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**Subject:** Addiction, Pain, and Inflammation

**Addiction & Inflammation: What’s the connection?**

Chronic pain drives many people to become addicted to pain medications. The addiction to pain medications may occur via two pathways: the analgesic pathway, and the euphoric pathway (or both). In the analgesic pathway, pain medication offers tremendous relief from chronic pain, so that the medication becomes strongly associated with relief. With time tolerance to the analgesic effect of pain medication develops. Escalating doses of the pain medication is required, with less and less benefit with each rise in dosage. Eventually, medication-induced pain relief is minimal, medication doses are high, as are side effects (such as sedation and depression). Despite realizing that the pain relief is not as great as it once was, the user is unwilling to give up what has become marginal pain relief. Even if one wants to discontinue the medication, it is often difficult to come off the pain medication because of a rebound in pain secondary to physiological withdrawal. The second “euphoric” pathway is mediated by the reward center of the brain (the nucleus accumbens). In this article I will focus on the the analgesic pathway to addiction.

**The analgesic pathway to addiction.**

Chronic pain almost always has a significant underlying component of inflammation, and so inflammation plays a starring role in the analgesic pathway. Because of this, it is clear that if one can reduce or eliminate inflammation, pain will be reduced, and it becomes possible to come off pain medication, as the need for analgesia diminishes. Thus, treating inflammation removes one of the triggers driving addiction to pain medication.

**What is inflammation?**

Inflammation is classically defined as a local tissue response, which occurs in reaction to injury or destruction of tissues as a result of a variety of stimuli. These triggers of inflammation can be infectious (e.g., viruses, bacteria, molds), chemical (toxic inhalation of chemical solvents for example), mechanical (a sports injury), radiation (for cancer), high temperature (burns) etc. The inflammatory process is directed at containing, destroying, or diluting the injurious trigger, repairing the injured tissue and restoring it to normal function. Acute inflammation is a self-limiting process in which the inflammatory mechanisms- along with other interventions- restores homeostasis (normal function). Chronic inflammation is a state of prolonged activation of the immune response, which results in chronic tissue and organ damage, which causes symptoms and specific diseases to develop.

Acute inflammation and chronic inflammation involve a series of cellular, molecular, genetic mechanisms which compromise function and create symptomatology, which varies with tissue(s) involved as well as with the severity of the immune response. Symptoms of chronic inflammation are both organ specific, and more general. These symptoms include pain, fatigue, fever, reduced cognitive function/emotional regulation, restriction of function of organs involved, restrictions of function of musculoskeletal system, and psychosocial dysfunction.

Chronic inflammation is known to be a major underlying mechanism in the majority of chronic illnesses affecting western societies. While our focus here is how inflammation, and the pain that results, creates addiction, its worth identifying illnesses which are caused by inflammation, so you realize how wide-spread the problem is. These illnesses include, but are not limited to: all “-itis” disorders (e.g., arthritis, sinusitis, prostatitis, cystitis, thyroiditis, cholecystitis, etc.), chronic skin conditions such as acne vulgaris, cystic acne, drug induced acne (e.g., lamotrigine), folliculitis; some chronic pain syndromes, such as sciatica, costochondritis, fibromyalgia; diabetes;

cardiovascular disease; mood and cognitive disorders; auto-immune disorders; chronic infectious diseases (e.g., Lyme);

environmentally caused disorders (e.g., mold induced Sick Building Syndrome); cancers.

As we age two things happen. First stress accumulates. We are exposed to acute stresses (a broken bone, a psychological trauma) and long-term stresses. These stresses may be physical (e.g., arthritis, chronic infections) or psychological (stress increases inflammation thru several mechanism). Second, our reserve, or buffering capacity gradually becomes diminished. With time and trauma, and modified by our genetic endowment, we gradually slide, some people sooner than others, into a state of long-term inflammation. This wears down our biological systems, from specific organs, to our energy producing capacity. We feel this decline in specific ways (e.g., arthritis), or general ways (fatigue). Organs that are most vulnerable, whether due to genetics, previous injury (e.g., a knee injury), or ongoing stress (liver damage from alcohol, or pancreatic damage from a diet too high in sugars, or vascular disease from vessel damage and cholesterol) will exhibit symptoms specific to that organ. As we get older, we have more and more trouble controlling inflammation, and we often end up in a vicious cycle where the effects of inflammation actually cause more inflammation. This is contrary to what happens normally, where inflammatory molecules turn off the production of more inflammatory molecules, thereby reestablishing balance.

**Mainstream medicine’s approach to inflammation**

Current mainstream medicine approaches inflammation by trying to get to identify and treat the cause (e.g., find the infection), and where no common cause can be found, with medications. Commonly used medications are too often inadequate and have significant potential for serious side effects. These anti-inflammatory approaches, (and analgesic approaches, which are included here because one of the cardinal signs of inflammation is “dolor”-i.e. pain) for chronic conditions fall, primarily, into two broad categories: Steroidal and Non-steroidal;

1. Steroidal medications are associated with long-term dangers including diabetes, osteoporosis, fracture, glaucoma, dependence etc.
2. Non-steroidal approaches include:
3. Narcotics (e.g., tramadol, oxycodone, codeine)
4. Prostaglandin Inhibitors (acetaminophen)
5. COX 1 and 2 inhibitors (e.g., ibuprofen, celocoxib)
6. Salicylates (e.g. aspirin)
7. Cannabinoids (e.g., Marinol, medical marijuana)
8. Interleukin 1 inhibitors (e.g., Rilonacept, an orphan drug)
9. Cys-LT-inhibitors (Monteleukast-used specifically for asthma, as these receptors are present in the lung)

Chronic use of all of the above compounds is associated with a significant potential for serious side effects such as:

1. Hepatic injury(acetaminophen),
2. Renal dysfunction COX 1 and 2 inhibitors (e.g., ibuprofen, celocoxib),
3. Ulcers and hemorrhage (e.g. aspirin, ibuprofen),
4. Addiction (e.g., codeine),
5. Cognitive dysfunction (e.g., medical marijuana, narcotics),
6. Infection (Rilonacept)

**Complementary and alternative approaches to inflammation**

As a replacement for the above approaches, or in addition to them, natural and herbal interventions may be employed with great success. At the end of this article I provide an overview of such a program. In this section, I would like to review natural and herbal approaches to inflammation, and how these substances work to reduce chronic inflammation.

There are scores of substances, which have been shown, in clinical and basic science studies, to have a beneficial effect on pain and inflammation. Below are some of my favorites, along with some of the scientific mechanisms of anti-inflammatory action.

1. Omega 3-essential fatty acids. EPA and DHA are two related essential fatty acids, commonly found in cold-water fish. They help with inflammation by enhancing the conversion of certain inflammatory molecules (COX) to prostaglandin E3 (PG-E3), which is a natural anti-inflammatory. PG-E3 inhibits production of the strong pro-inflammatory molecule, PG-E2, as well the pro-inflammatory cytokines, TNF-alpha, and Interleukin 1b. These two fish oils also inhibit the 5-lipoxygenase (5-LOX) pathway, which converts arachidonic acid (present in the cell membranes) to inflammatory leukotrienes. In cartilage, these two Omega 3’s inhibit actions of matrix metalloproteinase (MMP), which breaks down intercellular tissue, (and is a cause of tissue damage in chronic inflammation), and aggrecanase (a degrading enzyme, which affects the integrity of cartilage).
2. Frankincense (Boswellia serrata) is an herb used for millennia and for good reason. In fact, its use is described in biblical texts written around 586 BCE. While used in religious ceremonies (it was used for its aromatic effects), it was very likely also used for its anti-inflammatory pain relieving effects. We now know that this herb has at least 8 anti-inflammatory actions, some of which prevent the breakdown of tissue (inhibition of MMP’s which breakdown connective tissue) and sparing of GAG’s (which help protect connective tissue). Additionally this herb has effects on the above-mentioned molecules, NF-Kappa-B, and TNF-alpha. Boswellic acids (11-keto-Beta-boswellic acid is the most potent of all boswellic acids) inhibit Leukotriene B4 (a molecule that promotes inflammation) synthesis by inhibiting 5-LOX, thereby reducing inflammation; It reduce the white blood count in joints (a measure of inflammation), and inhibits an enzyme (leukocyte esterase) which is elevated in rheumatoid arthritis.
3. Stinging Nettle (Urtica Dioica). This herb, which grows ubiquitously, is often considered a weed, yet there is a great deal of research indicating it has very potent anti-inflammatory properties. One of the actions of this herb is to stabilize the two molecules that are the ‘grand central stations’ of inflammation—TNF-alpha and NF-Kappa Beta. When those molecules are activates, a symphony of inflammatory molecules are made by the your genes. This activation is very helpful for acute inflammation, but very often damaging in chronic inflammation. Additionally, it has effects on the synthesis of other molecules of inflammation such as the leukotriene’s and prostaglandins. Importantly, boswellia (above) and stinging nettle don’t suppress the activity of these molecules below normal. They merely restore normal levels. This is important because excessive suppression of inflammation is, in its own right, dangerous.
4. Turmeric (curcumin) is a Cox 1 and 2 inhibitor, NF-Kappa Beta inhibitor. However, absorption in significant quantities is a challenge. It takes 14-21 days for levels of the inflammatory cytokines to begin to be reduced, and high blood levels of the active compound are needed. When used continuously in cooked foods, it likely confers an anti-inflammatory benefit.
5. Green tea contains polyphenolic compounds called catechins. One of these, called epigallocatechin-3-galate (E3G) inhibits interleukin 1b, and reduces the activation of NF-Kappa B. NF-Kappa B mediated signal transduction has been implicated in the regulation of viral replication, auto-immune diseases, the inflammatory response, development of tumors and cell death (apoptosis). Green tea also protects cartilage. Green tea extract can cause stomach irritation and contains caffeine (but can be decaffeinated).
6. Pycnogenol (pine bark) contains polyphenols, which inhibit TNF-alpha activation caused by bacteria, and also inhibits MMP activity. Pycnogenol should not be used by those being treated with immune-suppressants or steroids; it can cause diarrhea or upset stomach.
7. Resveratrol contains polyphenolic compounds. It is found in plant skins (e.g. red wine grapes). These polyphenols are potent inhibitors of TNF-alpha and interleukin 1-B induced NF-Kappa-Beta activation. Resveratrol should not be taken if blood clotting is an issue; In fact use of any herb should be screened before use, if one has a clotting problem, or is on anti-coagulant medication such as warfarin, heparin or Coumadin.
8. Cat’s Claw (Uncaria tomentosa): once again contains polyphenols which inhibit activation of NF-Kappa Beta and inhibit TNF-alpha production; These may cause nausea, and two case reports of acute renal failure have been reported;
9. Horsetail (Equisetium Arvensae). Horsetail like other herbs in this listing inhibits TNF-Alpha based inflammatory response.
10. Celery (Apium Graveolens) inhibits the production of COX-2, which is blocked by the usual over the counter and prescription anti-inflammatories (e.g., Advil). It also is a weak diuretic, thereby reducing swelling in tissues, and reducing excess blood flow to tissues.
11. Garlic (Allium Sativum) enhances white blood cell production (white blood cells fight infections which cause inflammation), increases the ability of white blood cells to ‘eat’ bacteria, increases natural killer cells, which are a first line of defense against viruses and bacteria.

**Summary and what to do**

At sometime during our lives, we have serious physical pain, which often leads to exposure to pain medications. These medications and the relief the initially give may activate an addictive process in those who are vulnerable. For those people addicted to pain medication due to chronic pain (as opposed to those addicted due to the ‘high’), treating inflammation can be the answer to achieving and maintaining sobriety, and overall improvement in many areas of health and a significantly improved life.

To be effective in normalizing inflammation, one must use natural substances in a synergistic manner, along with other approaches. Below is a flow chart, which illustrates how using a combination of herbs can attack several points in the inflammatory cascade, working upstream in the domino-like process, to support normal levels of inflammation. This is a more logical and thorough approach to inflammation, than using one substance to attack one point in the inflammation cascade, as common medications (e.g., ibuprofen) do.

My advice is that in concert with an integrative health care practitioner, you work on identifying and cleaning up your sources of inflammatory stress: diet, psychological stress, chronic infections, etc. Are the sources in your gut, your nutrition, your air (mold), your sinuses, your thoughts, your hormonal stress system (adrenal)? Are they in your lifestyle? Once you have identified these sources of inflammation, a clear prescription for reducing inflammation is easy. Implementing it takes time, and is best done with a good friend, who is pursuing similar goals.

1. A well balanced minimally processed diet, low in grains, and high in small fish (e.g., sardines, mackerel, herring) and colorful vegetables and fruits are a fabulous start.
2. Use a couple of probiotics. This is a great second step, as will help reduce the inflammation coming from your gut. This is a major source of inflammation. I often recommend Culturelle, and MegaFoods MegaFlora.
3. Use a broad-spectrum herbal anti-inflammatory blend on a regular basis.
4. Life is stressful. We cannot avoid that, nor can we usually remove the stressful situations from our life. Engage in some form of meditation, music, art—something which will slow down your worrying, obsessing brain, and calm your body, reducing your adrenalin ‘over-drive’ do 5 minutes of appropriate stretching daily and exercise 3 or 4 times per week;
5. Get involved and stay involved in a community organization, which is service, oriented. This has been shown to improve long-term health, if done before illness starts.

