

Chronic Pain

Pain serves a valuable function by alerting the body that something is functionally or structurally wrong. A simple example is the reflex response that occurs when you accidentally touch your hand to a hot stove. Sensors in the skin sense pain. These sensors send signals along special nerve pathways to the spinal cord, which in turn sends signals to provoke a reflex that causes you to jerk your hand away from the heat source, thereby limiting damage to your hand. This is all done automatically, without thinking.

Pain may be chronic or acute, sharp or dull, throbbing or steady, or intermittent or constant. Chronic pain is a significant source of discomfort and lost productivity in today's workplace.

In the doctor's office, pain is often measured on a scale from 1 to 10 (called a visual analog scale) or by using words such as "mild," "moderate," "severe," or "excruciating." Pain itself is not a disease; it is a symptom of a disease or condition. Pain can be perceived in remarkably varied ways. For example, some people have very high pain thresholds and can endure a great deal of pain with relatively little complaint. For others, even a slight amount of pain is difficult to tolerate.

The ability to sense and locate pain depends in large part on where it is in the body. Pain sensors are distributed unevenly throughout the body and have different levels of specificity. For example, the skin has many pain receptors that are very sensitive. People who have had a skin injury can often tell if a sharp object, a blunt object, a flame, or some other source caused the injury without having seen the injury occur. By contrast, pain that occurs in the intestines is difficult to locate and describe. Similarly, pain may also occur in the form of referred pain. In a case of referred pain, the pain is felt in one area of the body even though the problem may be located elsewhere. A good example of this is pain that radiates to the left arm during a heart attack.

Pain may also be psychogenic, meaning that it arises from a disturbance in the psyche or emotions. True psychogenic pain, in which there is no injury, is relatively rare. More common is pain that has a psychogenic element. In other words, the patient is feeling pain out of proportion to the injury or condition. It's important to note that, even if some portion of the pain may be due to psychogenic reasons, it is still important to treat the pain. The perception of psychogenic pain is no less debilitating than pain directly caused by an injury.

This chapter focuses on chronic pain, or lasting pain that does not signal an immediate injury such as surgery, trauma, or a heart attack. Chronic pain has been defined as pain lasting 3 months or more (Koch H 1986). Pain can be caused by numerous medical conditions, including (Burris JE 2004; Lethbridge-Cejiku M et al 2004):

- Osteoarthritis
- Rheumatoid arthritis
- Back problems
- Osteoporosis
- Peripheral vascular diseases
- Cardiovascular diseases
- Cancer
- Fibromyalgia
- Multiple sclerosis
- Phantom limb pain (pain felt in the area of an amputated limb)
- Parkinson's disease
- Neuralgia (pain along the course of a nerve)

Chronic pain affects up to 50 percent of the elderly (Burris JE 2004). This percentage rises to 80 percent in residents of hospices or nursing homes (Burris JE 2004). According to the National Institutes of Health, lower back pain is one of the most significant health problems in the United States and is the most frequent cause of limited activity in people younger than age 45 years. Approximately 65 percent to 80 percent of people have back pain at some time in their life (Harris L 1999).

Some other facts about pain:

- Women report having chronic pain more frequently than men (Lethbridge-Cejiku M et al 2004).
- Asian Americans report migraine, neck pain, or back pain less frequently than whites, African Americans, American Indians, or Alaskan Natives (Lethbridge-Cejiku M et al 2004).

- Studies show that effective pain relief helps reduce hospital stays, promotes recovery, and reduces the risk of developing chronic pain (Carli F et al 2002; Linton SJ et al 1993).
- Undertreatment of pain is a major, worldwide problem (Lander J 1990; Martin R et al 2005).

NATURAL PAIN DEFENSES

We can sense pain because of the presence of nerve cells throughout the body that are activated by painful stimuli. These cells react to a variety of disturbances, including pressure, temperature, and chemical stimuli. There are several kinds of pain receptors for different kinds of stimuli. Once stimulated, a pain receptor sends an impulse along a network of special nerves called afferent nerves to the spinal cord and brain. Signals are transmitted along the afferent nerves by neurotransmitters, including substance P (Guyton AC et al 2001).

In addition to transmitting signals along the nerve pathway, substance P enhances local sensitivity, lowering the pain threshold (Guyton AC et al 2001). Prostaglandin E2 also enhances local sensitivity. During an injury, prostaglandin E2 is increased as a result of the local inflammatory response, which is initiated by the cytokines interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-alpha). Prostaglandin E2 is a target for nonsteroidal pain relievers such as aspirin and ibuprofen.

The body has its own pain-killing system (analgesic system) that blocks pain signals before they reach the brain (Guyton AC et al 2001). Endorphins are a central part of the analgesic system (Guyton AC et al 2001). They are produced by the hypothalamus and secreted into the bloodstream during times of pain or stress (Berne RM et al 1988). Endorphins bind to opioid receptors on the afferent nerves (Guyton AC et al 2001). By stimulating opioid receptors, they prevent neurotransmitters from transmitting the pain signal (Guyton AC et al 2001).

CONVENTIONAL PAIN MANAGEMENT

Pain management represents a large and very important part of modern clinical medicine. Physicians typically rely on pain medications to dull the sensation of pain. In the United States, there are various categories of medications available for treating pain, including (Aronson MD 1997):

- Simple analgesics (acetaminophen)
- Nonsteroidal anti-inflammatory drugs (NSAIDs), including nonprescription NSAIDs (such as ibuprofen or naproxen) and prescription NSAIDs (such as nabumetone and diclofenac)
- Opiates (such as codeine, morphine, and oxycodone)
- Corticosteroids
- Various adjuvant agents (such as antidepressants, anticonvulsants, benzodiazepines, and GABAergics) (Ashkenazi A et al 2004)

Some medications work peripherally at the local level on pain sensors and some work centrally on the central nervous system (Cashman JN 1996). Consequently, each is effective in treating a different type of pain. The adverse effects of pain drugs vary, depending on the drugs, but can be lethal and very dangerous.

Besides being taken orally, anesthetics can be rubbed on the skin, delivered by an adhesive patch applied to the skin, or injected directly into the painful area (Ashkenazi A et al 2004). Topical applications include lidocaine and capsaicin (from cayenne pepper) creams (Ashkenazi A et al 2004). Neural blockage (nerve block) can also be an effective treatment of chronic pain (Ashkenazi A et al 2004). Physicians may inject a local anesthetic or corticosteroid to reduce inflammation or block nerve function in a specific area, temporarily stopping pain messages from reaching the brain (Ashkenazi A et al 2004).

In patient-controlled analgesia, the patient has the ability to self-administer a low level of a narcotic pain reliever through an infusion pump. The number and size of doses is pre-set so the patient cannot overmedicate. Patient-controlled analgesia has been shown to be a very effective method of relieving pain, in part because the patient has some control over his or her own pain relief.

Ziconotide is a novel type of painkiller approved by the US Food and Drug Administration (FDA) in 2004; it is the first of a new class of painkillers (Miljanich GP 2004). Ziconotide is a nonopioid treatment of severe chronic pain (Miljanich GP 2004). It is the synthetic version of omega conotoxin M seven A (omega-MVIIA), which is a component of the venom of a marine snail (*Conus magus*) that blocks neuronal calcium channels to inhibit neurons that transmit pain signals (Miljanich GP 2004). This mechanism of action distinguishes ziconotide from all other analgesics (Miljanich GP 2004).

Ziconotide must be slowly injected into the cerebrospinal fluid. Adverse effects include psychiatric and neurological signs and symptoms such as memory loss, confusion, and speech disorders. These effects go away when the drug is discontinued. A higher incidence of confusion is found in patients older than age 65 years, which may limit use of ziconotide in older individuals.

The Lethal Side Effects of Pain Medications

Over-the-counter pain medications are some of the most popular drugs in the world. Millions of people regularly take drugs such as aspirin, acetaminophen, or NSAIDs to relieve common aches and pains. Because of their availability, however, few people are aware of the serious, and sometimes lethal, side effects that are associated with these medications.

Aspirin is an inexpensive and common painkiller that is used both to relieve minor aches and more serious conditions such as arthritis. In high doses, however, aspirin's adverse effects can include heartburn, nausea, vomiting, ringing in the ears, and hearing loss. Also, because it decreases the action of platelets, aspirin is associated with a risk of bleeding. Patients who are taking anticoagulants should never take aspirin. Aspirin has also been associated with increased bleeding if taken with alcohol.

Acetaminophen is a pain and fever reducer with adverse effects that can include trembling, lightheadedness, fatigue, fever, bleeding, and pain in the side or lower back. Long-term use can cause anemia, as well as liver and kidney damage.

Use of over-the-counter NSAIDs can also cause serious adverse effects. While prescription cousins of NSAIDs such as rofecoxib have attracted national attention for increased risk of heart attack, the over-the-counter NSAIDs can also cause adverse effects, including gastrointestinal upset and bleeding. Other adverse effects of NSAIDs include stomach pain, gastritis, peptic ulcers, headaches, nausea, dizziness, depression, vomiting, diarrhea, cramps, and convulsions.

Few prescription drugs, however, have the reputation of opiates when it comes to adverse consequences. People who take opiates run a risk of developing a tolerance and dependency on the drugs. Also, opiates may cause sedation and respiratory depression. Opiates are, however, the mainstay for treating severe pain (such as the pain caused by some forms of cancer) because they are so effective. The risk of dependency is much lower than many people assume. Nevertheless, because the drugs are commonly abused, many physicians are hesitant to prescribe opiates in situations that might otherwise warrant their use.

Nutrition and Pain

In many cases, chronic pain is caused by an underlying condition, such as arthritis or fibromyalgia. Treating the underlying condition is an effective way of relieving pain.

A number of nutrients have been studied for the ability to limit oxidative stress and inflammation. Some interfere with substance P. The nutrients discussed here have been studied in the context of various diseases, such as arthritis. Effective pain management may require different strategies for different people, depending on the nature of the pain. Anyone experiencing chronic pain should have a full evaluation by a licensed, experienced physician to determine the cause.

Phenylalanine and Pain

Phenylalanine is an essential amino acid found in milk and meat (Mahan LK et al 1996). It was first tested to treat pain in a 1978 study. Researchers discovered that injecting phenylalanine intraperitoneally (into the peritoneal cavity of the abdomen) blocked pain in 70 percent of mice subjected to painful stimuli. The pain-blocking action actually grew stronger with time (Ehrenpreis S 1978). Scientists later tested the pain-blocking capacity of phenylalanine on 10 patients who had chronic pain that did not respond to treatment. All patients found pain relief with this simple amino acid (Ehrenpreis S 1978). There were no harmful side effects, and no one became addicted (Ehrenpreis S 1978).

Phenylalanine does not work as rapidly as aspirin and other pain medications (Balagot RC et al. 1983). This is because phenylalanine helps relieve pain by increasing the body's supply of endorphins rather than by attacking pain directly (Kitade T et al 1990; Russell AL et al 2000). In animals, DL-phenylalanine has been shown to block the activity of carboxypeptidase, an enzyme that degrades enkephalins, endogenous morphine-like substances. DL-phenylalanine administered orally before acupuncture prolonged the pain relief induced by acupuncture. In 56 patients, tooth extraction was performed while the patients were under acupuncture anesthesia. In addition to the acupuncture, 18 of the 56 patients also received 4 grams of DL-phenylalanine orally 30 minutes before the extractions. The pain-relieving capacity was excellent in eight of the patients, good in six of them, fair in three, and poor in one. The patients who had excellent and good pain relief were compared to 38 patients who received a placebo. The effect in the patients who received DL-phenylalanine in addition to acupuncture was significantly increased ($P < .01$) by 35 percent (Kitade T et al 1990).

Some people cannot use phenylalanine. These include those who have a genetic deficiency called phenylketonuria (which prevents the body from metabolizing phenylalanine), people who have high blood pressure (phenylalanine can further elevate blood pressure in people who already have high blood pressure), and those who have cancer (phenylalanine can promote the division of cancer cells) (Guyton AC et al 2001; Mahan LK et al 1996).

Nutrients That Support the Joints

For joint-related pain, various supplements may help improve the integrity of joints:

- Glucosamine is particularly helpful in treating osteoarthritis because it plays a role in cartilage formation and repair (Moskowitz R et al 2004). Many clinical studies have shown that supplemental glucosamine slows or reverses degenerative joint changes, with resulting reduction in joint pain, tenderness, and swelling (Drovanti A et al 1980; Pavelka K et al 2002; Pujalte JM et al 1980; Vajjaradul Y 1981).
- Similarly, chondroitin sulfate provides building materials for cartilage damaged by osteoarthritis. It also increases blood flow to joints, allowing antioxidants and other healing substances to protect and repair body tissue (Vergés J 2004).
- Methylsulfonylmethane (MSM) is a naturally occurring organic sulfur compound found in human diets and in the diets of virtually all other vertebrates. In experiments using radioactive-labeled sulfur, MSM, after ingestion, gives up its sulfur to the essential amino acids methionine, cysteine, and other serum proteins, eventually finding its way into the collagen of skin, joints, and blood vessels. It is also incorporated into the keratin of hair and nails. Animal studies have shown that joints affected by osteoarthritis have lower sulfur content (Rizzo R et al 1995), and that arthritic mice given MSM experience less joint degeneration (Murav'ev luV et al 1991). In a double-blind trial of people who had osteoarthritis, study participants who received MSM experienced significant pain relief (Lawrence RM 1998). MSM is known to be very safe and nontoxic.

Although these supplements do not directly inhibit pain, by reinforcing damaged joints, they may help restore joint integrity.

For More Information...

Many conditions may cause chronic pain. For more information on underlying conditions associated with pain, please see the following chapters:

- Arthritis
- Carpal Tunnel Syndrome
- Fibromyalgia
- Lupus
- Migraine
- Neuropathy
- Osteoporosis
- Trauma

Melatonin

Melatonin is a hormone produced by the pineal gland. Besides inducing sleep, it has been shown to have a number of important functions (Arendt J 2005). Melatonin levels may be reduced in people who have irritable bowel syndrome, diarrhea, migraine, or ulcerative colitis (Bubenik GA 2001). The effects and mechanisms of melatonin on inflammation and immunoregulation have been studied (Bilici D et al 2002; Maestroni GJ 2001). Animal studies have shown that melatonin has significant positive effects on acute and chronic inflammation (Cuzzocrea S et al 2002). Patients who have cluster headaches found benefit in the form of fewer attacks when melatonin supplementation was used to raise subnormal melatonin levels, which is typical in people who experience cluster headaches (Peres MF et al 2001). Twenty-one patients who had fibromyalgia were given 3 milligrams (mg) of melatonin before they went to sleep at night. They reported significantly less pain on the visual analog scale. They also had lower melatonin levels than the control subjects (Citera G et al 2000).

Vitamins That Relieve Pain

Vitamin B1 (thiamin) and benfotiamine. Some animal studies have shown a decrease in pain with a combination of vitamin B1, vitamin B6, and vitamin B12 (Franca DS et al 2001; Jurna I 1998; Wang ZB et al 2005). The fat-soluble form of vitamin B1, called benfotiamine, has been used effectively to treat alcoholic and diabetic neuropathies. The most marked pain relief from benfotiamine occurred in patients with diabetic neuropathy after only a 3-week trial period (Anisimova EI et al 2001; Haupt E et al 2005; Winkler G et al 1999).

Niacin. Niacin has been shown to increase joint mobility and decrease joint pain (Jonas WB et al 1996). Fifty years ago, researchers reported that high-dose niacinamide was beneficial in the treatment of osteoarthritis and rheumatoid arthritis (Kaufman W 1955). A more recent double-blind study confirms the efficacy of niacinamide in treating osteoarthritis (Jonas WB et al 1996).

Vitamin B6 (pyridoxine). Studies show that vitamin B6 is effective in treating pain associated with headache and carpal tunnel syndrome. A study comparing amitriptyline (a tricyclic antidepressant used to treat pain) and vitamin B6 in the treatment of headache demonstrated equal effectiveness, with fewer side effects in those using vitamin B6 (Bernstein AL 1990). It is likely that vitamin B6 works to reduce pain by raising serotonin levels (Bernstein AL 1990). People who have chronic pain or headaches may have a serotonin deficiency (Bernstein AL 1990).

Vitamin B6 has a well-established record in the management of certain chronic pain syndromes. It may offer an alternative to surgery for carpal tunnel syndrome, which may be caused in part by a vitamin B6 deficiency (Aufiero E et al 2004; Ellis J et al 1981). A combination of B vitamins has also been demonstrated to allow a shorter course of treatment for people who have painful degenerative spinal diseases (Vetter G et al 1988). The painful response to thermal injury was inhibited by the combination of niacin, B6, and B12 in laboratory rats (Wang ZB et al 2005).

Many older people may be deficient in vitamin B6 either because of low intake, a higher requirement, or health problems that alter vitamin B6 levels (Mahan LK et al 1996). People who have multiple health problems have a higher risk of vitamin B6 deficiency (Mahan LK et al 1996). Up to 20 percent of women who take birth control pills have a deficiency in vitamin B6 (Mahan LK et al 1996).

Studies examining toxicity in long-term use of vitamin B6 found that adults using 100 to 150 mg daily for 5 to 10 years had minimal or no toxicity (Bernstein AL 1990).

Vitamin B12. A link between vitamin B12 levels and pain has been noted (Bernard MA et al 1998). Older individuals who have vitamin B12 deficiency experience more pain than those who have normal vitamin B12 levels (Bernard MA et al 1998).

In a study examining vitamin B12 and pain, patients with lower back pain received injections of vitamin B12 or placebo into muscle tissue. Patients treated with vitamin B12 reported a significant decrease in pain and disability, and used less acetaminophen, compared to placebo-treated patients. These findings are particularly interesting because there were no signs of nutritional deficiency (Mauro GL et al 2000). Vitamin B12 has also been used successfully to treat the pain of degenerative neuropathy (Sun Y et al 2005).

Many animal studies have demonstrated the reduced pain that occurs in response to combining vitamin B12 or B complex with conventional pharmaceuticals used to treat neuropathic or inflammatory pain (Caram-Salas NL et al 2004; Granados-Soto V et al 2004; Medina-Santillan R et al 2004; Reyes-Garcia G et al 2004; Rocha-Gonzalez HI et al 2004).

Vegetarians who completely avoid animal foods may develop vitamin B12 deficiency, which is linked to neuropathy; older people are also at risk because absorption decreases with age (Mahan LK et al 1996). Poor vitamin B12 status may cause painful neuropathy. On the other hand, in one study, a strict vegan diet rich in lactobacilli produced significant reduction in pain and other symptoms of rheumatoid arthritis, despite lower vitamin B12 levels (Nenonen MT et al 1998).

Vitamin C. Vitamin C, a versatile antioxidant, is another natural shield against pain (McAlindon TE et al 1996). One study found that pain and cartilage loss associated with knee osteoarthritis was reduced in people who had a high vitamin C intake (McAlindon TE et al 1996). Another study looking at the effects of 1000 mg daily of calcium ascorbate (a buffered vitamin C) taken for 14 days by 133 patients who had osteoarthritis found significant decrease in pain on the visual analog scale, as well as improved function of the joints compared to the placebo group (Jensen NH 2003).

Vitamin E. Vitamin E (tocopherol) blocks pain, enhances natural endorphin activity, and acts as an antioxidant (Kryzhanovskii GN et al 1988; Machtey I et al 1978). A study of women who had painful menstruation found that vitamin E reduced discomfort and increased endorphin levels (Kryzhanovskii GN et al 1988).

Vitamin E was tested for effectiveness against pain in a double-blind study involving 50 people who had primary degenerative

osteoarthritis. Participants were given either vitamin E or placebo. After 6 weeks, the vitamin E group reported less pain while moving or at rest and less pain when joints were subjected to pressure (Blankenhorn G 1986).

In another test of vitamin E against osteoarthritis, 29 patients were given vitamin E for 10 days. The same 29 patients were then given only a placebo for the next 10 days (Machtey I et al 1978). When the patients were taking vitamin E, 52 percent reported relief from pain. Only 4 percent reported pain relief while taking the placebo (Machtey I et al 1978).

Herbs That May Relieve Pain

Capsaicin. Capsaicin, a chemical found in cayenne and other peppers, is a prime ingredient of over-the-counter and prescription analgesic ointments. Capsaicin works by stimulating the release of substance P from pain-receptor cells called C fibers. Prolonged exposure to capsaicin depletes the C fibers, making them incapable of transmitting painful stimuli. Capsaicin has been shown to reduce the pain of shingles, postherpetic neuralgia, osteoarthritis, and diabetic nerve pain (Deal CL et al 1991; Pfeifer MA et al 1993; Rains C et al 1995; Tandan R et al 1992). Rubbing capsaicin on the skin produces an immediate sensation of heat and a temporarily increased sensitivity to pain (hyperalgesia) as substance P is released (Ashkenazi A et al 2004). Thirty percent of patients discontinue using capsaicin because of these unpleasant, temporary side effects (Ashkenazi A et al 2004). These adverse effects typically disappear after the first week of treatment, so it is well worth sticking with the treatment to achieve the long-term pain relief that capsaicin can provide (Rains C et al 1995).

Curcumin. Curcumin is the active ingredient in turmeric root that adds color and flavor to curry and other foods. It has anti-inflammatory properties and has been used to combat the pain and swelling of arthritis (Lodha R et al 2000). Curcumin can inhibit the release of inflammatory mediators and inhibit the COX enzyme (Huang MT et al 1991; Joe B et al 1997). It may also work as an enkephalinase inhibitor (the enzyme that degrades natural endorphins), serving to increase levels of natural endorphins by slowing their destruction (Kita A et al 1997).

Devil's claw. Several pharmacologic studies using animal models of inflammation have found that devil's claw root produces powerful anti-inflammatory and analgesic effects (Blumenthal M 2000). In one study, 122 patients who had osteoarthritis of the knee and hip were treated with either devil's claw or the drug diacerhein for 4 months (Chantre P et al 2000). Both groups experienced similar pain relief, but the group taking devil's claw experienced significantly decreased side effects, particularly less gastrointestinal distress (Chantre P et al 2000). Other studies in Germany and France have found that the herb's ability to alleviate pain and inflammation compares favorably with that of cortisone and phenylbutazone (Blumenthal M 2000; Brady LR 1981). In another study, people who had lower back pain felt significant relief after taking 2400 mg of devil's claw daily for 4 weeks (Blumenthal M 2000).

Ginger root. Ginger root has exhibited anti-inflammatory and analgesic effects and has also been used to treat headache, nausea, and vomiting. One component in ginger, called (6)-shogaol, has a capsaicin-like chemical structure and works to deplete stores of substance P (Onogi T et al 1992). Similar to NSAIDs, components in ginger can inhibit the COX enzyme, which reduces inflammation (Kiuchi F et al 1992). Clinical trials show that ginger can reduce the pain associated with arthritis (Srivastava KC et al 1992).

Proanthocyanidins. Proanthocyanidins possess extraordinary antioxidant properties that may be of value in reducing pain (Li WG et al 2001). Proanthocyanidins have shown analgesic and anti-inflammatory activity in mice (Subarnas A et al 2000). A small study found that grape seed proanthocyanidin extract reduced the frequency and intensity of abdominal pain associated with chronic pancreatitis (Banerjee B et al 2001). For chronic pain, 100 mg of proanthocyanidins can be taken twice daily for 4 to 6 months; then the dosage can be reduced by half.

Fatty Acid Nutrition and Pain

Essential fatty acids have special value in fighting pain. Gamma-linolenic acid (GLA) is an omega-6 fatty acid derived from evening primrose, borage, and black currant oils (Leventhal LJ et al 1994). Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are omega-3 fatty acids that are derived from flax and perilla and are found in fish oils (Mahan LK et al 1996). These essential fatty acids are important in manufacturing prostaglandins E1 and E3, which help to reduce inflammation and pain, while reducing proinflammatory prostaglandin E2 (Mahan LK et al 1996). In fact, infusions of prostaglandin E1 are commonly used to treat intermittent claudication, a painful, chronic, vascular condition caused by poor blood flow.

The omega-3 fatty acids have been found not only to protect against heart disease but also to reduce the inflammation and pain of rheumatoid arthritis. Studies show that patients with rheumatoid arthritis experience a decrease in joint stiffness and tenderness after 3 months of treatment with omega-3 fatty acids (Fortin PR et al 1995; Kremer JM et al 1985). Other studies have found that patients who consume fish oil were able to significantly reduce their intake of NSAIDs, compared with subjects in a control group (Lau CS et al 1993; Skoldstam L et al 1992).

Part of the effectiveness of omega-3 fatty acids may come from their ability to inhibit proinflammatory cytokines (such as TNF-alpha and IL-6) (James MJ et al 1997). For more information on reducing inflammation, see the chapter Inflammation.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

The approach to pain depends on what type of pain is present and what underlying conditions are causing the pain. Injuries, such as trauma or burns, may require immediate prescription analgesic therapy. Chronic pain, however, is a different story and may be more effectively treated with natural approaches that do not cause dangerous side effects.

People who have chronic pain may consider the following nutrients, which may reduce the need for stronger prescription painkillers. Nutrients that have been shown to reduce general pain and inflammation include:

- **DL-phenylalanine**—Take 500 to 1000 milligrams (mg) in the morning or afternoon.
- **Fish oil**—Use a highly concentrated fish oil supplement that provides at least 1400 mg of EPA and 1000 mg of DHA in four capsules. Distributing the fish oil over four capsules helps prevent gastrointestinal upset. In addition, take 285 to 570 mg of GLA daily.
- **Vitamin C**—1000 to 3000 mg daily
- **Vitamin E**—400 international units (IU) daily
- **Melatonin**—3 to 10 mg, 15 to 30 minutes before bedtime
- **Vitamin B1**—500 mg daily
- **Curcumin**—900 to 1800 mg daily
- **Grape seed extract**—one to two capsules daily (contains proanthocyanidin)
- **Ginger**—60 mg

For neuropathic pain:

- **Fat-soluble vitamin B1 (benfotiamine)**—150 mg one to three times daily
- **Niacin**—500 mg daily (for arthritis take 500 mg three to six times daily)
- **Vitamin B6**—250 mg daily
- **Vitamin B12**—500 micrograms (mcg) one to four times daily (up to 40 mg daily in the form of methylcobalamin)

For healthy joint function:

- **Ginger**—60 mg
- **Glucosamine/chondroitin sulfate**—one capsule up to eight times daily (each capsule contains 400 mg of glucosamine and from 400 to 450 mg of chondroitin sulfate)
- **MSM**—1000 to 3000 mg daily

CHRONIC PAIN SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Chondroitin Sulfate

- Consult your doctor before taking chondroitin if you are taking warfarin sodium or if you have hemophilia. Chondroitin can have antithrombotic activity.
- Use a salt-free chondroitin preparation if you need to restrict your salt intake.
- Chondroitin can cause gastrointestinal symptoms such as epigastric distress, nausea, and diarrhea.

Curcumin

- Do not take curcumin if you have a bile duct obstruction or a history of gallstones. Taking curcumin can stimulate bile production.
- Consult your doctor before taking curcumin if you have gastroesophageal reflux disease (GERD) or a history of peptic ulcer disease.
- Consult your doctor before taking curcumin if you take warfarin or antiplatelet drugs. Curcumin can have antithrombotic activity.
- Always take curcumin with food. Curcumin may cause gastric irritation, ulceration, gastritis, and peptic ulcer disease if taken

on an empty stomach.

- Curcumin can cause gastrointestinal symptoms such as nausea and diarrhea.

D,L-Phenylalanine

- Do not take D,L-phenylalanine if you have phenylketonuria.
- Do not take D,L-phenylalanine if you are taking nonselective monoamine oxidase inhibitors (MAOIs).
- Do not take D,L-phenylalanine if you have schizophrenia. D,L-phenylalanine can exacerbate tardive dyskinesia (involuntary facial movements) in people who have schizophrenia.
- Consult your doctor before taking D,L-phenylalanine if you have high blood pressure. D,L-phenylalanine can exacerbate high blood pressure. D,L-phenylalanine can also cause high blood pressure.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Ginger

- Do not take ginger if you have a bile duct obstruction or gallstones. Ginger may stimulate bile production.
- High doses of ginger (6 grams or more) can cause damage to the stomach lining and ulcers.
- Ginger can cause allergic skin reactions.
- Consult your doctor before taking ginger if you take blood thinners such as warfarin (Coumadin). Ginger can increase the risk of bleeding.

Glucosamine

- Consult your doctor before taking glucosamine if you have diabetes. It is unknown if glucosamine will increase insulin resistance in humans but glucosamine has been shown to increase insulin resistance in healthy animals and in animals with diabetes. Animals given intravenous glucosamine were found to have a significantly decreased rate of glucose uptake in their skeletal muscle (this effect was not observed, however, in animals given oral glucosamine).
- If you have diabetes, are overweight, or have difficulty with glucose tolerance and take glucosamine under medical advisement, monitor your blood glucose level frequently. Your doctor will need to adjust your medication levels accordingly.
- Glucosamine can cause gastrointestinal symptoms such as nausea and diarrhea.

Melatonin

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a "heavy head," or gastrointestinal symptoms such as nausea and diarrhea.

MSM

- MSM can cause headache or gastrointestinal symptoms such as nausea and diarrhea.

Niacin (nicotinic acid)

- Do not take high doses of nicotinic acid (1.5 to 5 grams daily or more) if you have liver dysfunction, an unexplained elevation in your serum aminotransferase (transaminase) level, active peptic ulcer disease, arterial bleeding, or if you consume large amounts of alcohol.
- Consult your doctor before taking high doses of nicotinic acid if you have a history of jaundice, peptic ulcer disease, gastritis, disease of the liver or bile ducts, gout, kidney dysfunction, or cardiovascular disease (especially acute myocardial infarction or unstable angina).
- Consult your doctor before taking high doses of nicotinic acid if you have diabetes. High doses of nicotinic acid can negatively affect glucose tolerance. Monitor your serum glucose level frequently if you take nicotinic acid and have diabetes.
- Have your doctor monitor your serum aminotransferase level if you take high-doses of nicotinic acid.

- Nicotinic acid may cause flushing, principally of the face, neck, and chest. This flushing is thought to be prostaglandin-prostacyclin mediated. Histamine may also play a role in the flushing.
- Nicotinic acid can cause dizziness, palpitations, rapid heartbeat, shortness of breath, sweating, chills, insomnia, nausea, vomiting, abdominal pain, and muscle pain.
- High doses of nicotinic acid can cause blurred vision, macular edema, toxic amblyopia, and cystic maculopathy.

Vitamin B1 (Thiamin)

- Consult your doctor before taking vitamin B1 for a thiamin deficiency, lactic acidosis secondary to thiamin deficiency, Wernicke-Korsakoff syndrome, Wernicke's encephalopathy, or Korsakoff's psychosis.

Vitamin B6

- Individuals who are being treated with levodopa without taking carbidopa at the same time should avoid doses of 5 milligrams or greater daily of vitamin B6.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

For more information see the Safety Appendix

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