference:

Burnstein SL, Liakos S. Parasitic rheumatism presenting as rheumatoid arthritis. J Rheumatol 1983;10:514-515.

Parasitology

Microscopic Exam Results

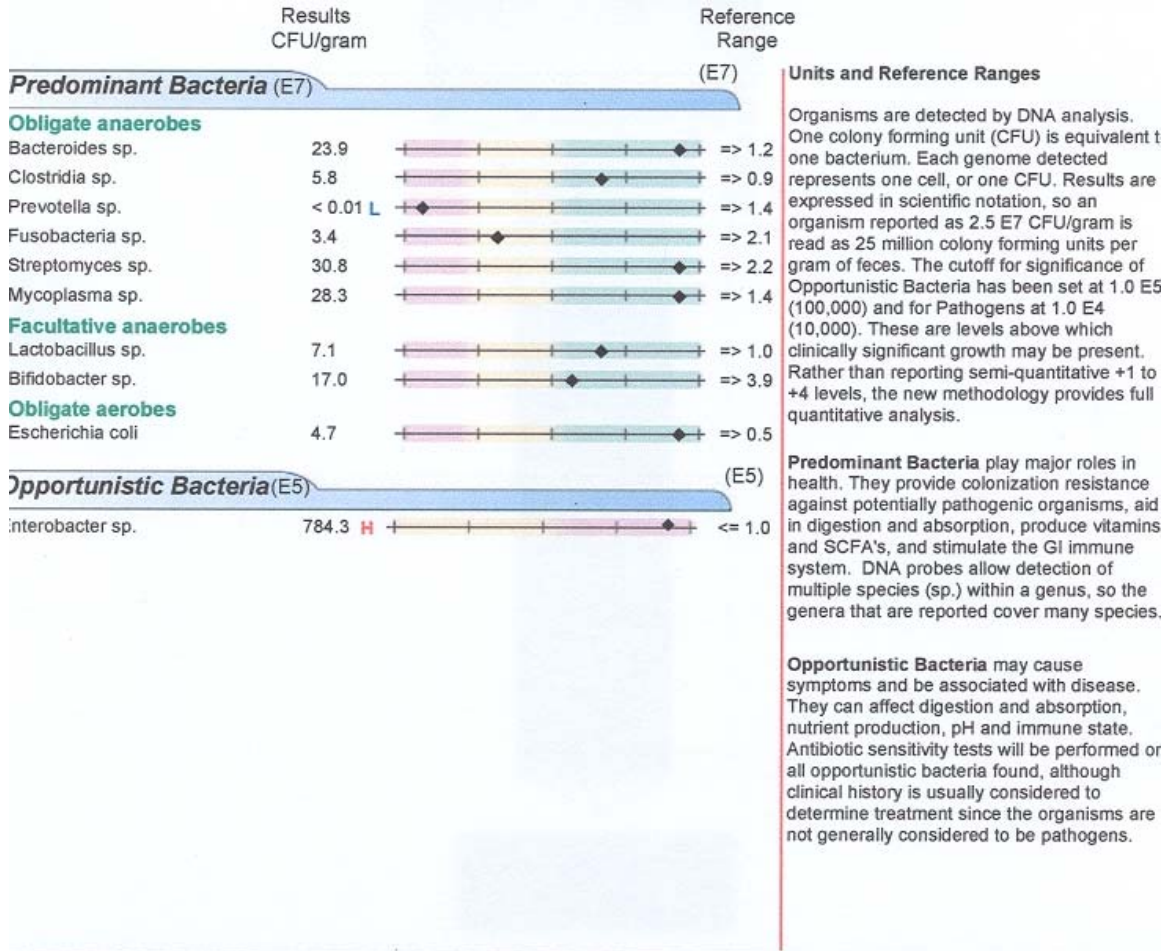
Blastocystis hominis: Many
Endolimax nana: Few Trophozoites
Entamoeba hartmanni: Moderate Trophozoites & Cysts

Specimen Tested: Stool

Parasitology EIA Tests

	Inside	Outside	Reference Range
Cryptosporidium	<input type="text" value="Not Ordered"/>	<input type="text"/>	Negative
Giardia lamblia	<input type="text" value="Not Ordered"/>	<input type="text"/>	Negative
Entamoeba histolytica/dispar	<input type="text" value="Not Ordered"/>	<input type="text"/>	Negative

Reference Range for EIA tests is Negative.



These test results are not for the diagnosis of disease. They are intended to provide nutritional guidelines to qualified healthcare professionals with full

	Results CFU/gram		Reference Range (E4)
Pathogens (E4)			
Pathogenic Bacteria			
H. pylori	< 0.001	◆	<= 1.0
C. difficile	< 0.001	◆	<= 1.0
Campylobacter	< 0.001	◆	<= 1.0
E.H.E. coli	< 0.001	◆	<= 1.0
Pathogenic Parasites			
Entamoeba histolytica	< 0.001	◆	<= 1.0
Giardia lamblia	< 0.001	◆	<= 1.0
Cryptosporidium	< 0.001	◆	<= 1.0
Mycology (E5)			
Rhodotorula sp.	1,067. H	◆	<= 1.0
Parasitology			
No Ova or Parasites			
Adiposity Index			
Firmicutes	75	◆	<= 80
Bacteroidetes	25	◆	=> 20
Drug Resistance Genes			
aacA, aphD	Pos	gyrB, ParE	Neg
mecA	Neg	PBP1a, 2B	Neg
vanA, B, and C	Neg		

Pathogens
Helicobacter pylori (H. pylori)
 bacterium causes peptic ulcer disease and has been associated with increased gastric

Clostridium difficile is a gram-positive bacterium that can cause diarrhea. C. difficile infection can have symptoms closely resembling Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD).

Campylobacter, a gram-negative bacterium, is a frequent cause of mild to severe diarrheal disease from contaminated food.

Giardia can cause acute or chronic infections. Acute symptoms include nausea, low-grade fever, epigastric pain and explosive watery stools. Chronic symptoms include recurrent diarrhea, distention, belching and heartburn.

Enterohemorrhagic E. coli or similar strains of E. coli produce toxins that may cause severe gastrointestinal disease. Transmission of these bacteria is commonly from contaminated or inadequately cooked beef and milk products.

Entamoeba histolytica is a tissue-invading parasite. Approximately 10% infected patients have clinical symptoms. Symptoms may appear in asymptomatic carriers following stresses that diminish GI immune response. Most symptomatic patient present with dysentery or colitis.

Cryptosporidium usually infects the brush border of the intestine. Symptoms include diarrhea, nausea and cramping. The disease is usually self-limiting in immunocompetent patients.

These test results are not for the diagnosis of disease. They are intended to provide nutritional guidelines to qualified healthcare professionals with full knowledge of patient history and concerns to assist in their design of an appropriate healthcare program.

Recommended Treatments:

- 1: Identification of microbial sensitive pharmaceutical and/or natural agents
- 2: Re-inoculate beneficial bacteria

Enterobacter sp.

	Sensitive	Resistant
Pharmaceuticals		
Ampicillin/Sulbactam		R
Clindamycin	S	
Erythromycin	S	
Levofloxacin	S	
Penicillin G	S	
Tetracyclin	S	
Botanicals		
Berberine		R
Black walnut		R
Caprylic acid		R
Cats Claw		R
Goldenseal		R
Oregano		R

Microbial Sensitivity Profile

Rhodotorula

	Sensitive	Resistant
Pharmaceuticals		
Fluconazole	S	
Amphotericin B	S	
Ketoconazole	S	
Nystatin	S	
Botanicals		
Berberine		R
Black walnut		R
Caprylic acid		R
Cats Claw		R
Goldenseal		R
Oregano		R

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