Chronic diseases are the major cause of death and disability worldwide. Non-communicable conditions such as cardiovascular disease, diabetes, obesity, cancer and respiratory diseases now account for 59% of the 57 million deaths annually and 46% of the global burden of disease. Chronic diseases affect more than 90 million United States citizens. Inflammation is at the root of many chronic problems, including cardiovascular disease, cerebrovascular disease, cancer, stroke, and Alzheimer’s dementia, all of which are among the top 10 causes of mortality.

Inflammation is a part of the body’s natural defense system. An excessive or constant elevation of inflammatory markers, however, can cause harm. In Western biomedical medicine, inflammation is commonly controlled with prednisone, non-steroidal anti-inflammatories (NSAIDs), or other medications. Treatment modalities exist that are potentially effective, have fewer negative effects, and provide the affected patient with greater control. The anti-inflammatory diet is one of these modalities.

**Anti-Inflammatory Diet**

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**LINKING DIET TO INFLAMMATION**

An inflammatory response includes hundreds of chemical reactions. Multiple laboratory markers are used as correlates for how much inflammation exists. Some of these include C-reactive protein (CRP), Interleukin-6 (IL-6), and tumor necrosis factors such as TNF-α. Trans-fat consumption, fiber intake, essential fatty acid consumption, glycemic index, fruit and vegetable consumption, and overall diet quality as scored by various measurement instruments are all known to influence the levels of these inflammatory markers. Furthermore, a number of chronic illnesses have been found to be associated with elevated serum levels of these and other biomarkers.

Foods influence inflammation in multiple ways. Some foods, including trans-fats and charred foods, have pro-oxidant effects. Foods with high glycemic index or glycemic load values are more pro-inflammatory (Diabetes mellitus Type II is preceded by elevations in inflammatory markers). In addition, many food compounds directly alter specific biochemical pathways, the most researched of these being essential fatty acids (EFAs).

The body is unable to synthesize omega-6 and omega-3 fatty acids, so they must be obtained in the diet. Omega-6 fatty acids are overall pro-inflammatory. Omega-3 fatty acids decrease inflammation by decreasing the metabolism of arachidonic acid into inflammatory prostaglandins and leukotrienes. Common omega-3 fatty acids include alpha-linolenic acid (ALA), eicosapentanoic acid (EPA), and docosahexanoic acid (DHA). Since the Paleolithic era, the ratio of omega-6 to omega-3 fats in the human diet has steadily increased, from approximately 1-2:1 to over 25:1. This rise seems to correlate with the rise of many chronic illnesses.

Continued on page 2
WHAT IS AN ANTI-INFLAMMATORY DIET?
An anti-inflammatory diet is any diet that can help to prevent or decrease the body’s total levels of inflammation. Based on the research currently available, some essential steps include:

• Avoid unhealthy fats. Trans-fats and omega-6 fats, which are often found in animal products and any foods designed to have a long shelf life, cause inflammation. Mono-unsaturated fats, like olive oil, decrease inflammation.

• Eat fruits and vegetables. People with diets high in fruits and vegetables have decreased inflammatory markers and are at lower risk for a number of chronic illnesses.

• Eat fiber. Fiber intake also correlates with lower levels of inflammatory markers and lowers risk for disorders such as cardiovascular disease.

• Decrease consumption of high glycemic index/load foods. Foods that lead to a rapid release of high levels of insulin can increase inflammation.

WHO SHOULD TRY AN ANTI-INFLAMMATORY DIET?
The following conditions are linked to inflammation:

• Heart disease 15,16,17

• Stroke

• Cancer 18,19,20,21,22 (a recent JAMA systematic review questions the cancer benefit from omega-3 fatty acids) 23

• Chronic obstructive lung diseases (emphysema and bronchitis) 24,25

• Asthma 26,27,28

• Chronic pain (e.g., fibromyalgia 29 and neuropathy 30). Few studies on diet and chronic pain exist to date.


Food Intake Guidelines:28

<table>
<thead>
<tr>
<th>EAT MORE</th>
<th>AVOID EATING</th>
</tr>
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<tbody>
<tr>
<td><strong>FOODS HIGH IN OMEGA-3 FATS</strong></td>
<td><strong>FOODS HIGH IN TRANS- AND OMEGA-6 FATS</strong></td>
</tr>
<tr>
<td>• Cold water fish (salmon, sardines, herring, mackerel)</td>
<td>• Fatty red meats</td>
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<tr>
<td>• Ground flax seeds or flax oil</td>
<td>• High fat dairy products</td>
</tr>
<tr>
<td>• Leafy green vegetables</td>
<td>• Partially hydrogenated oils</td>
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<tr>
<td>• Walnuts</td>
<td>• Corn, cottonseed, grapeseed, peanut, safflower, soy, and sunflower seeds</td>
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<tr>
<td><strong>FOODS HIGH IN ANTIOXIDANTS</strong></td>
<td><strong>FOODS HIGH IN SIMPLE CARBOHYDRATES</strong></td>
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<tr>
<td>• Yellow, orange, and red vegetables (peppers, carrots)</td>
<td>(That is, foods with a high glycemic load. Foods that cause a rapid rise in insulin levels seem to cause more inflammation.)</td>
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<tr>
<td>• Dark leafy greens (spinach, Romaine lettuce)</td>
<td>• White breads or bagels</td>
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<tr>
<td>• Citrus fruits</td>
<td>• English muffins</td>
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<tr>
<td>• Black and green teas</td>
<td>• Instant rice</td>
</tr>
<tr>
<td>• Allium vegetables (onions, garlic)</td>
<td>• Rice and corn cereals</td>
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<tr>
<td><strong>FOODS HIGH IN FIBER</strong></td>
<td><strong>FOODS MORE LIKELY TO TRIGGER INTOLERANCE REACTIONS</strong> (these vary from person to person)</td>
</tr>
<tr>
<td>• Whole grain such as whole wheat, oat meal</td>
<td>• Dairy</td>
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<tr>
<td>• Fruits and vegetables</td>
<td>• Wheat</td>
</tr>
<tr>
<td><strong>SPICES THAT CONTAIN ANTI-INFLAMMATORY COMPOUNDS</strong></td>
<td>• Eggs</td>
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<tr>
<td>• Ginger</td>
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<td>• Rosemary</td>
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<td>• Turmeric</td>
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<td>• Oregano</td>
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<td>• Cayenne</td>
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<td>• Clove</td>
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<td>• Nutmeg</td>
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<td><strong>HERBS THAT HAVE ANTI-INFLAMMATORY PROPERTIES</strong></td>
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<td>• Boswellia</td>
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<td>• Willow bark</td>
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<tr>
<td>• Feverfew</td>
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Continued on page 3
• *Diabetes mellitus* Type II and the metabolic syndrome 31,32
• Inflammatory bowel disease (Crohn’s or ulcerative colitis) 33,34
• Alzheimer’s disease and other dementias 35,36,37
• Autoimmune disorders (e.g., rheumatoid arthritis 38,39)
• Cystic fibrosis 40,41

An anti-inflammatory diet tends to be nutritionally balanced. The anti-inflammatory guidelines may be tailored to individual patient’s needs based on motivation, the degree to which the diet needs to be modified, and the extent of illness.

**OTHER DIET-PRESCRIBING TIPS**
When prescribing an anti-inflammatory diet, keep the following in mind:

• The overall effect may take as long as 6 weeks to 6 months.

• Consider supplementing DHA and EPA, a total of 1,000 mg daily. For every gram of fish oil, there is 300 mg total omega-3 fatty acid content. For flax, it is 700 mg omega-3 fatty acids per gram of flax oil. Cod liver oil has 200 mg/gram but also contains very high levels of vitamin A (intake must be monitored to avoid hypervitaminosis). Many patients are unable to get adequate omega-3 fats through diet alone, or may be concerned about doing so because of contaminants and great variation in omega-3 levels in seafood.

• The anti-inflammatory diet guidelines may complement those medications prescribed by a physician (discuss these guidelines with your healthcare provider).

• Stress reduction and exercise also have significant anti-inflammatory effects.

• Remember to enjoy eating.

**CONCLUSION**
A recent review concisely summarized: We can no longer view different diseases as distinct biochemical entities. Nearly all degenerative diseases have the same underlying biochemical etiology, that is, a diet-induced proinflammatory state. Although specific diseases may require specific treatment, the treatment program must also include nutritional protocols to reduce the proinflammatory state. 42

The current body of available evidence supports the use of the anti-inflammatory dietary approaches as part of an integrative approach to dealing with a number of chronic, difficult-to-treat illnesses.

– AR

**Clinical Pearl**
If your patient has an elevated inflammatory marker, consider prescribing the following:

• Anti-inflammatory/Mediterranean Diet (omega-3 rich, fish, fruit, vegetables, whole grains, olive oil)

• Low Glycemic Load foods www.glycemicindex.com for list

• Attain an ideal body weight (especially those with trunkal fat distribution)

• Create an environment that allows positive emotions (vs. negative)

  **Tools to help with this:**
  – Mindfulness course
  – Breathing exercises
  – Yoga class

• Regular aerobic exercise (30-40 min/day)

If the above prescriptions are already in place, consider these additional prescriptions:

• Include a high-quality (preferably a whole food supplement) multivitamin, if the patient is diagnosed with diabetes

• Add 1 gram of cold-water derived fish oil daily (this may be increased to a maximum dosage of 4 grams, if needed to reduce inflammatory markers further)

• Include an aspirin 81-325 mg daily with food

• Consider statin therapy, if the patient is at high risk with elevated lipids

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Continued on page 4
Inflammation and inflammatory mechanisms demonstrate that there is no distinction between the mind and the body. Inflammation can be initiated in the periphery through immune recognition of a foreign invader, such as bacteria, or due to specific damage to a part of the body (e.g., a mosquito bite or a cut on the finger). The brain also has the ability to inhibit the inflammatory process through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medullary (SAM) axis, the major peripheral output systems of the brain’s stress responses.

**PATHOPHYSIOLOGY**

When the brain responds to stress such as anxiety or negative emotion, the sympathetic nervous system (SNS) is activated and prompts the release of neurotransmitters (e.g., serotonin) that stimulate the HPA axis and cortisol release. Each of these biological processes branch repeatedly and interact with other neuro-endocrine responses, each of which have effects on the peripheral immune system that involves cytokines (e.g., IL 1 and 6), Substance P (SP), and other biomolecules. These in turn, can act on the hypothalamus and other components of emotional circuitry in the brain. The existence of this bi-directional circuit implies that peripheral inflammatory processes can cause psychological distress, and conversely, that psychological distress can initiate inflammatory processes. A review of asthma and depression illustrates the empirical validity of both processes.

**ASTHMA AND DEPRESSION**

Asthma and depression are examples of the mind-body-inflammatory-stress loop; the former being a condition more routinely associated with the body and the latter more routinely associated with the mind.

**DEPRESSION TRIGGERED BY THE BRAIN**

Depression can be caused by negative life events, exacerbated by negative self-attributions, and maintained by rumination. This may result in feelings of hopelessness and suicide. When a negative event occurs that is psychological (e.g., the letter F represents a failing grade), the stressor activates emotional circuitry in the brain which results in a complex neurotransmitter cascade including the release of norepinephrine (NE) and activation of the HPA axis, one pathway for the brain’s influence on peripheral immune function and inflammatory processes. In this case, epinephrine and NE can down-regulate the expression of glucocorticoid receptors. In the immune system, this results in a reduced ability to constrain inflammatory processes. Furthermore, psychological stress or emotion can activate systems relevant to SP, a neuropeptide that can trigger inflammation in the absence of an invading pathogen or chemical irritant.

**DEPRESSION TRIGGERED BY THE IMMUNE SYSTEM**

Analogous to the brain, the immune system interprets events as negative and can stimulate depression-like symptoms when a pathogen, detected in the periphery, causes the release of cytokines. This occurs when a pathogen, detected in the periphery, causes depression. When a pathogen enters the periphery, immune cells recognize these pathogens, and produce pro-inflammatory cytokines that trigger a brain cytokine system (largely through IL-1) that initiates the sickness response. This response includes the activation of the HPA axis and behavioral patterns associated with sickness (e.g., reduced food intake and low energy). Peripheral cytokine activity alters an individual’s motivational state and priorities to react to threat. Furthermore, chronic inflammation and the inability of glucocorticoids to suppress immune function can result in prolonged activation of the brain’s stress response, a condition associated with depression and other mood disorders. This may be why prolonged administration of IL-2 as a treatment for some cancers or viral infections (hepatitis C) results in depressive episodes for 20-30% of the population. Disorders associated with chronic inflammation, such as atherosclerosis and coronary heart disease, also have the same prevalence of depression. Finally, drugs that block the neurokinin-1 receptor, the receptor through which SP exerts its inflammatory effects, are as effective as conventional anti-depressants in alleviating depressed moods in some studies. Thus, both peripheral and central mechanisms exist to initiate and maintain a depressive episode.
ASTHMA
When an asthmatic episode occurs, the brain is alerted to the presence of inflammation, most likely via sensory nerves and cytokine activity. Evidence suggests that this alert is communicated to brain regions that process and respond to emotion, and may influence the ensuing inflammatory response. In short, asthma symptoms can be initiated peripherally but may be maintained or exacerbated by brain mechanisms. Evidence suggests the strength of the inflammation message to the brain may be increased in some asthmatics or that the descending influence from the brain (especially emotional neural circuitry) to the lungs is stronger. This increase may contribute to the emotion- and stress-related flare-ups common in asthma where both ends of the mind-body loop are sensitized.

This relationship between inflammatory processes and psychological or physical stressors challenges the idea of a clear distinction between the mind and the body. The examples of depression and asthma demonstrate the lack of this distinction. Furthermore, the nature of the inflammatory response suggests a continuous loop involving the entire body including the brain. Such a loop explains why events interpreted as negative by the brain affect the body and why events interpreted as negative by the body affect the brain. The loop also suggests that some physical problems (either central or peripheral) can be alleviated through psychological means and some psychological problems can be alleviated through physical means. Changing the mind will change the body because the mind is the body. The reverse is also true.

CONCLUSION
As the biochemical distinction between the mind and body becomes more blurred, both mind and body specialists will benefit from recognizing the impact of the body on the mind and the mind on the body. Paying attention to both physical and psychological symptoms is required. Such a perspective may remind practitioners to treat the whole human being, encourage patients to think more holistically about their current concerns, and access therapies (e.g., mindfulness, psychotherapy, journaling) and insights that bring resolution to the physical symptoms by addressing the thoughts and emotions that can initiate and exacerbate them.

– DM, MR

Treating the Whole Person
There is good evidence that treating the whole person, as opposed to just the symptoms, reduces negative health outcomes. For example, a meta-analysis of 23 studies demonstrated that people receiving psychosocial treatments in addition to standard cardiac rehabilitation regimens had reduced mortality and morbidity, psychological distress, and other risk factors compared to those receiving only standard cardiac care. Another meta-analysis of 37 studies showed that utilizing stress management techniques versus traditional allopathic care reduced cardiac mortality by 34% and MI recurrence by 29%. Depression increased the risk of heart disease by about 50%. Happy people have lower risk factors for heart disease (e.g., fibrinogen levels) than unhappy people. Meditation (transcendental meditation technique) was twice as effective than progressive muscle relaxation in reducing systolic blood pressure. Laughter is associated with a healthy heart.

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Inflammation and Exercise

**EFFECTS OF EXERCISE ON INFLAMMATORY AND NON-INFLAMMATORY BIOMARKERS**

Who should exercise? What age group? How much? How long? When is it too much? In relation to exercise, are there nutrients that influence inflammation? These are just a few of the many questions that may arise when a practitioner is advising patients on exercise regimes.

In the following review, four clinical studies on various aspects of exercise and inflammation are presented. In this issue, the basic theory of inflammation in the progression of certain chronic disease states has been discussed. It should be noted that different inflammatory and anti-inflammatory biomarkers are evaluated depending on whether the chronic illness is cardiovascular disease, diabetes, asthma, or depression, for example. And in some instances these biomarkers overlap. In terms of exercise, the common biomarkers used in these four clinical studies included both inflammatory and anti-inflammatory markers (see Box).

These studies were chosen because they represent a broad sector of the population: Study 1, middle-aged and older adults; Study 2, severely obese subjects; Study 3, elderly; and Study 4, ultra-marathon runners.

**Study 1:** Increased physical activity among healthy middle-aged and older adults resulted in significantly lower inflammatory markers. When the results were adjusted due to confounding factors, the relationship between physical activity and inflammation remained significant for CRP and WBC. **Of particular note is that those who engaged in more frequent physical activity (4-21 per month) had lower CRP levels than those who exercised less frequently.** The authors suggest the coronary heart disease patients may benefit from reduced inflammatory markers due to the effects of regular exercise. The frequency may be more beneficial on inflammation than the duration.1

**Study 2:** Twenty-seven severely obese patients were put on a hypocaloric diet and exercise regime. The lifestyle intervention induced reduction in inflammation in plasma and adipose tissue (AT), paralleled by a significant improvement in metabolic status. In the circulation CRP, IL-6, IL-8 and MCP-1 were reduced and adinopectin (an anti-inflammatory marker) increased. **This study demonstrated that weight loss obtained through lifestyle intervention induced a pronounced reduction in macrophage infiltration in subcutaneous fat paralleled by a reduction in inflammation (reduced CRP, TNF-a, IL-6, IL-8 and increased adiponectin).**2

**Study 3:** The authors found, among 1004 people aged 65 years or more, consistent associations between physical activity and performance, lower ESR, and lower plasma levels of fibrinogen, CRP, and IL-6. These benefits were based on light to moderate physical activity.3

**Study 4:** This study demonstrated attenuation, albeit transient, of both the adrenal stress hormone and anti-inflammatory polypeptide response to prolonged exercise in runners who supplemented with Vitamin C 1500 mg/day when compared to 500 mg/day. The authors noted that circulating adrenaline concentrations were reduced significantly following the stressful competitive event when compared to those in the unsupplemented runners.4

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**INFLAMMATORY MARKERS**
- Adrenaline
- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR)
- Fibrinogen
- Interleukin (IL) IL-8 cytokines
- IL-6 cytokines
- Monocyte chemoattractant protein (MCP)-1
- Tumor necrosis factor (TNF)-α
- White blood cell (WBC)

**ANTI-INFLAMMATORY MARKERS**
- Adiponectin
- IL-10 cytokines
- IL-1ra cytokines

**PRACTICAL ADVICE**
- Frequency of exercise may be a more important factor than the actual duration or intensity.
- Middle-aged, obese, and elderly in these clinical study sample populations appear to benefit from reduced inflammation that accompanies mild to moderate exercise.
- Elite athletes (i.e., ultra-marathon runners) may benefit from a Vitamin C supplement (1500mg/day—better in divided doses) pre- and post-event in order to decrease inflammatory responses.
- Excessive exercise can be potentially pro-inflammatory. A balanced approach is always strongly encouraged.

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Relaxation Response

Stimulation of the vagus nerve and the parasympathetic nervous system (relaxation response) has been found to prevent the release of tumor necrosis factor, which is one of the key cytokines in stimulating inflammation. In fact, tumor necrosis factor (TNF) inhibitors (Infliximab, etanercept, adalimumab) are an exciting new class of medications used to treat rheumatoid arthritis and inflammatory bowel disease.

Unfortunately, suppression of this important arm of the immune system can also lead to opportunistic infections and an increased incidence of malignancy.

Breathing exercises should be taught as a way to inhibit tumor necrosis factor release to help reduce the need of the TNF inhibiting drug which is associated with more side effects.

References

ANTI-INFLAMMATORY DIET


Clinical Pearl

Consider prescribing abdominal breathing exercises. This is a great way to stimulate the vagus nerve, induce relaxation, reduce inflammation, improve oxygenation, increase blood flow. Many meditation traditions (i.e., Vipassana, prana nigraha, etc.) focus on the breath and on expanding the breath to include abdominal breathing. In order to avoid hyperventilating consult a teacher of meditative practices. Remember, breathing doesn’t cost a cent!
REFERENCES


INFLAMMATION AND EXERCISE


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The information regarding these findings was prepared based on previous and current research. We are sending you this information to assist in your clinical practice.

Additional research and findings on this topic continue to occur.

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