

ACPA Resource Guide To Pain Medication and Treatments



American Chronic Pain Association

ACPA Resource Guide

To

Chronic Pain Management

An Integrated Guide to
Medical, Interventional, Behavioral,
Pharmacologic and Rehabilitation Therapies

2019 Edition

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Special thanks to Yvonne Selden for her editing assistance.



A STATEMENT FROM THE ACPA BOARD OF DIRECTORS

Since 1980, the American Chronic Pain Association (ACPA), a non-profit, tax exempt organization, has offered a support system for people with chronic pain through education in pain management skills and self-help group activities. To learn more about the ACPA and how to become a member, please visit our web site at <https://www.theacpa.org> or call the National Office at 800-533-3231.

The American Chronic Pain Association (ACPA) advocates a multi-modal strategy for addressing chronic pain. The ACPA focuses on pain management skills and self-help strategies that individuals can use in conjunction with modalities discussed with and approved by their health care professionals.

The ACPA considers the use of medication and other treatments to be a matter for individuals to determine in conjunction with their health care professionals. The ACPA takes no position on medical treatment choices. Thus, information the ACPA provides in this resource guide about medical care is educational and informative only.

The ACPA Resource Guide to Chronic Pain Management combines practical clinical experience and the most recent scientific information presented in an easy to read format for consumers and professionals. Input comes from many sources, including from individuals, from industry sources, some of which support the ACPA with grants. Dr. Feinberg, Senior Author and Editor, receives no funds from industry. As lead author, Dr. Feinberg receives input from many sources but takes full responsibility for the content of this Guide. Dr. Feinberg and the ACPA welcome input regarding any recommended changes, additions or deletions.



INTRODUCTION

The ACPA believes that people with chronic pain benefit from being well informed about their treatments. This knowledge may relieve the fears that can interfere with receiving maximum benefits from carefully and appropriately selected treatments. Education can also prevent unrealistic expectations that lead to disappointment with no benefit or even a bad outcome from treatment.

This Guide is not meant to serve as medical advice for medical conditions or guidance regarding treatment needs. Remember that the best source of information about one's health and treatment needs is through open dialogue with a qualified health care professional.

With the emerging and ever-increasing growth of the Internet, information is now available on almost every topic. Finding information is easy, but finding reliable, understandable and factual information that answers your questions is NOT so easy.

The information in this ACPA Resource Guide to Chronic Pain Management covers general information compiled from multiple sources. It is updated yearly and includes web links for certain medications and treatments and relevant Internet sites of interest. For medications, generic names are primarily listed with brand names in parentheses.

Unfortunately, there are risks (some serious) associated with certain treatments for chronic pain; especially invasive interventions as well as medications. There is also the potential of missing benefit from avoiding some chronic pain treatments. The best approach is for people with pain to ask questions about the benefits and risks or side effects when they are about to embark on any treatment approach or new medication. How often is this treatment effective -- compared to other options? Does the risk justify the possible benefit? How do the risks and benefits compare with those of other treatment options?

Although this ACPA Resource Guide covers many medications and treatments, the topics covered are not exhaustive. This Guide is primarily written for an audience of adults. See the section on Special Populations for basic advice for pregnant women, children, and older persons. If something is not mentioned in this Guide, that does not imply that it is not useful. Contact the ACPA with comments, corrections, or recommendations for topics to be covered in future updates and editions at <https://theacpa.org/Contact/>.

The best advice the ACPA can offer is to discuss all treatment and medication questions with a health care professional! In this Guide, this term includes physicians, prescribing advanced practice nurses, nurse practitioners, physician assistants, and others who do not prescribe medications but provide other health care services including psychologists, pharmacists, physical and occupational therapists and others. Practitioners of complementary and integrative health approaches may also be helpful in their areas of specialty.



The ACPA considers the use of medication and other treatments to be a matter for individuals to determine in conjunction with their health care professionals. The ACPA takes no position on medical treatment choices. Thus, information the ACPA provides in this Resource Guide about medical care is educational and informative only.



OVERVIEW OF CHRONIC PAIN TREATMENT

It's hard to know how to move forward once chronic pain has changed your life. It often seems like all you need is the right medication or treatment to take away the pain to increase your function. But sometimes that is not enough – especially in the case of chronic pain. Realistically, some treatments will provide substantial pain relief, while some will provide no benefit, and unfortunately, some can worsen your condition and pain. Perhaps the best to expect is that medication, injections or surgery will hopefully provide partial benefit, perhaps 25 or 30 percent pain relief.

WHAT DOES SUCCESSFUL PAIN TREATMENT LOOK LIKE?

Imagine a car with four totally flat tires, going nowhere. That's what life can look like for someone whose life has been totally changed by chronic pain. Medical treatment only puts air in one of our tires. We still have three flat tires and can't move forward. The ACPA's definition of "successful" treatment of a person with chronic pain is that the person has learned how to independently self-manage his/her condition in a way that allows life to continue, maximizing participation in everyday life activities, minimizing discomfort and side effects, and avoiding other bad consequences of treatment. Note: This does not mean that the person will be pain free but rather will be able to manage pain, get back on track, and lead a productive, satisfying, and happy life.

So, it is important to ask what else we need to fill our other three tires so that we can resume our life's journey. Unlike traditional medicine where the "patient" is a passive participant, living a full life with pain requires that the person take an active role in the recovery process. The individual needs to work with his or her health care providers to get what is needed to fill up the other three tires. Biofeedback, physical therapy, counseling, pacing of daily activities, nutritional counseling, a support group, life coaching, mindfulness practices, and a host of medical modalities are a few examples of the ways we can fill those other tires.

For each person, the combination of therapies and interventions needed may differ, based on individual need. It is the responsibility of the person in pain to decide whether any particular health care professional has actually helped them get their "car of life" moving forward again -- and if not, to make a change.

Once we have all four tires filled, it is our responsibility to maintain our car. We would not take our car back to the dealer and ask them to fill it up with gas or wash our windshield. That is our responsibility---to take good care of our car. We take it in for inspections and if something goes wrong, we go to a professional. It's the same with our wellness. You see, pain management is much more than one simple modality. It takes a team effort, with the person with pain taking an active role, to live a full life in spite of chronic pain. Go to *A Car With Four Flat Tires* at the ACPA web site at <http://www.theacpa.org/pain-management-tools/videos/support/> to watch a short educational video narrated by ACPA Founder and CEO, Ms. Penney Cowan.



PAIN TYPES, SOURCES & CLASSIFICATION

Many pain specialists recommend that the term “chronic pain” should be referred to as “persistent pain” – which can be continuous or recurrent and of sufficient duration and intensity to adversely affect a person’s well-being, level of function, and quality of life. This document continues to use the term “chronic pain” given its universal acceptance.

Acute pain is characterized as being of recent onset, transient, and usually from an identifiable cause.

Chronic (or persistent) pain can be described as ongoing or recurrent pain, lasting beyond the usual course of acute illness or injury healing, more than 3 to 6 months, and which adversely affects the individual’s well-being. Another definition for chronic or persistent pain is **pain that continues when it should not**. The International Association for the Study of Pain defines pain as a negative sensory and emotional experience. As such, the definition recognizes the important role of processes in the nervous system and brain (both neurological and psychological) in the experience of pain. Therefore, the nervous system and brain are very important therapeutic targets.

Chronic pain is classified by pathophysiology (the functional changes associated with, or resulting from disease or injury) as nociceptive (due to ongoing tissue injury) or neuropathic (resulting from damage to the nervous system – the brain, spinal cord, or peripheral nerves). The experience of pain can be due to either nociceptive and neuropathic changes or both -- but it is *always combined with the brain’s reaction* to incoming information, including the brain’s interpretation of what that incoming information means, what the brain learns as a result, and the responses it generates.

Central pain syndrome is a neurological condition caused by a process that specifically affects the central nervous system (CNS), which includes the brain, brainstem, and spinal cord. The disorder occurs in people who have or who have experienced strokes, multiple sclerosis, Parkinson's disease, brain tumors, limb amputations, brain injuries, or spinal cord injuries. It may develop months or years after injury or damage to the CNS. This also includes conditions such as chronic headaches, fibromyalgia, and Complex Regional Pain Syndrome (CRPS). In central pain syndromes, pain feels as though it is emanating from a specific place in the body, but the sensation is actually being generated by the nervous system and brain.

Continuous pain is pain that is typically present for approximately half the day or more.

Flare-up pain (the term break-through pain was coined to refer to cancer-related flare-ups) can be described as a transitory increase in pain in someone who has relatively stable and an adequately controlled level of baseline pain. It may be caused by changes in an underlying disease including treatment, or involuntary or voluntary physical actions such as coughing or getting up from a chair or other changes in activity level. It can also be caused by stress and emotions such as anxiety, anger, fear, or worry. Activity imbalance—doing too much or too little—can also flare pain.



PAIN IN SPECIAL POPULATIONS

Pain in Pregnancy

In January 2015, the U.S. Food and Drug Administration provided an FDA Drug Safety Communication: FDA has reviewed possible risks of pain medicine use during pregnancy – see <http://www.fda.gov/Drugs/DrugSafety/ucm429117.htm>.

The following is an abstracted summary:

The U.S. Food and Drug Administration (FDA) is aware of and understands the concerns arising from recent reports questioning the safety of prescription and over-the-counter (OTC) pain medicines when used during pregnancy. As a result, we evaluated research studies published in the medical literature and determined they are too limited to make any recommendations based on these studies at this time. Because of this uncertainty, the use of pain medicines during pregnancy should be carefully considered. We urge pregnant women to always discuss all medicines with their health care professionals before using them.

Severe and persistent pain that is not effectively treated during pregnancy can result in depression, anxiety, and high blood pressure in the mother. Medicines including nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and acetaminophen can help treat severe and persistent pain. However, it is important to carefully weigh the benefits and risks of using prescription and OTC pain medicines during pregnancy.

Pregnant women should always consult with their health care professional before taking any prescription or OTC medicine. Women taking pain medicines who are considering becoming pregnant should also consult with their health care professionals to discuss the risks and benefits of pain medicine use.

Pain in Children

Chronic pain is a significant problem in the pediatric population, conservatively estimated to affect 20 to 40 percent of children and adolescents around the world. The most common chronic pain conditions in children and adolescence are musculoskeletal pain, headaches, and abdominal pain. They may experience physical and psychological pain and their families may experience significant emotional distress and social consequences as a result of pain and associated disability. Research suggests that the family dynamic and how parents respond to their child's pain can have a significant impact on the course of the child's pain and on their function. One of many resources is the book "Conquering Your Child's Chronic Pain: A Pediatrician's Guide for Reclaiming a Normal Childhood" by Lonnie K. Zeltzer, MD, and Christina Blackett Schlank.



Childhood pain brings significant direct and indirect costs from health care utilization and lost wages due to parents taking time off work to care for the child. In addition, longitudinal studies provide convincing evidence to suggest that childhood chronic pain predisposes the continuation of pain later in life and the development of new forms of chronic pain in adulthood (from Assessment and Management of Children with Chronic Pain, A Position Statement from the American Pain Society (January 4, 2012) http://americanpainsociety.org/uploads/about/position-statements/Pediatric_Pain_Policy.pdf). In addition, resources to help adolescents with pain was created by the ACPA and is accessible via dedicated website: www.growingpains.org.

Pain in Older Persons

The likelihood of experiencing chronic pain increases with age. An estimated 65% of US adults over the age of 65 report suffering from pain and up to 30% of older adults report suffering from chronic pain. The US Centers for Disease Control and Prevention estimates 15% of Americans over the age of 65 use a prescription pain relief drug. Older adults are more likely to have additional health problems that can cause or complicate chronic pain. Mobility and balance issues, common in older adults, both may impact their ability to engage in daily therapeutic exercise. While medications are certainly an important part of treating chronic pain, use in older persons is fraught with potential problems. Physical rehabilitation and other interventional therapies, which may include targeted injections and acupuncture, can be helpful to reduce pain, increase strength and physical function, and decrease the need for medications. In fact, the medical literature is full of studies showing the advantage of regular physical exercise in older adults. Additionally, psychological supports including relaxation techniques, mindfulness practices, and positive self-talk should always be considered for managing pain in elderly people. Finding a support group for people with chronic pain is also most beneficial.

In addition to chronic pain, older adults are more likely to have multiple medical conditions and to be taking multiple medications. Medication risks are greater for an individual when multiple medications are taken, and it is important to discuss all medications (including over-the-counter or herbal/homeopathic medications with your health care provider). Certain medications carry greater risks than others, especially when used in combination. Some older individuals may be more sensitive to medications, more likely to experience side effects, and more likely to be using multiple drugs with the associated risk of interactions between the drugs.

In general, 30 percent of hospital admissions among the elderly may be linked to an adverse drug-related event or toxic effect from opioids and sedatives (i.e., a tranquilizer). Nearly one-third of all prescribed medications are for persons over the age of 65 years. Unfortunately, many adverse drug effects in older adults are overlooked as age-related changes (general weakness, dizziness, and upset stomach) when in fact the person is experiencing a medication-related problem.

When using medications, they should be initiated at a low dose and adjusted slowly to optimize pain relief while monitoring and managing side effects. Multi-modal analgesia, which is the careful use of multiple pain-relieving drugs together, can be seen as potentially advantageous. Combining smaller doses of more than one medication may minimize the dose-limiting adverse effects of using a particular single drug. This statement is not meant to endorse certain drug combinations such as opioids with benzodiazepines which we know are hazardous.



The American Geriatrics Society (<http://www.americangeriatrics.org>) provides guidance on the topic of *Pharmacological Management of Persistent Pain in Older Persons* at the following website:

<https://www.nhqualitycampaign.org/files/AmericanGeriatricSociety-PainGuidelines2009.pdf>

This organization also offers patient-level information on medications for pain, and identifies medications with risks that may be greater than their benefits for people age 65 and older (also known as the *Beers Criteria for Potentially Inappropriate Medication Use in Older Adults*) at the following website: <http://www.healthinaging.org/medications-older-adults/>

The National Library of Medicine also offers information on a wide range of topics about chronic pain, including non-pharmacologic treatment alternatives, at the following website: <https://medlineplus.gov/chronicpain.html>

The Gerontological Society of America has a publication, *Addressing the Societal Burden of Opioid Misuse: Focus on a Balanced Approach to Older Adults with Chronic Pain*, which could be obtained by adding it to your cart for free at:

<https://www.geron.org/online-store/gsa-products/product/10-from-publication-to-practice-addressing-the-societal-burden-of-opioid-misuse-focus-on-a-balanced-approach-to-older-adults-with-chronic-pain>

The following infographic is from the NIH Pain Consortium:

https://painconsortium.nih.gov/sites/default/files/aging_and_chronic_pain_infographic_508.pdf



MAJOR TYPES OF INTERVENTIONS FOR PAIN

Passive interventions are treatments that can be received without any active participation by the person with pain. The physician or therapist delivers the treatment and the person with pain simply needs to be present. Massage, acupuncture, medications, injections and surgery are examples of passive interventions.

Active interventions require the person with pain to exert energy – to use their mind and/or body as part of the treatment. Active treatment requires the person with pain to be engaged, to participate and do things, to interact with the therapist or instructor -- or even to carry out the intervention or treatment independently (at home or outdoors by themselves). Yoga is an example of an active intervention. As a general rule, studies have shown active treatments to be more effective than passive ones over the long run.

Self-directed interventions can be carried out independently by the person with pain. By definition, self-care and self-management techniques are active interventions. Self-directed interventions do not require supervision by a health care professional beyond initial instruction. Self-directed activities may occur solo or in a class environment. Examples of self-care techniques for reducing pain include progressive relaxation exercises, mindfulness meditation and distracting oneself with pleasurable activities. Examples of self-management of chronic conditions include yoga, physical reconditioning, and competently managing complex medication regimens on a daily basis.

Functional restoration is a whole person approach to relieving pain and distress with the goal of restoring the person with pain's ability to engage in life in meaningful ways. Functional restoration refers to a unique philosophy and approach to medical care that focuses not just on the biology (injury/illness and associated pathology) but also on the individual as a whole person in the context of their life -- including its psychological and social aspects.

- **Interdisciplinary care or programs** means the involvement of several health care professionals (physician, pharmacist, psychologist, physical therapist, occupational therapist) providing coordinated services and communication at the same facility.
- **Multidisciplinary care or programs** involves the same kinds of practitioners providing services and communication as interdisciplinary care -- but the practitioners are in different locations. Coordination among practitioners is often challenging in multi-disciplinary programs.

FUNCTIONAL RESTORATION APPROACHES & PROGRAMS

The process of functional restoration enables an individual to acquire the skills, knowledge, and behavioral changes necessary to assume or re-assume primary responsibility for his/her physical as well as emotional well-being. Functional restoration thereby empowers the individual to achieve



maximum functional independence, to have the capacity to regain or maximize activities of daily living, and to return to vocational and avocational activities.

Fundamental elements of a functional restoration approach include assessment of the person's dynamic physical, functional, and psychosocial status. This is followed by a treatment plan that includes directed conditioning and exercise, physical and occupational therapy, cognitive behavioral therapy, patient/family education, and counseling, functional goal setting, ongoing assessment of participation, compliance, and complicating problems, and progress toward achievement of goals. Put all together, this is called a biopsychosocial approach.

Functional restoration treatment team members act as educators, de-emphasizing passive and/or palliative therapies, while emphasizing independent self-management. There should be a shift of health and well-being responsibility from the health care professionals and therapists to the person.

A functional restoration approach can include a more comprehensive adjustment of medications focusing on decreasing and/or eliminating unnecessary analgesic use, integrating adjunctive medications, focusing on improving mood, and sleep quality. The overlying goal is to coordinate appropriate interventions for the specific purpose of supporting the individual's effort to reach and maintain maximum functional improvement; institution of preventive measures, expectation management, education for relapse prevention, proper activity and work pacing, ergonomic accommodation; and when appropriate, transitional return to gainful employment with as little disruption to the work site and coworkers as possible.

Functional restoration involves objective measures of physical performance that guide treatment progression. At the same time, physical and occupational therapists, psychologists, nurses, and case managers provide education on pain management, coping skills, return to work issues, and fear-avoidance beliefs ("it hurts when I move, so I better not move"). They often use a cognitive behavioral therapy (CBT) approach consistent with the biopsychosocial view of chronic pain/disability. Additional psychological interventions may include acceptance and mindfulness interventions.

Ultimately, successful individuals with chronic pain take control of and re-engage in life activities and have achieved mastery over when and how to access the medical community in a way that is most beneficial for them. The goal is a mitigation of suffering and return to a productive life despite having a chronic/persistent pain problem.

While the functional restoration approach is a philosophy, there are coordinated functional restoration programs which involve an integrated team of professionals providing intensive, coordinated care, which may include pain specialist physicians/health care professionals, physical therapists, occupational therapists, psychologists, vocational counselors, nurses, and case managers providing individualized treatment in a structured setting.

These programs can be part-time or full-time but involve the individual with a chronic pain problem treated at a center where the physician, psychologist and physical therapist are based at that location. Services are coordinated 4-6 hours a day, 3-5 days a week for 4-6 weeks. These



programs focus on medication optimization, education, emotional stability and physical reactivation with a goal of better pain management and return to functional and life activities including work.

SELF-DIRECTED INTERVENTIONS

Self-Care, Self-Management, Self-Development

Information is power. Several effective self-care techniques to manage pain symptoms and reduce distress exist. So do techniques for self-management of chronic medical conditions, and techniques for self-management of nutrition, sleep, and general wellness. Most physicians and other healthcare professionals do not have the time to teach these self-directed treatments (or are unaware of them), but self-directed interventions are a very good way to regain a sense of independence and maximize over-all well-being and quality of life.

In addition, living with chronic pain sometimes creates challenges and life predicaments that are bigger than a person is accustomed to dealing with -- which makes pain and distress even harder to bear. It is important to recognize when this type of problem is due to lack of the knowledge or skills required to cope effectively with a particularly trying situation. In these situations, self-development is the ideal solution. Gaining knowledge and techniques for coping will strengthen skills and build the confidence needed to deal with the situation more effectively. Many psychologists and other mental health providers are trained to teach these self-development methods.

Self-management includes the systematic application of education and supportive interventions often suggested by health care professionals to increase patients' skills and patients' confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support. It is clear that patients who develop these skills and who have confidence to deal effectively with chronic pain, experience pain differently. Becoming more active and independent results in better outcomes in chronic pain treatment.

Resources to support self-care and self-management run the gamut from simple online tools, websites, print materials, and videos to local and virtual support groups. The ACPA provides information for many of these resources at <https://theacpa.org/>.

ACPA Groups

A significant part of being involved in your recovery is being involved with your peers. ACPA groups welcome anyone who is living with an ongoing pain problem. The goal of an ACPA group is to provide support, validation, and education in basic pain management and life skills. Groups are facilitated by group members themselves and the success of the group is a shared responsibility. ACPA groups do not focus on symptoms or provide treatment of any kind. Rather, they are a means for people to share what they have learned and to encourage others to create more satisfying lives. Hear members' thoughts about the value of the kind of peer support offered by ACPA groups at <https://theacpa.org/about-us/support-groups/>.



Classes in Chronic Pain & Chronic Disease Self-Management

Another self-management treatment pathway involves structured educational self-management programs. Two widely acclaimed self-management programs include the Chronic Pain Self-Management Program and the Chronic Disease Self-Management Program. Both group educational programs consist of 6 classes (meeting once weekly) with each class lasting 2.5 hours. Research has shown these programs improve outcomes for participants. The class leaders in these structured programs all use the same manual, so participants receive the same information in every city and state where the program is being delivered. The programs are peer-led by persons with lived experience who have received their trainer certification. The programs are designed to help people living with chronic pain and medical conditions live better lives by learning how to self-manage symptoms and various life factors. The Chronic Pain Self-Management Program was initiated in 2015 and is currently available in nine states in the U.S. and in Canada and availability is rapidly expanding.

In some areas, the courses are delivered for a fee, but many closed payer systems, state and municipal public services, and health care centers offer one, or both, of these self-management programs to their members **free of charge**. Check with your health care organization, or you may search online to learn about local chronic pain self-management programs. If you wish to conduct an online search, include “Chronic Pain Self-Management Program” plus your city (or nearby cities) or healthcare organization. You can do the same search for the Chronic Disease Self-Management Program.



ACTIVE INTERVENTIONS – DELIVERED BY PROFESSIONALS

Active interventions delivered in concert with a professional get the individual with pain involved in learning and making positive changes that allow them to increase function and reduce pain. Active interventions help people change their lives in ways that create lasting benefits with the lowest risks.

Active interventions can be divided into two main groups: those that educate and retrain the body and those that educate and retrain the brain and mind. However, since pain is always the result of interactions and communications between body, brain, and mind, and they cannot actually be entirely separated, most of the active interventions below address both to some degree.

Following is a list of treatment options that fit within the concept of active interventions delivered in concert with a professional. Some require a clinician's involvement and others only an experienced practitioner. The list is not mutually exclusive so utilizing more than one, in combination or in sequence, might prove beneficial. Trial and error might be required to select the most appropriate treatment(s) that reduce risk but improve the level of activity and function. The primary goal is to find what works for the individual.

Information Therapy: Reconditioning the Brain

Number one should be education of the patient and the family -- as soon as the pain has been identified as chronic. However, today many persons with chronic pain and their practitioners often think of education last, after medications, passive therapy, other invasive interventions, and surgery. Without careful and thorough education about their situation, many patients have ended up with incorrect ideas or false beliefs that get in the way of their rehabilitation and actually increase their pain and disability.

Patients need and deserve information in easy-to-understand terms about the nature of chronic pain, how it gets started and perpetuated, and the best and most effective ways to treat it. Information is power. New facts often change the way both patient and family see the problem and their situation and open up opportunities for action.

No treatment plan is complete without addressing issues of individual and/or group education as a means of facilitating self-management of symptoms and prevention. It is critically important for persons with chronic pain to actually become well-informed about it.

Early topics should include helping a person understand that they may not end up “fixed” but rather, that they will discover they can manage their pain, which will reduce the suffering and distress that go along with it.

It can be helpful to think of chronic pain similar to other chronic diseases such as diabetes. A person needs to manage his or her diabetes and prevent it from getting worse and causing other



problems. Diabetes is not quickly cured or fixed. The same is true for chronic pain. Further education on chronic pain should also include understanding that pain is not “all in your head” (but it surely affects your brain) and that an active approach that focuses on the whole person is the most effective way to treat chronic pain.

Once pain becomes chronic, a safe level of activity should be defined as clearly as possible. Many times, the only guidelines a person may hear are restrictions given right after the injury or surgery. For example, rest immediately after surgery may be beneficial. In the case of chronic pain, however, prolonged rest can contribute to additional problems, such as deconditioning, increased stress, and additional pain problems. As the tissues heal after an injury, many restrictions can be lifted, and a person can safely return to higher levels of activity. Unfortunately, it is also common that patients have either been told incorrect information or have misinterpreted education from a past health care provider. Many health care providers lack experience in assessing or treating chronic pain. Inconsistent information can be confusing. Phrases like, “the back of an 80-year-old man” or “you will end up in a wheelchair if you sneeze,” can keep a person fearful and disabled.

Reconditioning the Body: Exercise and Body Awareness

For most people with chronic pain, the main thrust of an effective pain treatment program is to keep them as physically active as possible. The human body is designed to be used. Inactivity can actually make pain worse over time, despite the temporary relief that often accompanies it. Gradual but continual advancement of activity levels is recommended.

There is strong evidence that regular physical activity and therapeutic exercise programs are beneficial for persons with chronic pain. They restore flexibility, strength, endurance, function, and range of motion, and can decrease discomfort. In addition, active exercise, particularly walking, has positive effects on brain chemicals. It usually improves mood and has been recognized as one of the most effective treatments for depression. Also, research has shown that walking and other appropriate exercises are usually the best treatments for chronic low back pain.

The American College of Sports Medicine has started a global health initiative called Exercise is Medicine. Their focus is to encourage health care providers to include physical activity when designing any treatment plan.

After consultation with a health care professional and/or physical therapist, a therapeutic exercise program should be initiated at the start of any chronic pain treatment program. Therapeutic exercise can be classified to include 1) range-of-motion exercises; 2) stretching; 3) strength training; and 4) cardiovascular conditioning. Such programs should emphasize education, independence, and the importance of an on-going self-directed exercise regimen.

Aquatic therapy or exercise may be beneficial for individuals who have other medical problems or conditions that make weight-bearing exercise inadvisable, or for those whose pain or weakness limits them from participating in even a low-level land program. The buoyancy of water can provide decreased stress on weight-bearing joints. After gaining strength and flexibility in the water, the person should transition, at least in part, to a land-based exercise program. Many times,



an individual's aquatic program can serve as an ongoing part of their long-term maintenance exercise program.

Persons with chronic pain can become discouraged when their pain temporarily increases due to therapeutic exercise, and they will sometimes terminate treatment too early before achieving maximal benefit. A flare-up of pain with exercise should be expected even with safe exercise, but can also be due to poor body mechanics, guarded or stiff movement, high levels of demand on an injured site, or compensatory movements. It is important to have a health care professional who is knowledgeable about treating chronic pain assist not only with setting up a graded and careful exercise program, but also with distinguishing new symptoms that may signify problems from the "good" discomfort that normally goes along with an increasing exercise program.

Pilates

Pilates is a method of exercise performed on a mat or using special apparatus that consists of low-impact and endurance movements. Pilates is named for its creator, Joseph Pilates, who developed the exercises in the early 1900s. The Pilates method emphasizes the breath, core strength and stabilization, flexibility and posture. Improving these areas can be beneficial when learning to manage chronic pain. Mat work may be too challenging as a starting point for people with chronic pain. Because it lacks the support associated with the Reformer and the Trapeze table (exercise machines used in Pilates), mat work can result in excessive strain to the body resulting in a poor movement. Appropriate modifications and simplifications to mat exercises do exist, which can be incorporated into a home program.

Yoga

Yoga creates a greater sense of health and well-being by emphasizing mindful practice, breath awareness, and proper body alignment. Yoga helps to manage chronic pain through movements that increase flexibility, strength, and relaxation. People with chronic pain should begin with a gentle, slow-paced class where props are available for support. Benefits of a regular yoga practice include improved sleep and reduced stress and anxiety. Studies have shown that yoga is beneficial for fibromyalgia, among other pain conditions.

Working with a Yoga Therapist on a one-to-one basis is an excellent way to experience the benefits of yoga in a safe environment and with a professional who is trained to modify different poses for specific conditions.

These styles of yoga are good for beginning students:

- Viniyoga refers to a therapeutic style of yoga that adapts the practice to the unique conditions and needs of each individual. It emphasizes repetitive movement combined with breath work. Although all yoga is therapeutic, Viniyoga's emphasis on the individual's physical needs makes it especially so.



- Iyengar Yoga utilizes straps, blocks, and chairs as props to assist participants in the precise alignment of their poses. Because of this assistance, Iyengar is an ideal style of yoga for beginners or those suffering from chronic pain. Unlike ‘flow yoga,’ Iyengar poses are held in order to focus on safe alignment and to build endurance.
- Yin Yoga focuses on the body's connective tissue, ligaments, and joints as opposed to the muscles. Yin Yoga is practiced on the floor, and most poses are either sitting or reclining. To affect change in the connective tissue, poses are held for time – sometimes up to 10 minutes. Although challenging, Yin Yoga has a deeply soothing effect on the nervous system and for that reason is more relaxing than Iyengar Yoga.
- In Restorative Yoga, the body is supported in the poses by a variety of props. This encourages passive stretching and deeper awareness of the breath. Because of their passive nature, restorative poses are often held for up to 20 minutes.
- Hatha Yoga has come to represent a gentle, basic yoga classes with no flow between poses. However, Hatha actually describes any kind of yoga in which poses are done. Therefore, before participating in a Hatha Yoga class, it is important to clarify what type of Yoga will be taught.
- Therapeutic Yoga combines restorative yoga, breath work, and meditation techniques to bring the body into a greater sense of balance and reducing stress. What makes this type of Yoga Therapy unique is that the instructor has the skills to prescribe specific poses or breathing techniques for specific conditions. The instructor may build a program ranging from gentle to a more vigorous program depending on the individual's needs. Group classes can be designed for those with particular therapeutic needs.

These styles of yoga require strength and endurance:

- Ashtanga Yoga is characterized by constant movement, or flow, from one posture to another. It is vigorous and fast-paced, earning it the nickname of “Power Yoga.” The focus is on deep breathing during each pose.
- Vinyasa is similar to Ashtanga Yoga in its emphasis on flowing through postures, particularly Surya Namaskar (Sun Salutation). The goal of Vinyasa is to improve coordination, strength, and balance by following the sequence of active poses.
- Bikram or "hot" Yoga literally refers to the fact that the practice studio is heated to 104 degrees Fahrenheit. The practice consists of 26 poses that are repeated twice. The intense sweat produced is thought to purify the body. This type of yoga should not be attempted without permission of your physician.
- Kundalini Yoga focuses on purifying the emotions, the mind, and the body while placing emphasis on the effects of breathing in each pose. Chanting mantras and meditation are



common practices of Kundalini. The word Kundalini refers to an energy, which is said to reside at the base of the spine. The intention of Kundalini practice is to release this energy.

Feldenkrais

The Feldenkrais Method® uses gentle movement and directed attention to improve ease and efficiency of movement, increase range of motion, and improve flexibility and coordination. This method is based on the principle of becoming aware of one's habitual movement patterns through movement sequences. The Feldenkrais Method is taught through Functional Integration® and Awareness Through Movement®. Functional Integration is a hands-on approach in which the practitioner subtly positions the client through gentle touching and cueing to allow improved positioning and movement. Awareness Through Movement classes use verbal instruction to guide the participant through movement sequences. Chronic pain can lead to guarded and stiff movement and Feldenkrais can be used to allow improved ease of movement and body awareness.

Postural Re-Training

There is considerable debate regarding the link between posture and spinal pain and much of the research indicates that there is either a weak correlation or no correlation between posture and pain. However, most clinicians believe that poor posture is a risk factor to spinal pain and maintaining good posture can benefit other structures of the body. Many rehabilitation programs focus on improving posture. Below are three common methods.

The Egoscue approach focuses on posture therapy and claims to get to the root of your chronic pain by returning your body to proper alignment, function, and balance. Egoscue uses a series of gentle exercises and stretches to return musculoskeletal balance and symmetry back to the body.

The Gokhale Method focuses on regaining healthy posture and movement to help restore the body's structural integrity. This approach emphasizes correcting positioning in everyday movement rather than periodic exercise sessions.

Global Postural Reeducation (GPR) is an approach based on the idea that the muscular system can face shortening resulting from genetic factors and body type, behavioral, and psychological factors. Treatment includes a thorough analysis and observation of a person's individual anatomy, physiology, and their presentation of symptoms and the consequences of such symptoms. GPR focused on each individual body, as a whole, with the understanding that the true cause of a problem could arise from a different part of the body. Part of the philosophy is that there are different series of interconnected muscles (or muscle chains) that have specific roles in function. GPR makes use of a series of specific postures adapted to each patient according to the chain of muscles that are affected while taking into account the whole body. The ultimate goal of this approach is to improve postural symmetry, which is believed to reduce pain and disability.



Alexander Technique

The Alexander Technique is a method that teaches how to find an improved balance in one's body by releasing unnecessary tension and changing inefficient habits of movement. The philosophy of this technique includes bringing attention to tensions throughout the body that have previously gone unnoticed, and that these tensions are very often the root cause of many common ailments. It is not a series of treatments or exercises, but rather a reeducation of the mind and body. The Alexander Technique allows one to become aware of balance, posture, and coordination while performing everyday actions.

Brain Motor & Sensory Retraining

Research has shown that there are altered connections and reorganization of the brains of those who suffer from chronic pain, although it is not clear whether these changes are a consequence of the chronic pain or they may have led to the pain becoming chronic. Treatment of chronic pain includes techniques called graded motor imagery, desensitization, and sensory re-education which focus on brain re-training. A brain motor and sensory exercise program can help you re-develop healthy nerve connections and brain organization. Certain pathways in the brain are activated when the brain needs to recognize a body part (sensory) and before and during a movement of that body part (motor). The goal of these treatments is to reorganize the brain and its pathways to diminish pain and sensitivity.

Graded Motor Imagery

Graded motor imagery is a set of rehabilitation processes used to treat pain and movement problems related to an altered nervous system. The three different treatment techniques include limb laterality training, motor imagery exercises, and mirror therapy. These techniques are delivered sequentially or individually.

People suffering from chronic pain often lose the ability to identify left or right images of their painful body parts. Limb laterality training includes viewing photographs of left or right body parts in a variety of postures focused on improving speed and accuracy. Motor imagery involves thinking about a movement but not actually performing that movement. By imagining movements, similar areas of the brain are used as would be used when the person performs the same movement. This technique is commonly used in competitive sports training. Mirror therapy involves movement of the limb inside a mirror-box such that visual feedback of the affected hand is replaced with that of the (reflected) unaffected hand. Mirror therapy is thought to reconnect motor output and sensory feedback and active pre-motor cortices. Mirror therapy has been found to be effective for CRPS and phantom limb pain in particular.

Desensitization

With chronic pain, a painful area can become more sensitive (hypersensitivity) than expected and the area of sensitivity can become bigger over time. Light touch, pressure, warm or cold temperatures, vibration and even the contact of the clothes on the skin can be painful. Desensitization is a treatment to slowly reduce the hypersensitivity of the affected area by introducing normal types of touch and temperature. A desensitization program provides frequent but short periods of stimulation to the affected area. The stimuli may consist of smooth to rough textures/fabrics, heat or cold, light or deep pressure and vibration. Desensitization programs progress gradually from



stimulation that produce the least painful response to the most painful. The course may take several days to several months, depending on the level of hypersensitivity.

Sensory Re-education

The ability of the brain to recognize the affected body part and its sensations is affected. Sensory re-education helps to adapt the brain's response to injured areas to normalize object shape, size, texture, and location. The brain is retrained for constant touch compared to moving touch, where on the skin the touch is actually occurring and what direction the touch is moving in. Treatment may incorporate unaffected areas using the same procedure so that the sensation on the two sides may be compared.

Virtual Reality

Although still in the early stages of research and development, scientists started looking at the power of virtual reality to ease suffering more than 20 years ago. Researchers don't know exactly how virtual reality impacts pain. One theory is that it provides a powerful distraction from pain. Another theory suggests that virtual reality could affect the "gating" system of how pain is transmitted to the brain and processed by the brain. Some have proposed that it can help interfere with how pain is processed in the brain and/or central nervous system. Virtual reality is also being used for Mirror Visual Feedback therapy based on the theories of mirror box therapy that is thought to affect the sensory maps in the brain. Virtual Reality is not readily accessible to most people yet and is now mostly limited to researchers who are [conducting clinical trials](#) for treating chronic pain or in select hospital settings.

Functional Activity Training

Chronic pain can limit even the simplest daily activities as well as the ability to perform higher-level work activities. A successful active program focuses on increasing the ability to perform functional tasks. For example, this could mean being able to perform household tasks or return to work again. Being more independent leads to a higher quality of life. Functional activity training is just as important as performing a daily exercise program. Lifting, carrying, pushing, pulling, reaching, bending, finger dexterity, and gripping/grasping are all examples of functional movements that are used on a daily basis. Functional Activity Training also includes the ability to tolerate sitting and standing for long periods of time. It is helpful to think of practicing daily activities similar to performing exercises. It is important to first determine the current ability to perform this task. Each task is then practiced with appropriate pacing of activity, flare management, and slow progression. Recreational activities are included in this category. The ability to perform a higher level of recreational activities serves many purposes including exercise, socialization, time utilization, and general enjoyment.

Personal Goal Attainment Program

One approach is the Personal Goal Attainment Program (PGAP) which consists of a series of 10 face-to-face or telephonic sessions with a trained PGAP provider, most often a vocational rehabilitation consultant, occupational therapist or physical therapist. The purpose of the program is for the individual with chronic pain to identify specific daily activities that are important or meaningful but have been given up due to the pain – and then gradually and safely restore them. In the process, confidence increases, and negative thinking and fears recede. The program was



developed by a psychologist at McGill University and has been shown to be very effective in reducing fear avoidance, catastrophic thinking and perceived injustice – and facilitating return to work. Referral is made by the treating physician. An interview and administration of screening questionnaires during an evaluation session determines eligibility for the program. The number of certified PGAP providers varies from community to community.

See <https://www.pgapworks.com/en/index.php>.



PSYCHOLOGICAL & BEHAVIORAL APPROACHES

Chronic pain can impact every corner of a person's life, not just their physical functioning. The longer the pain condition lasts, the more emotional and mental distress a person tends to feel. This distress can make pain worse over time and decrease functioning. Chronic pain is best treated by the biopsychosocial model, which addresses the emotional, mental, and social aspects of pain as well as the physical.

Mental health care is an essential component of the multidisciplinary team. These interventions lead to less stress, more positive behaviors and a focus on functioning rather than cure.

Choosing to engage in a multidisciplinary approach and focus on managing pain rather than curing it is not “giving up.” On the contrary, it is letting go of the illusion of being pain-free and simply choosing to live life to the fullest and find ways to thrive, despite pain. With the right mindset and coping strategies, a life with pain can still be a life full of hope and joy.

Pain Psychology

The International Association for the Study of Pain (IASP) defines pain as a negative sensory and emotional experience. As such, psychology is built into the definition of pain. Psychological experiences (e.g., stress, anger, depression, anxiety, worry about pain, over-focusing on pain) will increase pain intensity, whereas happiness, joy, love, and relaxation have been shown to provide pain relief. Pain psychology recognizes that every person can benefit from learning information and skills they can use to reduce their pain and suffering, even while other pain treatments are being pursued. In fact, some research suggests that the combination of medical, physical, and psychological pain treatments can provide best results.

Living in constant pain can be emotionally distressing and result in depression and anxiety or can worsen existing mental disorders. This does not mean that the person in pain is weak, but rather is having an understandable reaction to a stressful situation. Other psychological factors that impact pain and functioning include, but are not limited to, life stress, fear of movement and reinjury, avoidance behaviors, lack of motivation, sleep disturbance, poor social support, substance abuse and negative thinking patterns. Treatment of chronic pain in the biomedical model neglects to address the psychological and social issues that can worsen chronic pain.

Pain Psychology is the cutting edge of where psychology meets medicine. Utilizing a combination of Cognitive Behavioral Therapy, relaxation strategies, and education, Pain Psychology can help empower a person to manage their pain more independently by helping them understand their neurological gates in the central nervous system. The foundation of Pain Psychology is the Biopsychosocial Model, which treats the patient as a “whole” and not as an injured body part. Often individuals are relieved when exposed to the Biopsychosocial model because they have only been offered few, typically not helpful, tools to help them cope with the emotional and mental distress they have been experiencing. It is important to remember that Pain Psychology is not meant to “cure” the patient, but rather provide strategies to maximize one's ability to participate



in valued life activities that are most meaningful to them.

TREATMENT APPROACHES

Cognitive Behavioral Therapy for Pain (Pain-CBT)

Cognitive Behavioral Therapy is a common form of psychological treatment for many different problems, such as depression, anxiety or eating disorders. Pain-CBT is a specific form of CBT designed to address the common mental, emotional, and behavioral concerns that individuals with chronic pain face.

Pain-CBT provides foundational education on the role of the mind in the experience and treatment of pain, including the relationships between thought patterns, emotion, actions, and pain. Key CBT skills include learning to identify the negative thoughts/behaviors that serve to worsen pain and establishing different thought patterns that serve to reduce distress, calm the nervous system, reduce pain, and lead to better health choices. These are interventions that patients can learn to do independently. Once the individual understands how to help themselves feel better mentally and emotionally, it is easier to make healthier choices that support good pain control.

CBT also addresses core underlying beliefs that may be serving to keep an individual stuck in feeling hopeless or out of control with their pain. As such, negative beliefs can impact the functioning of an individual living with chronic pain and prevent them from engaging in active rehabilitation.

1. Sinister beliefs are when a person believes that pain is indicative of tissue damage. This belief is associated with fear, which keeps people from engaging in activity that may be beneficial, although physically uncomfortable.
2. Disability beliefs are when a person believes his or her pain is disabling them. The more disabled a person thinks he or she is, the more disabled the person will act. The person is not exaggerating or lying about the condition, but just perceives him or herself as very disabled and acts accordingly.
3. Reliance on medication or a medical intervention. If someone believes that only a medical intervention will cure them, then they will put their effort into seeking medical interventions and not into trying self-management techniques. They may also experience high levels of distress when their medications are unavailable or treatment they believe will cure them is not authorized. Often people become depressed or anxious when their surgeries or treatments fail.
4. Catastrophic beliefs are when people believe an event or situation is a disaster. For example, a patient may think of a pain flare as an indication that their condition is worsening rather than a temporary elevation in pain levels.



These types of pain beliefs can trigger emotional distress, such as sadness, anxiety, fear, hopelessness, or anger. As such, it's important to address such pain beliefs to best ensure a good response to medical treatment, and engagement in self-management principles.

Pain-CBT is the best-studied psychological treatment for pain and is considered the gold-standard because of decades of accumulated evidence showing benefit for people living with chronic pain. Pain-CBT is typically delivered in person or telephonically by trained mental health professional, pain psychologist or health psychologist in individual or group format. To locate a qualified therapist, consider utilizing the “find a CBT Therapist” tool at the website for the Association for Behavioral and Cognitive Therapies (<http://www.abct.org/Home/>) or the “Find a Psychologist” link at the American Psychological Association website at (<http://www.apa.org/helpcenter/index.aspx>).

Brain imaging studies show that pain-CBT works, in part, by decreasing attention to pain. It's common for people to ruminate on pain and to worry about it, and unfortunately these experiences serve to increase distress and amplify pain processing in the nervous system. Through CBT, people learn skills to better control pain-related distress—and stress caused by other life factors. Without the right understanding and skills, it's easy for pain and stress to cause people to react in ways that end up being unhelpful. For instance, most physicians could tell you that their patients engage in negative behaviors that harm their health. This may include smoking, lack of exercise, or poor eating habits. Most people know these habits are not healthy; but they probably do not understand what triggers them to engage in these harmful behaviors. Human beings are always acting on their thoughts, many of which become patterned over time—for better or for worse!

While pain-CBT is an appropriate treatment for pain, it can also be used to treat the psychological factors that impact pain including depression, anxiety, and sleep disturbance. In fact, pain-CBT often includes content on addressing sleep problems and factors that contribute to low mood. A combination of education, behavioral modification, and the changing of thinking patterns can help alleviate these psychological issues, resulting in improved functioning. Leaving psychological symptoms untreated can be costly. For example, a patient may be too depressed to be motivated in physical therapy and will be unlikely to benefit from other interventions until the depression is under control. Patients may also be taking higher doses of medication to cope with psychological distress, which can put them at risk for prolonged use, polypharmacy, addiction or substance abuse.

Acceptance and Commitment Therapy (ACT)

Acceptance and Commitment Therapy (pain-ACT) is a variant of pain-CBT. Like pain-CBT, pain-ACT includes education about pain, relaxation skills training, and some meditative elements shown to improve pain control. Unlike pain-CBT, pain-ACT emphasizes non-reactivity to negative thoughts as a way to diffuse their ability to amplify pain and distress. ACT guides participants toward acceptance of one's available choices and committing oneself to doing what will move them closer to attaining valued goals. Rather than “fighting against the pain” participants are guided to develop positive, attainable goals (that honor current physical limits) that are consistent with their values. Importantly, pain-ACT emphasizes engagement in activities with pain present, rather than waiting for pain to subside. Such an approach can help individuals reclaim their control over pain.



Locate an ACT therapist anywhere in the world:

<https://contextualscience.org/civcrm/profile?gid=17&reset=1&force=1>

Motivational Interviewing

Motivational interviewing is a counseling method that helps people resolve ambivalent feelings to find the internal motivation they need to change their behavior. It is a practical, empathetic, and short-term process that takes into consideration how difficult it is to make life changes.

Motivational interviewing is often used to address addiction and the management of chronic health conditions such as diabetes, heart disease, chronic pain, and asthma. This intervention helps people become motivated to change the behaviors that are preventing them from making healthier choices. It can also prepare individuals for further, more specific types of therapies. Research has shown that this intervention works well with individuals who start off unmotivated or unprepared for change. Motivational interviewing is also appropriate for people who are angry or hostile. They may not be ready to commit to change, but motivational interviewing can help them move through the emotional stages of change necessary to find their motivation.

The process includes a motivational interviewer encouraging patients to talk about their need for change and their own reasons for wanting to change. The role of the interviewer is mainly to evoke a conversation about change and commitment. The interviewer listens and reflects back the patient's thoughts so that the patient can hear their reasons and motivations expressed back to them. Motivational interviewing is generally short-term counseling that requires just one or two sessions, though it can also be included as an intervention along with other, longer-term therapies.

Fear Avoidance Therapy

Many people avoid activity after an injury due to the fear this will cause more pain and/or additional injury. Immediately after an injury, this fear is natural and helps to remind us to avoid further damaging the area. For example, immediately following an ankle injury, you avoid further pain and therefore do not put weight on the ankle. If you have just sprained your ankle, this is a good idea so that it can heal itself. However, once the pain becomes chronic, avoidance is not beneficial and can lead to physical de-conditioning, loss of flexibility, loss of muscle strength and an increase in pain. Therefore, this fear can prevent or delay recovery.

Unfortunately, people who have higher levels of fear tend to avoid more activity than normal and tend to focus more on the amount of pain they have when they attempt daily activity. Healthcare providers unknowingly contribute to this fear with messages such as “Don’t do an activity that is painful”, “You have the back of a 90-year-old” or “If you fall, you can be paralyzed”. Reducing or eliminating pain-related fear can be a powerful intervention for those with chronic pain.

The Fear-Avoidance Model of Musculoskeletal Pain (FAM) describes how the pain experience can lead to negative thoughts, fear, avoidance, disability, depression and physical disuse. It states that in some situations, an individual connects specific movements with harmful consequences. These movements are considered threatening and cause fear, muscle tension, anxiety and thoughts of having more pain. Avoiding painful movement leads to short term positive outcomes including



a reduction in pain and a decrease in muscle tension and anxiety. However, in the long term, avoidance has negative consequences.

Treatment to overcome fear avoidance includes awareness of the patient's current beliefs regarding their pain, education, repeated exposure to activities that have been avoided, setting short and long-term goals and taking an active role in recovery. It can be helpful to learn the difference between pain sensations and tissue damage. Instruction on safe positioning, safe activity and appropriate progression of activity are important. Relaxation, breathing and meditation skills can be useful since an increase in pain with a higher level of activity is common. This type of treatment is often performed with both a psychologist and physical therapist, either separately or in a co-treatment session.

Stress-reducing Interventions

Often people dealing with chronic pain feel that their mind and body are at war with each other and this causes stress for the individual. Modern medicine has known for some time that stress can be harmful for the body. It increases heart rate, breathing rate, blood pressure, releases stress hormones, and impacts the digestive system. Short term stress is not necessarily harmful, but long-term stress, like the stress associated with living with chronic pain, can negatively impact the mind and body. Stress reduction is a critical component to pain management. There are numerous stress reduction mind-body interventions including relaxation, meditation, guided imagery, biofeedback, hypnosis, and art and music. These treatments can be used individually or as part of Cognitive Behavioral Therapy.

Many people feel that they are relaxing when they are sitting in front of the TV, but active relaxation takes effort and time. Active relaxation strategies can harness the mind in order to harness the body. The mind is a powerful tool and being able to relax it at will is one of the most important skills a person with chronic pain can learn.

ACPA offers a five-minute relaxation video. This five-minute relaxation exercise can help you let go of physical stress and begin to reduce your sense of suffering. The relaxation video can be found at <http://www.theacpa.org/pain-awareness/september-is-pain-awareness-month/relaxation-video/>.

Mindfulness-based Stress Reduction (MBSR)

There are a variety of meditative practices; the most studied one for chronic pain being mindfulness-based stress reduction (MBSR). It is a variant of meditation that has been applied to stress reduction and created by biologist Jon Kabat-Zinn. In recent years, studies have found that patients who used MBSR reduced medication use, increased their activity levels, and felt increases in self-esteem. A 2016 study published in the Journal of the American Medical Association revealed that MBSR effectively reduced chronic pain in people with chronic low back pain and did so equally as effective as structured 8-week CBT. It is thought that MBSR works by helping decrease attention to pain and pain-related distress, thereby dampening pain processing the nervous system. MBSR cultivates a greater awareness of the relationship between the mind and body. This awareness can highlight, in a non-judgmental manner, how our negative thinking and emotions adversely impact our actions and our health. This technology is an excellent supplement to CBT, but also a treatment intervention on its own. For more information on Mindfulness, read *"Mindfulness for Beginners: Reclaiming the Present Moment-and Your Life,"* by Jon Kabat-Zinn.



The University of California (UCLA) Mindful Awareness Research Center offers free on-line guided meditations available in English and Spanish at the following web site: <http://marc.ucla.edu/mindful-meditations>.

Relaxation and Guided Imagery

Another way to relax the mind is to use guided imagery. This technique uses the imagination to take the mind to a relaxing place, such as the beach or the forest. Imagery can also be used to increase self-confidence by helping patients imagine themselves being successful at a task or reaching their goals. This technique of visualizing success has often been used by sports psychologists to help athletes improve their performance.

Art & Music

Art and music are creative forms of expression and have been used for some time in psychotherapy to help people express their thoughts and feelings. While these creative tools can help chronic pain patients maintain their emotional stability, they can also impact them biologically. Art and music stimulate the healing process by helping to decrease stress and release neurotransmitters that can decrease the experience of pain. Engaging in creative activity can release endorphins, which are the body's natural pain killers. Many people, when engaged in the creative arts, report that they are less aware of their pain. Research suggests that listening to music during medical and minor surgical procedures can reduce pain and anxiety – and it is free. Art and music are excellent tools for any pain management plan and can be personalized to the taste and preferences of the individual. See additional resource at <https://theacpa.org/pain-management-tools/the-art-of-pain-management/>

Biofeedback

The above strategies can help the psychological components of stress, but there are also strategies that target the biological components of stress. Stress has several biological features, like increased heart rate and muscle tension. Biofeedback uses feedback from sensors and a computer to give information about the body's stress response and then teaches the patient to control the stress response. This may involve consciously relaxing muscles or changing breathing. Biofeedback has been particularly helpful for headaches and chronic pain, which often causes increased pain due to muscle tension and fatigue.

Hypnosis

Hypnosis is a state of deep relaxation that involves selective focusing, receptive concentration, and minimal motor functioning. A National Institutes of Health Technology Panel found strong support for the use of hypnosis for the reduction of pain. Individuals can be taught to use hypnosis themselves (self-hypnosis), and the use of self-hypnosis can provide pain relief for up to several hours at a time.



Reconditioning Brain and Mind

Social Isolation and Building Social Support

One of the biggest negative impacts of chronic pain is social isolation. Individuals may stop making plans out of fear of having to cancel on late notice again. Relationships may grow distant, particularly if one is unable to work. When someone has an acute injury, their support system is quick to offer help. However, when the pain does not resolve in a few months, the support system starts to become strained and dwindles. Friends and family return to their lives and the person in pain feels like he or she is struggling alone. Also, being in pain can be an emotional roller coaster and this can negatively impact communication with loved ones, which strains relationships.

Building social support is an important pathway to improving quality of life and reducing the impact of pain.

There are many ways to build support.

1. Communicate and reach out to others. It is important to start with expressing feelings, needs, and desires. Often, we assume others know what we need or want, and we become frustrated when they don't give it to us. One must be careful to not assume and start by expressing themselves clearly.
2. Reach out to new communities, such as support groups (see ACPA Support Groups at <https://theacpa.org/about-us/support-groups/>), neighbors, churches or other religious organizations. This can be challenging at first but can really be beneficial. One must be careful when choosing a structured chronic pain support group. Some groups can feel negative depending on the format and it is important to find groups that highlight successes and strengths and explores coping. These groups can be in person or online.
3. Health care team members can also be part of your support system. This includes doctors, nurse case managers, and mental health practitioners.
4. Join an online pain support group. You can participate in discussions and receive social support from your own home.
5. Join a pain treatment group or health class, such as pain-CBT, pain-ACT, an arthritis water exercise group, a senior center stretching class, or gentle yoga for people with medical concerns.

Interrupting Learned Neural Circuits

Sometimes the brain itself may be the source of pain although the pain feels like it is coming from the body. For example, research has shown that the identical parts of the brain light up on functional MRI whether a person is experiencing the emotion of grief (a “broken heart”) or chest pain due to angina. Other studies have shown that acute pain lights up the parts of the brain that correspond to the injured body part on functional MRI. But just a few months later, that person's pain will no longer be lighting up that same part of the brain; it will now be lighting up the brain areas related to memory and emotion. Chronic pain of this sort is thought to be due to “learned neural pathways” or “learned pain circuits” in the brain – sort of like the repetitive sound of a scratched CD.

The Psychophysiological Disorders Society is an association of practitioners committed to



relieving symptoms due to stress-induced medical conditions. They help individuals with hard-to-explain chronic pain identify the connection between their pain and suppressed traumatic memories or emotions -- and then disconnect those experiences from their brain's pain circuits by using a variety of mind-body techniques. This approach has been particularly effective for people who had very difficult childhoods. Complete relief of pain and full return of function are possible. See for example the following web site: www.ppdassociation.org/.

Finding a Mental Health Therapist

There are a number of mental health therapists who offer psychotherapy for persons with chronic pain and who are specially trained and licensed by the state in which they practice.

- Psychiatrists have a Doctor of Medicine or Osteopathy (MD, DO) and provide psychiatric medical care services which includes diagnosis, treatment and prescription of medications.
- Psychologists have a Doctor of Philosophy (PhD) in Clinical Psychology or Counseling Psychology or Doctor of Psychology (PsyD) and specialize in human behavior and emotional health. They have training in working with individuals, couples, and families and do so either in group or individual sessions. They can also administer and interpret psychological tests. They have expertise in dealing with most emotional and behavioral problems. In some states, psychologists can prescribe medications for emotional problems.
- Social Workers have Masters Degrees (MA or MS) and are sometimes called Licensed Clinical Social Workers (LCSW). They receive specialized training in how people function in their environment and solve personal and family problems. Some also have experience in case management and can assist in finding government and local resources in the community that meet the needs of people with pain.
- Masters-Level Counselors have Masters Degrees (MA or MS) in either clinical or counseling psychology. They are sometimes called Licensed Marriage & Family Therapists or Licensed Professional Counselors. They have specialized training in dealing with individuals and families particularly in relationship problems.

It is important for the public to realize that few doctoral and masters programs offer courses in Pain Psychology and not all providers who treat chronic pain are focused on improving functioning. Some providers are simply offering support during difficult transitions while others are inadvertently reinforcing negative behaviors. The most common example is that a mental health provider may discourage a chronic pain patient from engaging in a certain activity because it is uncomfortable and distressing. A provider trained in Pain Psychology focuses on teaching skills so that the patient can engage in more activity, ask for support when they need it, and set realistic goals for themselves. In order to find a provider who is truly trained in Pain Psychology, it is important to ask them four questions:

1. Do they have the special expertise or training in chronic pain?
2. Do they understand the biopsychosocial model?
3. Are they trained in cognitive behavioral therapy and mindfulness?



4. Are they familiar with working with multidisciplinary teams? A good indication of this would be that the provider is associated with a functional restoration program or they are part of a clinic that includes biopsychosocial interventions.

Conclusion

Chronic pain can impact every corner of a person's life, not just their physical functioning. The longer the pain condition lasts, the more emotional and mental distress a person tends to feel. This distress can make pain worse over time and decrease functioning. Chronic pain is best treated by the biopsychosocial model, which addresses the emotional, mental, and social aspects of pain as well as the physical. A mental health practitioner is an essential component of the multidisciplinary team. These interventions lead to less stress, more positive behaviors and a focus on functioning rather than cure.

Choosing to engage in a multidisciplinary approach and focus on managing pain rather than curing it is not "giving up." On the contrary, it is letting go of the illusion of being pain-free and simply choosing to live life to the fullest and find ways to thrive, despite pain. With the right mindset and coping strategies, a life with pain can still be a life full of hope and joy.



COMPLEMENTARY, ALTERNATIVE & INTEGRATIVE MEDICINE (CAM)

Complementary and Alternative Medicine (CAM) includes a diverse group of healing systems, practices, and products that are typically considered allopathic medicine, although some have proven scientific validity and have become mainstream (e.g., acupuncture, meditation, hypnosis, yoga, certain herbal preparations, etc.). Other CAM approaches have strong followers, but their “proof” of value is really anecdotal rather than based on scientific fact.

In fact, what is considered to be CAM changes continually, as those therapies that are proven to be safe and effective become adopted into conventional health care and as new approaches to health care emerge.

Complementary medicine and alternative medicine are different from each other. Complementary medicine is used together with conventional medicine while alternative medicine is used in place of conventional medicine. Integrative or integrated medicine combines treatments from conventional medicine and CAM for which there is some high-quality evidence of safety and effectiveness. Always check with your health care provider or pharmacist as drug interactions can occur with many alternative or “natural” medications.

The reader is referred to the following Internet websites for further information.

The National Center for Complementary and Integrative Health (NCCIH) (<http://nccam.nih.gov>) is part of the National Institutes of Health (NIH) and is the lead agency for scientific research on CAM. Go to <https://nccih.nih.gov/health/integrative-health> for Complementary, Alternative, or Integrative Health: What’s In a Name?

The Mayo Clinic published an article for healthcare practitioners (Mayo Clin Proc. 2016;91(9):1292-1306), *Evidence-Based Evaluation of Complementary Health Approaches for Pain Management in the United States*. This article examines the clinical trial evidence for the efficacy and safety of several specific approaches including acupuncture, manipulation, massage therapy, relaxation techniques including meditation, selected natural product supplements (chondroitin, glucosamine, methylsulfonylmethane, S-adenosylmethionine), Tai Chi, and yoga as used to manage chronic pain and related disability associated with back pain, fibromyalgia, osteoarthritis, neck pain, and severe headaches or migraines. The article is available on the Internet at:

[http://www.mayoclinicproceedings.org/article/S0025-6196\(16\)30317-2/pdf](http://www.mayoclinicproceedings.org/article/S0025-6196(16)30317-2/pdf)



Traditional Chinese Medicine (TCM)

Traditional Chinese Medicine (TCM) originated in ancient China over five millennia ago. It is a medical philosophy built around the theory that diseases are caused by an imbalance of vital energy flow (Qi). Qi is thought to circulate around the body via multiple channels (meridians), predicated optimal functioning of all organs and tissues. Many additional concepts inform diagnosis and treatment, such as those of Blood, Yin and Yang, and Jing, among others. Such theories were recorded in writing and passed down generations for thousands of years, resulting in a robust theoretical and empirical framework of medical thought. Many of TCM's major concepts bear some correlation to contemporary Western notions about the physiological basis of bodily functioning. For more information on TCM's origins and approach, please visit <https://nccih.nih.gov/health/whatis/tcm/chinese/med.htm> and <https://www.tcmworld.org/>.

TCM is a complete medical system that can be used independently of any other system. Its principal modalities are as follows:

Herbs

The most important and powerful modality in TCM is herbal treatment, which corresponds to the pharmacological approach in modern medicine. Thousands of herbs and hundreds of animal materials, along with minerals, constitute TCM's pharmacopeia. These are combined in complex formulas and used to treat disease on an individual basis. A number of these compounds are used to treat chronic pain, and are dispensed in tea, pill, or topical form, as each case demands. They are prescribed by certified TCM practitioners. Practitioners' certification is regulated either by state or nationally and can be confirmed here: <http://www.nccaom.org>.

Acupuncture and Acupressure

The flow of Qi along meridians is thought to be modulated by application of specific points on these meridians. Classically, there are 362 points located along 14 meridians. They can be mapped using a specific, three-dimensional coordinate system. Meridian points are then stimulated, alone or in groups, using thin metal needles (acupuncture or needling), fingertips (acupressure), heat (moxibustion), cold (cryotherapy), electricity (with or without needles), or other stimuli. Typically, four to twelve points are stimulated per session, with sessions lasting from five to sixty minutes. A full course of treatment consists of ten to twenty sessions. These have traditionally been held daily, although contemporary American treatment more commonly takes place three times a week. There are multiple acupuncture techniques outside of TCM that have been derived from its system, although these have less empirical evidence of effectiveness than TCM.

Acupuncture has been gaining popularity in the United States since the 1970s, and, in wake of increasing acceptance by both the public and medical professionals, it is now covered by many insurance policies. In the field of chronic pain medicine, there is a strong body of research supporting the efficacy of acupuncture for headache, osteoarthritis, and musculoskeletal conditions, such as neck and lower back pain.

The National Library of Medicine website (<https://medlineplus.gov/acupuncture.html>) provides general information on acupuncture, including a link to locate a certified practitioner.



Moxibustion

An important modality of treatment in TCM consists of applying heat to meridian points, either in combination with needles or by itself. This is known as moxibustion. Cigars made of different herbs, small cones of fine sawdust, electrical heating devices or lasers can all be used to provide a steady flow of heat and thereby enhance or substitute the effects of acupuncture in harmonizing Qi flow. Moxibustion is often used to treat chronic pain or insomnia, and for relaxation.

Cupping

Cupping is a TCM treatment modality in which cups are placed on the skin to create suction. Traditionally, cups were made of wood, clay or horn; glass or plastic cups are used today. In cupping, a vacuum is created within the cup by setting a flammable substance on fire inside of it and then allowing it to cool, or by using a rubber pump. The underlying tissue is, in result, sucked partway into the cup. Small blood vessels are broken by the vacuum suction, and cupping causes light bruising around the circumference of the cup. The cups may be placed over acupuncture needles, on their own, or moved around to provide vigorous massage of large body areas. Cupping is used to regulate Qi flow and help with pain, inflammation, blood flow, and relaxation. There is limited research on cupping, and its benefits in alleviating pain have not been proven. Some believe that cupping has no scientific basis.

Gua Sha

Gua Sha is a TCM treatment modality involving scraping areas of skin with plates, traditionally made of horn, usually together with application of herbal oil. Scraping causes light bruising and is thought to promote Qi flow and help with chronic pain, inflammation and circulation. As with cupping, the benefits of Gua Sha have not been proven, and some believe that it has no scientific merit.

Tui Na

Tui Na is a combination of massage, mobilization and manipulation techniques. It is widely used in TCM in treatment of musculoskeletal disorders but has no wide recognition by Western conventional medicine.

Tai Chi

Tai Chi was developed in China as an ancient martial art and is practiced for both defense training and health benefits today. It has gained popularity worldwide as an exercise form and for health enhancement. In this context, Tai Chi refers to a sequence of choreographed slow, soft flowing movements with the body that incorporate a straight spine, abdominal breathing, and a natural range of motion. Each specific movement corresponds with either the inhalation or exhalation of a deep, gentle breath. The slow movement and weight bearing required by Tai Chi contributes to musculoskeletal strength and joint flexibility, while the meditative focus of Tai Chi improves concentration and mindfulness, thus improving mood, and functions of the immune and autonomic nervous systems. In recent years, Tai Chi has received increased attention from researchers worldwide looking for alternative and complementary approaches to treating chronic pain. Research studies has suggested that Tai Chi can provide benefit for pain from osteoarthritis, osteoporosis, and



low back pain with practice longer than five weeks. Other studies have found benefits of Tai Chi in postherpetic pain in herpes zoster, rheumatoid arthritis, and stroke. It has not yet been conclusively demonstrated that Tai Chi is superior at chronic pain control when compared to other active treatments. Tai Chi is not generally associated with significant adverse events.

Qigong

Qigong is another systematized form of movement, breathing, and mindfulness, cultivated in ancient China, and used today for health, longevity, and martial arts training. It seeks to harness and balance *qi*, or ‘life energy’ by coordinating slow movements similar to those of Tai Chi with deep breathing and a meditative state of mind. It, too, has been explored as an alternative or complementary therapy in the relief of pain. It has been recognized as a “standard medical technique” in China since 1989 and is included in the medical curriculum of some universities there, used in treatment not just of pain but hypertension, coronary artery disease, diabetes, fatigue, insomnia, myopia, and a host of other chronic conditions. Medical research, while promising, does not conclusively demonstrate whether Qigong can be helpful in chronic pain however more research is needed.

Nutrition

Diet, including use of dietary herbs, is an important and inseparable part of TCM. TCM practitioners with an oriental background generally hold an advantage over other providers in that they are intimately familiar with the nutritional products through lifetime cultural exposure rather than learned use of nutritional products in a classroom setting.

FINDING A Specialist in Traditional Chinese Medicine

Traditional Chinese Medicine originated largely as a holistic system of preventive medicine, with multiple treatment modalities as described above. In the United States it is regulated on a state and national level. Multiple schools offer a master’s degree in TCM or oriental medicine and a few offer a doctoral level, which is more important for continuous research in the field rather than in clinical training. Upon completion of master course, many states offer a licensing examination in acupuncture, which includes theory of TCM, diagnosis and multiple treatment modalities other than just acupuncture. The National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM®) is a non-profit organization established in 1982. The NCCAOM is the only national organization that validates entry-level competency in the practice of acupuncture and oriental medicine through professional certification. Most of the states either require or use NCCAOM certification/examination. In California, state acupuncture license is mandatory for practice. Alabama, Oklahoma and South Dakota have no acupuncture practice act. The best way to find a practitioner in TCM is through state boards or NCCAOM websites. <http://www.nccaom.org>

The American Academy of Medical Acupuncture (AAMA) is the professional society of physicians (MDs and DOs) in North America who have incorporated acupuncture into their traditional medical practice. The AAMA was founded in 1987 by a group of physicians who represented both East Asian and Euro-American styles of acupuncture. <https://www.medicalacupuncture.org/>

The American Board of Medical Acupuncture (ABMA) was formally established on April 26,



2000. The ABMA has been created as an independent entity within the corporate structure of the American Academy of Medical Acupuncture. The ABMA has a separate, independent Board of Trustees with full responsibility for the direction and operation of the ABMA. The mission of the American Board of Medical Acupuncture is to promote safe, ethical, efficacious medical acupuncture to the public by maintaining high standards for the examination and certification of physician acupuncturists as medical specialists. <http://www.dabma.org/>



PHYSICAL MODALITIES – NONINVASIVE INTERVENTIONS

Passive therapy (those treatment modalities that do not require energy expenditure on the part of the patient) can provide short-term relief during chronic pain flare-ups and is directed at controlling symptoms such as pain, inflammation, and swelling. Passive therapies may be useful over the short term but have limited benefit for chronic pain conditions overall.

Heat & Cold

Using cold (cryotherapy) or heat (thermotherapy) are inexpensive self-treatment approaches with minimal risks. While there are some individuals that find cold helpful for chronic conditions, it is mostly utilized for acute injuries when there are damaged superficial tissues that are inflamed, hot and swollen. Heat is more helpful for chronic muscle pain, contractures and spasm.

Cold treatment reduces inflammation by decreasing blood flow. It is usually applied within 48 hours after an injury. Heat treatment promotes blood flow and helps muscles relax. Alternating heat and cold may help reduce exercise-induced muscle pain. Heat and cold therapy modalities are often used despite prevalent confusion about which modality (heat vs cold) to use and when to use it. Most recommendations for the use of heat and cold therapy are based on empirical experience, with limited evidence to support the efficacy of specific modalities. There is limited evidence from randomized clinical trials supporting the use of cold therapy following acute musculoskeletal injury and delayed-onset muscle soreness. There is limited overall evidence to support the use of topical heat in general; heat-wrap therapy providing short-term reductions in pain and disability in patients with acute low back pain; and significantly greater pain relief of delayed-onset muscle soreness than does cold therapy. <https://www.ncbi.nlm.nih.gov/pubmed/25526231>

Therapeutic Massage

Therapeutic massage is different than the relaxing massage you may receive at the spa. The therapists use their knowledge of anatomy and physiology along with different manual techniques including but not limited to cross-fiber massage, friction massage, myofascial release, and trigger point therapy.

Soft tissue mobilization is a form of manual physical therapy where the physical therapist uses hands-on techniques on the muscles, ligaments and fascia with the goal of breaking adhesions. The goal of soft tissue mobilization (STM) is to break up inelastic or fibrous muscle tissue such as scar tissue, move tissue fluids, and relax muscle tension. This procedure is commonly applied to the musculature surrounding the spine and consists of rhythmic stretching and deep pressure.

Myofascial Release is a hands-on technique that involves applying gentle sustained pressure into



the myofascial connective tissue to release restrictions. The idea is that the gentle pressure over time will allow the fascia to elongate. Myofascial Release Treatment is performed directly on skin without oils, creams or machinery. This enables the therapist to accurately detect fascial restrictions and apply the appropriate amount of sustained pressure to facilitate release of the fascia.

While most therapists will use only their hands, tools or instruments can be used with therapeutic massage. The Graston Technique is when a tool is used to perform a specialized form of massage/scraping of the skin.

Active Release Therapy (ART®) is a patented and specific set of hand techniques that combine soft tissue mobility with movement. The role of ART is to reestablish proper motion between muscles and fascia while reducing fibrous adhesions or scar tissue. This scar tissue can also compress nerves and cause trigger points. The provider uses his or her hands to evaluate the texture, tightness and movement of muscles, fascia, tendons, ligaments and nerves. The goals of ART include restoring normal mobility and gliding between muscular tissue and nerves. It can also help push joint fluid throughout the body and stimulate the lymphatic system, which helps lower inflammation.

Ultrasound

Ultrasound therapy is using ultrasonic waves or sound waves of a high frequency to stimulate tissues in the body. Ultrasound is applied using a round-headed wand or probe that is placed on a patient's skin. The ultrasonic waves are caused by the vibration of crystals within the head of the wand/probe. The sound waves that pass through the skin cause a vibration of the local tissues. Ultrasound gel is used in order to reduce friction and assist in the transmission of the ultrasonic waves. Ultrasound can also be applied under water. When done properly, ultrasound is not painful. Ultrasound is thought to improve healing through increases in tissue relaxation, local blood flow, and scar tissue breakdown. Phonophoresis is when ultrasound is used to help deliver topical medication. The medication gel is applied to the skin, and then the ultrasonic energy forces the medication through the skin.

Although ultrasound is a common modality used in physical therapy treatment, the evidence does not support the use of ultrasound as an effective treatment for pain.

Iontophoresis

Iontophoresis is a method of delivering medication using electrical stimulation. The electrical current is used to push ionized drugs through the skin's outermost layer. Different medications can be used depending on the purpose of the treatment. Iontophoresis is thought to decrease inflammation, decrease pain, decrease muscle spasm, decrease swelling and edema, reduce calcium deposits in the body and manage scar tissue. Iontophoresis is administered in a physical therapy clinic or the patient wears a small battery-operated patch for 24 hours.



Paraffin (wax)

A paraffin treatment uses warm oil-based wax most commonly used on the hands, elbows and feet to provide deep heat therapy. Liquefied paraffin wax is very efficient at absorbing and retaining heat. The affected body part is dipped into the paraffin and then removed to allow the paraffin to harden. This is repeated multiple times. The body part is then covered to maintain its heat. Paraffin provides the benefits of heat including increased blood flow, increased muscle flexibility and decreasing joint stiffness. Paraffin treatments also smooth and soften dry, chapped, rough and scaly skin. It can be helpful for chronic skin disorders such as eczema and psoriasis. Home units are available although one should always use paraffin wax heater which has automatic heat controller to maintain appropriate temperatures.

Infrared Light Therapy

Infrared Light therapy delivers light energy safely through the skin. The human eye can see a spectrum of light wavelengths. Light at longer wavelengths are no longer visible to the human eye and are called infrared. The longer the wavelength, the deeper it can penetrate into the body. Infrared Light therapy is thought to increase blood circulation, stimulate healing and reduce inflammation.

Spinal Traction & Spinal Decompression

Spinal Traction simply means providing a pulling force that provides a stretch to the spine. Traction is thought to decrease the intradiscal pressure to promote retraction of the herniated disc which would decrease the pressure on the adjacent nerve. However, muscles surrounding this area can contract as the body attempts to protect itself against the stretch, eliminating the benefit. Traction can be performed manually or with a machine. Spinal decompression claims to use computer-controlled force to achieve gradual and calculated increases in traction forces and angles to the spine that creates a vacuum action within the disc. The computerized decompression table continuously monitors spinal resistance and adjusts forces accordingly. The goal of treatment is to create a negative intradiscal pressure to promote repositioning of the herniated disc material and to cause an influx of healing nutrients and other substances into the disc.

Spinal Traction and Spinal Decompression have not been proven effective in treatment of pain. There is moderate evidence that home-based patient-controlled traction may be a noninvasive conservative option, if used along with other evidence-based conservative care.

Taping

Kinesiotape (KT) was originally developed to provide support for musculoskeletal structures without overly restricting them like other taping methods. Kinesiotape is made up of cotton fibers with polymer elastic strands and is lightweight with heat-sensitive acrylic adhesive. Clinicians that use the tape believe that it can improve blood and lymph flow, provide soft tissue and muscle support, allow for beneficial muscle activation and provide joint protection. Kinesiotape can be



applied in a variety of patterns on different body parts. The tape can remain on the skin for 3 to 5 days.

Despite the fact that the brightly colored Kinesiotape has been widely seen on Olympic and professional athletes, the scientific evidence for its use remains low. Kinesiotape may have a small beneficial role in improving strength, range of motion and fluid circulation in certain injured individuals, but multiple systematic reviews have found insufficient evidence to support the use of Kinesiotape for those following injury or those with chronic musculoskeletal pain.

Non-Elastic or Corrective Taping, often called McConnell Taping technique named after physical therapist Jenny McConnell who developed it, is characterized by tape with a combination of minimal elasticity and a high adhesive. Due to the highly adhesive backing of the tape (usually called Leukotape), a protective tape (usually called cover roll tape) is applied on the skin first. This type of taping technique is much more rigid and is used for structural support or alignment. McConnell taping is most frequently used for taping of the knee however the research is inconclusive for its benefit.

Manipulation & Mobilization

Spinal Manipulative Therapy (SMT) is a therapeutic intervention performed for what is described as “restricted joint(s)” in the spinal column.

Spinal manipulation is a historically recognized therapeutic intervention that has been employed in various cultures for thousands of years. In modern time, the procedure is utilized by Doctor of Chiropractic (DCs), Doctors of Osteopathy (DOs), and physical therapists (PTs). Chiropractors prefer the term "adjustment" whereas physical therapists apply the word "mobilization." Adjustment is described as a more specific type of SMT, often provided to address a specifically identified biomechanical fault.

Manipulation and mobilization are two types of manual (hands-on) therapies that include a wide array of different techniques and schools of thought. Traditional manipulation involves high force, high velocity, and low amplitude action (HVLA) forces with focus on moving a targeted, fixated or restricted joint(s). In general, mobilization involves assisted low force, low velocity movement often directed to one or more compromised vertebral segments and typically uses long lever arms to deliver the force. The term adjustment is commonly used a synonym for manipulation.

The effects of spinal manipulation include relief of acute and chronic back pain, improved spinal motion, and affecting the nervous system mostly at the local spinal level. There are research studies which support the benefits of SMT.

Overall, studies have shown that spinal manipulation can provide relief from acute and chronic low back and neck pain. SMT can be as effective, or more effective, than conventional medical treatments. In 2007 Guidelines, the American College of Physicians and the American Pain Society include spinal manipulation as one of several treatment options for practitioners to consider using when pain does not improve with self-care. Research studies have shown that spinal manipulation can be a more effective treatment for chronic back pain than bed rest, traction, topical



gels, or no treatment; some studies show superiority of SMT over acupuncture, physiotherapy, and school for low back pain.

Electrical Stimulation Devices (external)

Electrotherapy represents the therapeutic use of electricity and is another modality that can be used in the treatment of pain.

Transcutaneous electrotherapy is the most common form of electrotherapy in which electrical stimulation is applied to the surface of the skin. The earliest devices were referred to as TENS (transcutaneous electrical nerve stimulation) and are the most commonly used.

Interferential Current Stimulation (ICS) allows for deeper penetration of tissue, whereas TENS is predominantly a cutaneous or superficial stimulus. Interferential current is proposed to produce less impedance in the tissue, and the intensity provided is supposed to be more comfortable. Because there is minimal skin resistance with the interferential current therapy, a maximum amount of energy goes deeper into the tissue. It also crisscrosses, as opposed to the linear application of the TENS. This crisscrossing is postulated to be more effective because it serves to confuse the nerve endings, preventing the treated area from adjusting to the current.

Pulsed Electromagnetic Field Therapy (PEMF or PEMT) is a non-invasive treatment that creates micro-currents in the body's tissues through time-varying or pulsed electromagnetic fields. All cells produce electromagnetic fields and every organ in the body produces its own signature bioelectromagnetic field. As low frequency pulsed electromagnetic current passes through the body, it stimulates the electrical and chemical processes in the tissues. Therapeutic PEMFs are specifically designed to positively support cellular energy, resulting in better cellular health and function. PEMFs are believed to work to 1) Reduce pain, inflammation, and the effects of stress on the body; 2) Improve energy, circulation, blood and tissue oxygenation; 3) Improve tissue regeneration; 4) Accelerate repair of bone and soft tissue; and 5) Increase endorphin and serotonin release. Treatment times are typically 10-30 minutes and multiple areas can be treated at one time.

Diathermy uses high-frequency electric current to produce heat deep inside a targeted tissue. It can reach areas as deep as two inches beneath the skin's surface. The diathermy machine does not apply heat directly to the body. Instead, the waves generated by the machine allow the body to generate heat from within the targeted tissue. There are three main types of diathermy: shortwave, microwave, and ultrasound. Shortwave diathermy uses high-frequency electromagnetic energy, microwave diathermy uses microwaves and ultrasound diathermy uses sound waves. Heat is generated by the vibration of the tissue. This promotes blood flow into the area. Treating injuries with heat can increase blood flow which can accelerate healing. Treatment can also make connective tissue more flexible, minimize inflammation and reduce the incidence of edema, or fluid retention. There are risks to using Diathermy and you should consult a physician before use.



INVASIVE INTERVENTIONS

In general, interventions are meant to facilitate improved function and should be viewed as part of an overall rehabilitation treatment strategy combining behavioral and physical medicine approaches to pain management.

Dry Needling

Dry needling is a technique that uses a “dry” needle (meaning one that doesn’t release any medication). The needle is inserted through the skin into trigger points in muscle tissue. Trigger points can be tender to the touch and touching a trigger point may cause pain to other parts of the body. Dry needling is used to release the trigger points to relieve pain and tension or improve motion. Dry needling is also thought to normalize abnormal motor end plates (the sites that transmit nerve impulses to muscles). Dry needling can produce minor bleeding and some soreness but is a safe procedure when performed by a trained professional. Dry needling is not the same thing as acupuncture, a practice based on traditional Chinese medicine and performed by acupuncturists.

Trigger Point Injections

Trigger point injections are given to individuals with a myofascial pain syndrome, a regional painful muscle condition. These injections may provide short-term benefit only but are curative for some individuals.

A trigger point is a discrete focal tenderness located in a palpable taut band of skeletal muscle, which produces a local twitch in response to stimulus to the band. Trigger points may be present in up to 33-50 percent of the adult population. Myofascial pain syndrome is a regional painful muscle condition with a direct relationship between a specific trigger point and its associated pain region. These injections may occasionally be necessary to maintain function in those with myofascial problems when myofascial trigger points are present on examination.

Intra-Articular Steroid Injections

Invasive therapeutic interventions for osteoarthritis include steroid injections into the joint. Intra-articular steroids are effective for short-term (one to three weeks) pain relief but do not seem to improve function or provide pain relief for longer time periods. The number of steroid injections should be limited secondary to associated side effects including fat necrosis, loss of skin pigmentation, skin atrophy, avascular necrosis of the femoral head, Cushing’s disease, and in some cases, acceleration of joint degeneration. Following a steroid injection, the treated joint should be rested (limit its use) for a minimum of 24 hours in order to prolong and to improve effects on function and pain control.



Viscosupplementation

Viscosupplementation may be used for osteoarthritis (OA) of the knee. Viscosupplementation involves injecting lubricating substances (hyaluronic and hylan derivatives) into the knee joint. Proponents argue that viscosupplementation restores the lubrication of the joint, and as a result, decreases pain and improves mobility.

There are differences of medical opinions regarding use of viscosupplementation.

The American Academy of Orthopedic Surgeons (AAOS) does not recommend using hyaluronic acid for treatment of patients with symptomatic osteoarthritis of the knee (<http://www.orthoguidelines.org/guideline-detail?id=1214>).

The American College of Occupational and Environmental Medicine (ACOEM) states Intraarticular knee viscosupplementation injections are not recommended for treatment of moderate to severe knee osteoarthrosis based on a review of scientific evidence-based medicine research.

The American Medical Society for Sports Medicine (AMSSM) recommends the use of hyaluronic acid for patients above the age of 60 years with knee osteoarthritis. AMSSM feels that based on the response to those over 60, the evidence is moderate for those under 60. (http://journals.lww.com/cjsportsmed/Fulltext/2016/01000/AMSSM_Scientific_Statement_Concerning.1.aspx).

The American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee regarding the use of intraarticular hyaluronate injections states they are conditionally recommended in patients who had an inadequate response to initial therapy. <http://www.rheumatology.org/Portals/0/Files/ACR%20Recommendations%20for%20the%20Use%20of%20Nonpharmacologic%20and%20Pharmacologic%20Therapies%20in%20OA%20of%20the%20Hand,%20Hip%20and%20Knee.pdf>

Intraarticular hyaluronic acid treatment for knee osteoarthritis (OA) has a good safety profile and a moderately beneficial effect on symptoms similar to that observed with other pharmacologic modalities such as nonsteroidal anti-inflammatory (NSAIDs), according to a review by an international task force convened by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO).

Obviously, there is some controversy, but some orthopedists feel that viscosupplementation may provide some benefit short-term (weeks to months) for treatment of knee osteoarthritis; but the improvements in pain and function are not long-lasting.



Implantable Devices: Spinal Cord Stimulation & Implantable Drug Delivery System

For selected individuals with chronic pain, the health care provider may suggest an implantable device, such as a neurostimulator (also called a spinal cord stimulator) or a medication pump. A pain specialist is the best source for information regarding these devices, but the ACPA provides a video series with some basic information at <https://theacpa.org/pain-management-tools/videos/conditionstreatments/>

SPINAL CORD STIMULATION (SCS)

Neurostimulation therapy is delivered with a small device implanted under the skin, typically in the abdomen or buttock area. The neurostimulator generates mild electrical signals that are delivered to an area near the spine. The impulses travel from the device to this spinal area over thin insulated wires called leads.

Medical researchers are still investigating exactly how SCS controls pain and are considering multiple theories. The originally proposed mechanism of action of SCS is the “gate control theory.” This theory states that by providing a pleasant vibratory and touch sensation via the SCS system, pain signals that reach the brain are decreased.

The current SCS devices are programmable via a remote control that allows the patient to adjust the therapy within certain limits to help them receive the best pain relief each day, depending on his or her activity level or changes in pain during the day. It is not uncommon for patients being considered for a SCS to have a psychological evaluation as part of the overall evaluation process. The purpose of this psychological evaluation is to see if the person has any emotional or other difficulties that may adversely affect the surgery or recovery and to ensure the person has realistic expectations and goals for what can be achieved with the therapy. During the psychological evaluation, the person can expect to be asked questions about how the pain is currently affecting sleep, mood, relationships, work, and household and recreational activities. Some are also asked to complete paper-and-pencil tests. The results of this evaluation should be shared with the person with pain and the referring physician who will consider all the information to determine if SCS is an appropriate option.

Two stages are involved in SCS implantation. In both stages, a physician, guided by an x-ray, places a lead into the epidural space located within the bony spinal canal. The first stage is the trial phase, which provides information to predict the success of permanent implantation.

During the trial phase, one or two leads are placed via an epidural needle in the appropriate position. This is an outpatient procedure done under light sedation. Once the lead is in position, it is tested to see if the patient's painful area is covered with a tingling sensation (paresthesia). It is important that the patient is alert during the insertion and testing of the lead so he or she can inform the health care professional if the lead is in the appropriate position.

The lead is programmed with a computer. The patient then goes home for 3 to 5 days. He or she has an external power source and remote control that allows him or her to control the amount of



stimulation being received. During the trial, the patient should keep an activity record to determine if the treatment is helpful in relieving pain and improving function. At the end of the trial, the patient returns to the physician's office to discuss the results and have the lead removed.

Together, the health care professional and the patient decide whether or not to advance to permanent implantation. In this stage, the lead is again placed and implanted underneath the skin with a power source the size of a pacemaker battery. Either a rechargeable or non-rechargeable power source is implanted. For the non-rechargeable systems, the battery cannot be recharged and needs replacement every several years with a minor surgical procedure. The rechargeable system needs recharging when the power source runs low. While it typically lasts longer (up to 9 years) than a conventional system, eventually it will need to be replaced with a minor surgical procedure when it can no longer be recharged in a reasonable period of time. The SCS recipient goes home with a remote-control and battery charger (if they have a rechargeable battery). The patient is instructed to limit activity for about 12 weeks to allow for healing. Occasional re-programming will be needed to optimize coverage of the painful area.

The reader should understand that this discussion of SCS systems is limited. These devices are invasive and costly, and their use is limited to selected individuals as a treatment alternative for specific conditions after consideration of the risks, after failure of a reasonable trial of less invasive methods and following a successful temporary trial. There is some literature to suggest that in carefully selected patients, despite the initial cost, there may be long-term cost savings after a few years related to a reduction in the use of medications and other medical care services.

When utilized, spinal cord stimulation should be part of an overall rehabilitation treatment strategy combining behavioral and physical medicine approaches to pain management. Effectively treating pain by implanting an SCS system requires a responsive, long-term relationship between the person with pain and his or her health care professional. A significant advantage of a SCS system is that it is a reversible and nondestructive treatment option.

An important consideration is that the ability to obtain subsequent spinal imaging (such as an MRI) may be compromised after implantation of an SCS system. While some SCS systems are safe to use with MRI, others are not. Patients should discuss current and potential needs for MRI with their health care professional to ensure that they are being treated with a system that will meet their needs.

As with most treatments for chronic pain, it is important for the patient and health care provider to have realistic expectations regarding treatment, with the goal being pain reduction and control rather than complete elimination. It is also important for people with SCS to involve themselves in a multidisciplinary treatment plan if they are to get the best results. In appropriately selected individuals, SCS treatment can be a viable tool in a treatment plan and can significantly reduce pain and associated limitations.

In general terms, spinal cord stimulation is primarily suited to certain neuropathic and ischemic (loss of oxygenated blood flow) pain states. Currently, conditions that can respond favorably to



SCS treatment include:

- Failed back surgery syndrome with radicular symptoms
- Complex regional pain syndrome (previously known as reflex sympathetic dystrophy or RSD and causalgia)
- Peripheral neuropathic pain
- Peripheral vascular disease
- Ischemic heart disease

SCS has been proven to be effective for many of these conditions with lasting results in terms of pain relief, pain medication reduction, and improvement in quality-of-life indices and satisfaction scores. Although SCS can also be quite effective in relieving ischemic pain due to peripheral vascular disease and even coronary artery disease, these are currently not FDA-approved indications.

Potential complications that may occur include lead migration or fracture and infection. Lead migration after implantation may require revision surgery to regain appropriate coverage. An infection of any kind requires an immediate assessment by the physician. An unrecognized and untreated infection around the hardware can progress to more serious complications such as an epidural abscess or meningitis. There may also be limited access to imaging with MRI after implantation of such devices. More information available on ACPA website video or at <https://theacpa.org/pain-management-tools/videos/conditionstreatments/>

IMPLANTED INTRATHECAL DRUG DELIVERY SYSTEMS (PAIN PUMPS)

Unlike medications that circulate through the body and in the bloodstream, programmable intrathecal (injection into the sheath surrounding the spinal cord) drug delivery systems release medication directly into the fluid surrounding the spinal cord, which may lead to fewer or more tolerable side effects, and in some instances, is the only route possible for certain drugs.

Intrathecal Drug Delivery is an FDA-approved pain therapy for people who have not had success with other chronic pain treatments and meet the criteria for implantation. Intrathecal therapy has been used in long-term pain management for carefully selected patients with failed back surgery syndrome, complex regional pain syndrome, spinal stenosis, osteoporosis with compression fractures, pancreatitis, phantom limb pain syndrome, peripheral neuropathies, and in cancer pain.

With Programmable Intrathecal Drug Delivery Therapy:

- Pain medication is delivered via a drug pump directly to the fluid around the spinal cord in an area called the intrathecal space.
- The drug pump is connected to a thin, flexible tube called a catheter.
- Both the pump and the catheter are surgically implanted under the skin.
- Pain medication is dispensed according to instructions programmed by the physician, which allows noninvasive changes in dose and drug infusion patterns.



The reader should understand that this discussion of programmable, targeted implanted drug delivery systems is limited to a general overview. More information can be found in the anesthesia and pain medicine literature.

These systems are invasive and costly, and their use is limited to select individuals who find oral opioids beneficial but cannot tolerate the side effects and as a treatment alternative for specific conditions after consideration of the risks, after failure of a reasonable trial of less invasive methods and following a successful temporary trial. There is some literature to suggest that in carefully selected patients, despite the initial cost, there may be long-term cost savings after a few years related to a reduction in the use of oral medications and other medical care services.

A psychological evaluation of the person being considered for an intrathecal pump is usually recommended as part of the overall evaluation process. These are often done by a psychologist or psychiatrist. The purpose of the evaluation is to see if the person with pain has any emotional or other difficulties that may adversely affect the surgery or recovery and to ensure the person has realistic expectations and goals for what can be achieved with the therapy. During the psychological evaluation, the person with pain will be asked questions about how the pain is currently affecting sleep, mood, relationships, work, and household and recreational activities. Some may also be asked to complete paper-and-pencil tests. The psychologist or psychiatrist should share the results of this evaluation with the person with pain and with the referring physician who will consider all the information to determine if an intrathecal pump is an appropriate option.

A decision to proceed with an implanted drug delivery system should include:

- Failure of a reasonable trial of other conservative treatment modalities (medication, surgical, psychological, or physical);
- Intractable pain secondary to a disease state with objective evidence of pathology;
- Documentation that further surgical intervention is not indicated;
- Psychological evaluation has been obtained and evaluation states that the pain is not primarily psychological in origin and that benefit can be anticipated with implantation despite any psychiatric comorbidity;
- No contraindications to implantation exist such as body size too small to hold the pump; presence of spinal anomalies that may complicate the implantation and fixation of a catheter; the pump cannot be implanted 2.5 cm or less from the surface of the skin; or, presence of known or suspected meningitis, ventriculitis, skin infection, bacteremia, and septicemia;
- A life span of at least 3-6 months; and
- If the above criteria are met, a successful temporary trial of spinal (epidural or intrathecal) medications must be achieved prior to implantation as defined by a significant reduction in pain and improved function and associated reduction in oral pain medication use.

Opioids (e.g., morphine) are the most common medications delivered by intraspinal infusion. Other medications (e.g., bupivacaine, clonidine, and baclofen) may be added to opioids, particularly in patients with nerve injury pain states (neuropathic pain).



Just as when one is taking opioids orally or transdermally, the doses of intraspinal opioids should be limited to the lowest possible dose required to achieve pain relief and increased function, as complications can occur with any dose of opioids regardless of the route of delivery.

As with any opioid, constipation, urinary retention, nausea, vomiting, and pruritus (itchiness) are typical early adverse effects of intrathecal morphine and are readily managed symptomatically. Other potential adverse effects include amenorrhea, loss of libido, edema, respiratory depression, and technical issues with the intrathecal system with component failure and need for replacement.

Intrathecal Drug Delivery is an invasive treatment and risks of implantation can include infection, bleeding, headache, allergic reaction, spinal fluid leakage and paralysis.

High doses of intrathecally-administered morphine or opioid mixtures, including compounded drugs, have uncommonly been linked to the development of a chronic inflammatory or granulomatous mass (an abnormal tissue growth) at the tip of the catheter that can compress the spinal cord or associated nerve roots. Thus, vigilance is important just as is the case when one is taking opioids orally or transdermally. Patients on intraspinal morphine therapy should be monitored carefully by their health care professional for any new neurological symptoms because inflammatory mass can, in some cases, lead to neurological impairment, including paralysis. Even though a direct cause and effect relationship has not been established, the dose of continuously-administered intrathecal morphine should be limited to the lowest possible dose to achieve pain relief and increased function, as complications can occur with any dose of opioids regardless of the route of delivery.

Apart from morphine, chronic intrathecal infusion of preservative-free, sterile ziconotide solution is approved for the management of severe, chronic pain. Ziconotide (Prialt®) is a non-opioid analgesic reserved for patients who are refractory to or who cannot tolerate intrathecal morphine. Typical side effects include dizziness, nausea, vomiting, and states of confusion. Other potential adverse effects include psychosis, convulsions, rhabdomyolysis (muscle breakdown), and problems with the intrathecal infusion system. These side effects can be prevented entirely or may be well managed by raising the dose very slowly to achieve the right level of pain relief with the least amount of drug.

The only drugs that have been approved by the FDA for continuous intrathecal use with implanted intrathecal delivery devices include ziconotide, morphine, and baclofen.

The FDA has recently advised that other medications (e.g., hydromorphone, bupivacaine, fentanyl, clonidine and compounded medications) are not approved for use in intrathecal pumps may increase risks of adverse effects and pump device failure.¹

¹ FDA alerts doctors, patients about risk of complications when certain implanted pumps are used to deliver pain medications not approved for use with the devices
https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625840.htm?utm_campaign=112718_PR_FDA%20warns%20about%20risks%20of%20using%20off-label%20medications%20in%20implanted%20pumps&utm_medium=email&utm_source=Eloqua



Epidurals, Nerve & Facet Blocks & Radiofrequency Ablation (Rhizotomy)

An epidural steroid injection involves the injection of steroid into the epidural space in the cervical spine (neck) or lumbar spine (low back). Sometimes, a local anesthetic (numbing medicine) may be injected with the steroid. The epidural space is located in the spine just outside of the sac containing the spinal fluid. Epidural steroid injections are often provided to individuals with herniated discs, degenerative disc disease, or spinal stenosis who have associated nerve pain in the arm or leg.

The steroids are injected into the epidural space in order to reduce inflammation in and surrounding the spinal nerve roots and adjacent tissues. By reducing inflammation and compression, the level of pain may be decreased. Epidurals are most useful in patients with acute nerve pain from the above conditions. A majority of individuals (80 to 90 percent) with acute low back pain and associated nerve pain will recover spontaneously within three months, therefore, these injections should be viewed as a way to facilitate earlier pain relief and return to function. These injections have not been demonstrated to provide long-term successful pain relief for people suffering solely from chronic (long-standing) back pain or chronic nerve pain.

Epidurals rarely provide long lasting benefit but may be useful in these chronic pain conditions to manage a flare-up. Some people who have residual pain after the first injection may receive a second epidural steroid injection. However, individuals who do not receive any relief from the first injection are unlikely to benefit from a second injection. Furthermore, the number of steroid injections per year should be limited in order to avoid side effects that may occur including osteoporosis (weakening of the bones) and avascular necrosis (bone cell death often seen in the hip). Diabetic patients receiving epidural steroids should monitor their blood sugars closely following the procedure since an elevation can occur.

Nerve and facet blocks use a combination of local anesthetic and steroid for diagnostic purposes to identify pain generators. These blocks can also be used therapeutically to “block” a painful condition. Unfortunately, these procedures do not provide lasting benefit and are best used as part of an overall treatment plan to relieve discomfort temporarily while the patient engages in an active rehabilitation program.

Radiofrequency ablation (rhizotomy) or lesioning involves inserting a probe to destroy the nerve that supplies the facet joint. The facet joint, a small joint that connects the back portion of the spine, can become arthritic and cause neck or back pain. Facet joints allow bending and twisting movements in the back and neck. These movements can be very painful and may limit daily activities in an individual with facet joint disease. People with lumbar (low back) facet joint syndrome often complain of hip and buttock pain, low back stiffness, and pain that is made worse by prolonged sitting or standing. People with cervical (neck) facet joint syndrome often complain of neck pain, headache, and/or shoulder pain. In addition, they will often have pain when they rotate or bend their neck.



In order to determine if facet joints are responsible for neck or back pain, medial branch blocks are performed. A medial branch block is a block that is performed under fluoroscopy (x-ray), and local anesthetic (numbing medicine) is injected on the nerves that supply the facet joint in the back or neck. Following the procedure, patients are asked to keep a pain diary in order to record any pain relief, the amount of pain relief, and for how long pain relief lasts. Based on the response to this block, it can be determined if the person is a candidate for medial branch radiofrequency ablation (rhizotomy). Patient selection is imperative for achieving successful results.

Following radiofrequency ablation, patients are often asked to resume physical therapy for flexibility and strengthening exercises. Radiofrequency usually blocks the signal for a prolonged period of time (six months to a year). Eventually, the nerve grows back and can allow the pain signal to be transmitted again. If this happens, the procedure can be repeated. This procedure often does not relieve all back pain, but it relieves the pain associated with facet joint arthritis.

Denervation of the spinal muscles is possible with rhizotomies, thus repeated rhizotomies can cause atrophy of these muscles and lead to other untoward effects.

As with any procedure, there are certain risks involved which should be discussed with a treating physician. In order to achieve optimal results, it is important that these interventions be incorporated into a multidisciplinary treatment plan.



MEDICATIONS

How Medications for Pain Can Help & Harm

The use of analgesics (pain relievers) and other medications is a common method of chronic pain treatment. Pain medications can be helpful for some patients with chronic pain, but they are not universally effective. It is important to remember that each person may respond in a different manner to any medication.

Many people with chronic pain can manage adequately without medications and can function at a near-normal level. Others find that their overall quality of life, in terms of comfort and function, is improved with medications.

The use of any treatment, including medications, is judged by efficacy – does the benefit exceed the risk/harm? When all is said and done, is the individual better off for having undergone the treatment? This is not as simple as it sounds. For example, a medication may be successful in partially providing pain relief but may have a side-effect such as weight gain or mild loss of mental sharpness – Whether the side-effect is worth the benefit is totally individual specific.

It is important also to understand that even the most potent medications used for pain rarely completely eliminate pain but rather, may reduce its severity. As such, medications are rarely adequate alone and should be considered as an optional part of a comprehensive approach to pain management and functional improvements.

While medications can help relieve symptoms, they also can cause unpleasant side effects that at a minimum can be bothersome and at their worst can cause significant problems including death. These side effects can often be avoided or at least managed with the help of a health care professional.

It is important that the health care professional be aware of all prescription medications, over-the-counter (OTC) medications, and fitness, nutritional and herbal supplements that are being taken for general health or for pain or other medical conditions to ensure these are being taken appropriately and safely and that they do not interact with other prescribed medications or therapies. Some substances and drugs may cause serious side effects if they are combined with other medications. Even OTC and herbal preparations have possible side effects and the potential to cause serious interactions with other nonprescription and prescription medications and with each other. These include various OTC supplements and vitamins, homeopathic remedies, items grown in a home garden or bought in a store, and other “substances” such as caffeine, alcohol, tobacco, grapefruit (especially dangerous in combination with a benzodiazepine medication), and even marijuana and illicit drugs.



It is strongly advised that all current medications in the original bottles or boxes or tubes and other items that are active (including non-prescribed medications, vitamins and supplements) be taken to any appointments with the health care professional. It is essential that the health care professional be told about all substances that are being taken (even if they are not legal) or if obtained from someone other than the prescriber. Even medications that may be used only occasionally such as cough and cold medications can have significant medication interactions.

People with any medical condition including pain should keep a list of all their medications in their wallet or purse. This list will be useful in an emergency.

All opioid medicines and other controlled substances should be locked (in medication safe or other locked compartment) to prevent diversion or unintended intake by children or others.

All medications should be safely disposed of when no longer needed.

The U.S Drug Enforcement Agency (DEA) sponsors National Prescription Drug Take Back Days; local communities may also hold their own take back program. The DEA website (https://www.deadiversion.usdoj.gov/drug_disposal/takeback/index.html) provides information regarding dates, times and locations for this program.

Please discuss questions regarding drug disposal with your pharmacist. Some pharmacies have mail-back programs and disposal kiosks for unused medicines.

The FDA website also provides comprehensive guidance to dispose of medications at home (<https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm>)

The FDA recommends two ways to dispose of medicine, depending on the drug.

Disposing of medicines in household trash: Prescription and over-the-counter (OTC) drugs, liquids, drops, patches, creams, and inhalers can be thrown into your household trash.

Medications should be mixed with something undesirable, such as used coffee grounds, dirt, or cat litter. This makes the medicine less appealing to children and pets and unrecognizable to someone who might intentionally go through the trash looking for drugs.

This mixture should be placed into something you can close (a re-sealable zipper storage bag, empty can, or other container) to prevent the drug from leaking or spilling out before placing in the garbage.

The FDA also advises to scratch out all your personal information on the empty medicine vials to protect your identity and privacy prior to disposal.

Flushing medicines: Because oral and patch formulations of opioid medications could be especially harmful to others, there are specific directions to immediately flush them down the sink



or toilet when they are no longer needed. The FDA provides a list of these medications at the following website:

<https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm576167.htm>

Individuals who take medications should know what medications they are taking, why they are taking them, when they are taking them, how they are to take them, which should be taken every day, and which should be taken just when needed. Optimal pain relief depends on knowing how much and how often each medication should be taken and whether to take the medication before, with, or after meals or at bedtime. Medications can be confusing, especially if taken for more than one condition. The type of medication and dose may vary depending on the medical condition, body size, age, and any other medications that are taken. It is important to understand the potential side effects of the medications and how these can be prevented or managed effectively. Because of the possibility of interactions between drugs, some medications should not be taken together or should be taken at different times during the day to avoid unwanted reactions. This information can be obtained by reading the labels on the medication containers and/or asking the health care professional or pharmacist. If you are already taking prescription medications, do not take any OTC medication without consulting your health care professional.

The ACPA has a MedCard for keeping track of medications which can be found at https://www.theacpa.org/wp-content/uploads/2017/08/acpa_wallet_card2906.pdf

The FDA also offers “My Medicine Record” which can be completed and updated on-line at the following website:
<https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM095018.pdf>.

A Drug Interactions Checker is available at http://www.drugs.com/drug_interactions.php. Any concern for drug interactions should be discussed with your pharmacist or health care provider.

The label on the medication bottle may show a brand name (for example, Tylenol®) or the generic name (for example, acetaminophen) or both. It is often less expensive to buy medications by their generic name rather than by the brand name. The health care professional can be asked to prescribe generic rather than brand-name drugs to hold down the cost of prescription medications. The color and shape of the pill may be different, but FDA-approved generic drugs are considered to be interchangeable with brand name drugs. Generic drugs are required to show the same quality and effectiveness as brand name drugs before they are approved by the FDA. Any noticeable differences in the response to a drug if switching from one drug to another or a brand drug to a generic drug should be discussed with a health care professional. It is essential that the dose and directions written on the medication label be followed. The dose should not be changed without consulting the health care professional and medications that have been prescribed for someone else should never be taken.



If Medications Are Not Relieving Pain

Successful treatment can reduce a person's distress and restores health, function, and well-being so he or she can resume full participation in everyday life (although adjustments may need to be made).

If an individual has been taking pain medicine every day for a long time and it doesn't seem to reduce pain and allow the person to be more functional, the treatment plan should be re-evaluated. Often a treatment is unsuccessful because it needs to be changed.

It is important to periodically evaluate the big picture and ask how life is going overall. Even if months or years have passed, people with pain should tell their health care professionals whether they have regained the ability to engage in and enjoy everyday life activities. If not, it is time to discuss how to change the treatment plan. A minor tweak may be all that is needed but often bigger changes such as a more comprehensive approach may be required.

There are many other methods for pain relief besides pain medications. Symptoms can usually be greatly relieved by learning and strengthening self-care skills. Although some self-care methods can be self-taught, they often require instruction and supervision by an experienced peer or professional at the beginning.

Multidisciplinary pain programs and organizations like the ACPA teach many specific self-care techniques that can help to reduce pain. Mastering them may allow the person with pain to find relief and minimize the things that often make pain worse, such as stress, inactivity, uncertainty, feeling powerless, being out of shape, lack of sleep, boredom, fear, and anger, which are all normal human reactions to pain and life disruption.

According to scientific studies, there are several non-invasive medical treatments that often work as well or better than pills, patches, injections, and surgery. These treatments usually have fewer side effects, are less hazardous, and are more likely to restore a satisfying everyday life. A health care professional may be able to prescribe these treatments to help relieve the pain while the patient learns the self-care approaches that can help get life back on track.

Changing or discontinuing medications should always be done under the direction of a health care provider because it can be dangerous as well as uncomfortable to stop some medications too rapidly and without medical supervision. This is particularly true in those taking high doses or more than one medication. See the next section on "Tapering/Weaning Off Pain Medications."



Warning about Internet Medication Purchases

Buying medication over the Internet may seem like a good way to save money, but up to 96 percent of online drugstores don't meet U.S. pharmacy laws or practice standards. Standards for protecting the public are available from the National Association of Boards of Pharmacy (NABP - <http://www.nabp.net/>).

Internet sites may purport to be legitimate or in a country with drug laws comparable to the United States (e.g., Canada) but may (a) not be located in that country; (b) be located in that country but dispense prescriptions from another country that has no comparable law; (c) not handle and store medicines in a manner that maintains potency and shelf life; or (d) purchase medicines from dubious sources, including knowingly or unknowingly selling counterfeit medicines that may contain amounts of the expected pharmaceutical ingredients that vary from those stated, may contain other unnamed pharmaceutical ingredients, may contain no active pharmaceutical ingredients, or may contain toxic chemicals or microbial contaminants.

Patient Tips for Safe Medication Purchasing*

1. Purchase all medications from state-licensed pharmacies located in the United States.
2. When purchasing medications from online pharmacies, perform the following checks:
 - a. Ensure that the retailer is in good standing and is licensed to dispense medications in the United States. A pharmacy's status can be verified by contacting the appropriate state board of pharmacy or the National Association of Boards of Pharmacy (NABP) at <http://www.nabp.net> or calling 1-847-391-4406.
 - b. Examine the site to see if it has posted the Verified Internet Pharmacy Practice Sites (VIPPS) Accreditation Program seal of approval. The NABP established VIPPS to ensure that online pharmacies meet all appropriate state and federal regulatory and licensing requirements for proper operation. A list of VIPPS approved pharmacies can be found at <http://www.vipps.info>.
 - c. All legitimate online pharmacies will:
 - i. Make available a licensed pharmacist to answer any medication related questions you may have.
 - ii. Require a prescription from a physician or other licensed health care professional who can prescribe medications.
 - iii. Provide accurate contact information for customer inquiries.
 - d. Notify the FDA about problematic websites at <http://www.fda.gov/Safety/ReportProblem/ucm059315.htm>.
3. Be familiar with all your medications, especially their physical characteristics such as size, color, shape, smell, hardness, taste, or texture. Speak with your pharmacist immediately if anything appears suspicious after refilling a medication.
4. Be observant for any altered or open medication containers, variations in packaging, raised or hazy printing, flat printing (instead of imprinting or embossing), missing expiration dates or lot numbers on the package, or sticky residue on the container. All are signs of potential package tampering.
5. Carry a list of all medications you currently take (prescription, over-the-counter, herbal, dietary, and vitamin) with you when you visit your doctor or pharmacist so that they can screen for appropriate use and drug-drug interactions. Keep this list on your person at all times.
6. Be proactive. If you have questions about your medications, ask your pharmacist or physician.



* Federal Food and Drug Administration (FDA):

- Buying Medicines Over the Internet: Available at <http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/buyingmedicinesovertheinternet/default.htm>
- Buying Prescription Medicine Online: A Consumer Safety Guide. Available at <http://www.fda.gov/Drugs/ResourcesForYou/ucm080588.htm>

Biosimilar and Interchangeable Medications

Biological products are regulated by the Food and Drug Administration (FDA) and are used to diagnose, prevent, treat, and cure diseases and medical conditions.

There are two new types of biological products - biosimilar and interchangeable.

A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared.

Biosimilars are a type of biological product that are licensed (approved) by FDA because they are highly similar to an already FDA-approved biological product, known as the biological reference product, and have been shown to have no clinically meaningful differences from the reference product.

An interchangeable biological product, in addition to meeting the biosimilarity standard, is expected to produce the same clinical result as the reference product in any given patient.

Biosimilars have no clinically meaningful differences in terms of safety and effectiveness from the reference product to which they were compared. In addition, a biosimilar needs to have the same mechanism of action as the reference product to which it was compared, which means it will work in the same way as the reference product.

The FDA will only approve a biosimilar product if it has the same mechanism of action, route of administration, dosage form, and strength as the reference product. Additionally, a biosimilar can only be approved for the indications and conditions of use that have been previously approved for the reference product.

A biosimilar product can be prescribed by a health care provider in place of the FDA-approved reference product. The health care professional must write the specific name of the product on the prescription if they want to prescribe the biosimilar.

An interchangeable biological product may be substituted for the reference product by a pharmacist without the intervention of the health care provider who prescribed the reference product. That means the patient may receive the interchangeable instead of the reference product, even if the health care provider writes the prescription for the reference product.



For more information about Biosimilar or Interchangeable Products, go to:
<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm>

Medication Identification

It is always very important to be able to visually identify medications. If a pill cannot be identified, it is best to contact a pharmacist for assistance.

Pill identification resources can be used to confirm that the medication is correct. The most definitive tool for identifying a pill is the imprint code that can be on one or both sides of the pill.

Drugs.com has a Drug Pictures Database at:
http://www.drugs.com/pill_identification_drug_picture.html

Drugs.com also has a Pill Identifier at http://www.drugs.com/pill_identification.html where there is a Pill Identification Wizard. After clicking on “I Agree,” the drug name, imprint(s), shape, or color can be typed in.

DailyMed provides trustworthy information about marketed drugs in the United States. DailyMed is the official provider of FDA label information (package inserts). This website provides a standard, comprehensive, up-to-date, look-up and download resource of medication content and labeling found in medication package inserts. The website can be found at <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

The National Library of Medicine of the National Institutes of Health provides the following PILLBOX website and can be used to find rapid identification and reliable information regarding medications. Pillbox's image explorer is a photo album for pills. The website can be found at <https://pillbox.nlm.nih.gov/index.html>.



Medication Side Effects, Drug Allergies & Drug Interactions

Consumers and health care professionals can now go to a single web page on the U.S. Food and Drug Administration's website to find a wide variety of safety information about prescription drugs titled Postmarket Drug Safety Information for Patients and Providers at <http://www.fda.gov/Cder/drugSafety.htm>.

MEDICATION SIDE EFFECTS

Every person is unique in how they respond to a particular medication. Side effects are not uncommon but can usually be managed or tolerated. However, some side effects may be harmful to health or even life-threatening. It is important to notify a health care professional of any medication side effects.

When taking any medicine, it is important to be aware of any change in the body and to tell a health care professional if something unusual happens.

It may be hard to know if an adverse reaction is caused by a medical problem or by a medicine. The health care professional will want to know all medications that are being taken, when the symptoms started, and whether they are different from other symptoms that have occurred from an illness.

The following are some common adverse drug reactions that might be noticed (this list is not all-inclusive):

- | | |
|---|--|
| <input type="checkbox"/> Skin rash | • Diarrhea or constipation |
| <input type="checkbox"/> Itchiness (pruritus) | • Drowsiness |
| <input type="checkbox"/> Headache | • Confusion, mental/behavioral changes |
| <input type="checkbox"/> Dry mouth | • Anxiety |
| <input type="checkbox"/> Easy bruising or bleeding | • Breathing difficulties |
| <input type="checkbox"/> Edema (swelling) | • Abnormal heartbeat |
| <input type="checkbox"/> Stomach distress - pain, nausea/vomiting | • Increased blood pressure |
| | • Urinary retention |

DRUG ALLERGIES

Drug allergies should be documented appropriately in the medical record and should include a description of the reaction. Some medications can trigger an immune response in individuals with a drug allergy. In other cases, as in a type of reaction to drugs such as aspirin or niacin, allergy-like symptoms may occur but do not involve the immune system. Like many other allergies, a drug



allergy can cause a range of responses from a mild rash to life-threatening effects on many body systems.

When reviewing drug allergy information with the health care professional, it is important to differentiate drug intolerance or side effects (e.g., stomach upset) from true allergic reactions.

Some pain medicines such as opioid analgesics (e.g., morphine and meperidine) can stimulate histamine release that may seem like an allergic reaction. Common symptoms include lightheadedness, dizziness, a fast heart rate, facial flushing, sweating, or itching. In some cases, the symptoms can be treated with an antihistamine and the opioid analgesic can be continued. If symptoms are severe, an opioid that is not associated with histamine release or a non-opioid alternative may be substituted.

Allergic reactions to drugs can occur within hours or days to as much as three weeks after drug treatment is started. The person with an allergy may experience itching, welts, swelling, and wheezing. An uncommon effect of drug allergy is a life-threatening reaction called anaphylaxis, which is a severe whole-body allergic reaction. Symptoms of anaphylaxis develop very quickly, usually in a matter of minutes. Symptoms may include abdominal pain or cramping, anxiety, confusion, difficulty breathing, dizziness, hives/itchiness, nausea/vomiting, skin redness, slurred speech, and wheezing.

It is important to notify the health care professional immediately or possibly seek emergency medical help depending on the symptoms.

More information about drug allergies can be found at the Mayo Clinic web site at

<http://www.mayoclinic.org/diseases-conditions/drug-allergy/basics/definition/CON-20033346>

Other sources of information include emedicinehealth at

<https://www.emedicinehealth.com/search/emh/allergies>

or on the American Academy of Allergy, Asthma & Immunology (ACAAI) website at

<http://acaai.org/allergies/types/drug-allergies>

DRUG INTERACTIONS

A drug interaction occurs when the amount or the action of a drug is altered by the administration of another drug or multiple drugs. It is wise for individuals to try to use the same pharmacy for all their prescriptions so that the pharmacist can screen health information and current medications to prevent drug interactions. Drug interactions will be discussed in later sections that are more drugs specific.



OFF-LABEL MEDICATION USE

Prescription medications are often used for conditions not listed on their FDA-approved labels. This is called off-label use of the medication. It is legal for health care professionals to use a medication “off-label,” but the insurer, health plan, or pharmacist may question its use as recommended by the health care professional. Ask the health care professional to explain that the medication is being prescribed off-label and for what reason.

A medication is used off-label when the health care professional prescribes that medication for a medical use or a diagnosis other than the one that received FDA approval or for a dose or dosing schedule that differs from the approved label. Off-label prescribing is a commonly used and accepted medical practice. These medications do have FDA approval, but for a different use. For example, health care professionals frequently prescribe FDA-approved anticonvulsant medications for persons who do not have seizures, but who may have nerve related pain or an antidepressant to help with sleep; or prescribe an antihistamine to reduce anxiety.

Medications can have more than one effect. Because of this, a medication may be used for a variety of unrelated conditions. For example, aspirin is used to reduce inflammation and pain in arthritis but is also used as a blood thinner to prevent heart attacks. Thus, it may be confusing to think of aspirin as an “arthritis” or “pain” medicine alone.

Similarly, many of the medicines used to treat chronic pain were originally designed and marketed for unrelated conditions such as seizures, irregular heartbeat, and depression. The fact that a health care professional recommends such a medication for pain treatment does not mean that the person with pain has epilepsy or some other condition. The same is true with antidepressants; the fact that they are prescribed for chronic pain does not mean that the health care professional has made a diagnosis of depression.

The FDA (<http://www.fda.gov>) allows medications to be sold and advertised for specific conditions where data prove the drug is safe and effective for its intended use. Once on the market, medications can be prescribed for off-label usage for any condition, particularly those with clinical data supporting effectiveness. The process of obtaining FDA-approval for another use of the medication can be costly, so a company may not be able to fund research studies to prove all the uses for a medication. This approval issue is especially true if the medication is no longer protected by a patent and other companies can sell it.

Further discussion about off-label medication use can be found at <https://www.fda.gov/forpatients/other/offlabel/default.htm>

and on WebMD at <http://www.webmd.com/a-to-z-guides/features/off-label-drug-use-what-you-need-to-know>



Clinical Trials

Clinical Trials (see <http://clinicaltrials.gov> for more information) are health-related medical research studies in human beings that follow a pre-defined plan. Choosing to participate in a clinical trial is an important personal decision. It is often helpful to talk to a physician or other health care professional, family members, or friends about deciding to join a trial. The results of the clinical trial may lead to new treatments or therapies becoming available for many people coping with chronic pain.

Information about Learn About Clinical Studies can be found at <http://clinicaltrials.gov/ct2/about-studies/learn>

The Clinical Trials Transformation Initiative (CTTI) is a public-private partnership to identify practices that will increase the quality and efficiency of clinical trials at <http://www.ctti-clinicaltrials.org/> states that it is “Here to identify and promote practices that will increase the quality and efficiency of clinical trials.”

Medication Assistance Programs

There are many programs that help people in need get access to their prescription medicines at a savings or even for free. There are more than 475 public and private patient assistance programs offering access to over 2,500 brand name and generic medications for free or at a low cost. Pharmaceutical companies offer nearly 200 of these programs. To learn about programs that might be able to help you, you can either try visiting the website of the pharmaceutical company that makes your medicine. Alternatively, you can also visit the following websites which provide links to the assistance programs available for many medicines. You will need to enter in the name of your medicine and answer a few other questions, and then you will be connected to the programs that might be able to help you.

- ❑ The Partnership for Prescription Assistance. <https://www.pparx.org/>
- ❑ NeedyMeds: <http://www.needymeds.org/>



MEDICATION TYPES FOR THE TREATMENT OF PAIN

There are four major types of medications used in the treatment of chronic pain:

1. **Non-opioids:** Aspirin (ASA), nonsteroidal anti-inflammatories (NSAIDs), and acetaminophen.
2. **Opioids:** Examples of opioids include but are not limited to morphine, codeine, hydrocodone, oxycodone, and methadone. Tramadol and tapentadol are considered opioids since they are biochemically similar and work on the same receptors.
3. **Adjuvant analgesics:** Medications originally used to treat conditions other than pain but may also be used to help relieve specific pain problems; examples include some antidepressants and anticonvulsants.
4. **Other:** Medications with no direct pain-relieving properties may also be prescribed as part of a pain management plan. These include medications to treat insomnia, anxiety, depression, and muscle spasms.

Some medications are available over-the-counter (OTC) without a prescription, and some require a prescription.

Prescription medications are lawfully available only from a licensed professional. The individual should only use medication that was prescribed for him or her by such a professional.

Do not use, buy, or sell prescription drugs from family members, friends, or others. Not only is it dangerous to your health and life, but also you could face criminal prosecution for possessing prescription drugs without a prescription. Illegal distribution of prescription drugs, including sharing, is a Federal drug violation, punishable by up to five years in Federal prison. The consequences are more severe if the illegal distribution leads to injury or death. Federal law makes it illegal for any person who does not have a license to write prescriptions to sell or give a prescription drug to another person (21 U.S.C. § 841(a)).



Non-Opioid Pain Relievers

The two most common types of non-opioid pain relievers are acetaminophen and NSAIDs, including aspirin. These non-opioid analgesic pain relievers are effective for pain and fever. Aspirin and NSAIDs are also indicated for pain that involves inflammation, whereas acetaminophen does not have anti-inflammatory activity.

These non-opioid pain relievers can be purchased without a prescription over-the-counter (OTC) but also are included in many combination prescription pain relievers.

Acetaminophen is an active ingredient found in more than 500 OTC and prescription medicines, including pain relievers, as well as for pain relief and fever reduction in cough suppressant and cold medication combinations.

NSAIDs are common medications used to relieve fever and minor aches and pains. They are found in over 900 medications; both OTC and via prescription. They include aspirin, naproxen, and ibuprofen. They can be found alone and in many OTC combination medicines taken for colds, sinus pressure, and allergies. They act by inhibiting an enzyme that helps make specific chemicals in the body responsible for pain and inflammation.

Over-the-Counter Medicines

OTC drugs are those drugs that are available to consumers without a prescription. A trip to the local drug store reveals numerous tablets, suppositories, patches, sprays, creams, lotions, and ointments, all with claims of providing pain relief.

The following article is from the FDA: **Educational Resources: Understanding Over-The-Counter Medicine** can be found at

<https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm277845.htm>.

The following Internet Link provides a good patient education handout regarding over-the-counter pain relievers to minimize toxicity:

<https://www.getreliefresponsibly.com/know-your-pain-medicines>

The traditional OTC pain group currently includes aspirin (e.g., Bayer®), acetaminophen (e.g., Tylenol®), naproxen (e.g., Aleve®), ibuprofen (e.g., Advil®, Motrin®IB), and various combinations. Most analgesic OTC drugs are based on one of these FDA-approved ingredients. Many manufacturers add other ingredients in an effort to tailor the medication to particular symptoms. For example, a pain reliever, such as acetaminophen, and an antihistamine, such as diphenhydramine (e.g., Benadryl®, Dramamine®, Sominex® and others) may be combined and sold as a nighttime pain and cold medication because the antihistamine induces drowsiness. Adding a decongestant makes a medication marketable for sinus problems.



When using OTC drugs, be aware that the brand name is often specific to the manufacturer and may not indicate the product's active ingredients. Look for active ingredients, usually listed by generic name, on the label. For example, this will provide information that Tylenol® PM not only contains acetaminophen but also contains diphenhydramine hydrochloride.

Some OTC medications are labeled “extra strength.” This usually indicates that the item contains more amounts (e.g., milligrams) of drug per dosage unit (e.g., tablet) than the standard product by the same manufacturer.

The key to the effective use of OTC medications is to understand the drug(s) that is/are taken and the maximum safe dosage of all ingredients. This requires reading the medication label and/or discussing OTC medications with the health care professional or a pharmacist before taking them, especially if prescription medications are also taken. The selected OTC medication should contain an appropriate amount of the drug needed to treat the symptom(s) and should not include medications or ingredients that are not needed.

OTC medications rarely cause significant health problems when used occasionally. In certain situations, however, they can be dangerous. This is especially true if used in combination with prescription medications or in dosage amounts that are higher than recommended.

OTC pain medications can be useful and effective. Even though they are considered safe enough to be dispensed without a prescription, remember they are real medicines. There is often a mistaken belief that because the medication can be obtained without a prescription, it is safe under all circumstances of use and without potential for harm. Nothing could be further from the truth.

Further information about OTC medicines is provided by the American Academy of Family Physicians at:

<http://familydoctor.org/familydoctor/en/drugs-procedures-devices/over-the-counter.html>.

The following is a link to a patient education video on over the counter pain relievers; including safely taking and storing pain medications. <https://www.youtube.com/watch?v=jE0-r2APdc>

The Safety of Non-Opioid Pain Relievers

“The Food and Drug Administration (FDA) advises consumers to follow directions when using common pain and fever reducers. **Using more than recommended can cause serious injury.**” The active ingredients, acetaminophen and NSAIDs, are safe and effective when the label directions or the advice from a health care professional or pharmacist are followed. This is especially important when taking both OTC medications and prescription medications. “Using Acetaminophen and Nonsteroidal Anti-inflammatory Drugs Safely” can be found at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/SafeUseofOver-the-CounterPainRelieversandFeverReducers/ucm164977.htm>



Nonsteroidal Anti-Inflammatory Drugs

The NSAIDs (aspirin, ibuprofen, naproxen, and others) have a host of potential side effects. They can cause toxicity when taken for a prolonged period or when taken in excess, but even low or regular dose or short-term therapy is not without risk.

NSAIDs can cause gastric distress. They can reduce the stomach's protective mucous layer and natural protection against irritation of the stomach lining from stomach acid. They can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. The risk of bleeding increases with age, dose, use with certain medications (such as warfarin), and duration of use.

NSAIDs also may cause kidney failure in people with damaged kidneys, liver disease, and certain other conditions such as high blood pressure. Use with diuretics, commonly called “water pills,” can increase this danger. Finally, the use of these medications has been associated with increased risk of cardiovascular disease (CVD), particularly in patients with risk factors for CVD or a prior history of CVD. The risk of heart attack or stroke can begin in the first week of NSAID use and the risks may increase with longer NSAID use and higher prescription doses. Individuals with any of these conditions should check with their health care professional before taking any NSAID medication. The following ACPA video on this topic may be helpful; view at <https://www.theacpa.org/pain-management-tools/videos/conditiontreatments/>.

The American Heart Association (AHA) recommends health care professionals change their approach to prescribing pain relievers for patients with or at risk for heart disease. Research in the AHA journal *Circulation* found that heart attack survivors who take NSAIDs face a significantly increased risk of a second heart attack or death.

There are 2 types of NSAIDs; selective and nonselective inhibitors.

The cyclooxygenase-2 (COX-2)-selective inhibitors are NSAIDs that can be prescribed and have a lower risk of gastrointestinal (GI) side effects with short-term use. The only agent of this type currently available in the United States is celecoxib (Celebrex[®]), which is more expensive than most of the generic nonselective NSAIDs and has not been definitively proven to provide better pain relief. Although celecoxib is associated with a lower risk for developing a stomach ulcer when taken for less than 6 months, serious stomach ulceration can still occur without warning with this drug. This is especially true if taking a daily aspirin – even if low dose – for protection of the heart. As with other NSAIDs, individuals who take celecoxib should be monitored for this serious side effect. Additionally, all NSAIDs are associated with potential kidney effects and heart (cardiovascular) complications, especially when taken for prolonged periods. Remember also that when acetaminophen (Tylenol[®]) is used in combination with NSAIDs, there may be an increased risk of developing kidney problems. This effect is usually only seen with long-term use.



While the increased risk of cardiovascular events, such as stroke and myocardial infarction, associated with COX-2 inhibitors has been well established, data are emerging that demonstrate similar risk increases associated with NSAIDs that are not selective for COX-2. Currently, data show that celecoxib 200 mg or less per day does not seem to increase the risk of cardiovascular events any more than the risk associated with traditional (nonselective) NSAIDs used at prescription doses. Discussing the risk-benefit ratio of NSAIDs with a health care professional is advised. The risk of experiencing adverse events or side effects with NSAIDs increases with the duration of use and the dose. Therefore, it is often recommended that these medications be used for the shortest period and at the lowest dose required to achieve therapeutic improvement. Individuals taking aspirin for its ability to protect the heart should consult with their health care professional or pharmacist prior to utilizing non-ASA NSAIDs on a long-term basis. The regular use of non-ASA NSAIDs inhibits aspirin's ability to protect the heart.

In order to improve the side effect profile of NSAIDs, topical NSAIDs have been developed and approved by the FDA. It is important to discuss the use of any topical medications with your health care professional, especially if you are also prescribed oral medications as taking both is duplicative therapy and may increase the risk of side effects.

Diclofenac Products*: Diclofenac Gel (Voltaren® 1% Gel) has been approved for the treatment of chronic pain associated with osteoarthritis in joints close to the skin surface. In 2007, a topical NSAID patch containing diclofenac (Flector®) was approved by the FDA for the treatment of acute pain due to minor strains, sprains, and contusions. In 2009, the FDA issued an advisory that transdermal and topical patches that contain metal, which includes Flector®, need to be removed prior to MRI procedures. A topical solution of diclofenac sodium 2% (Pennsaid®) is approved for the treatment of signs and symptoms of knee osteoarthritis. Topical delivery of any NSAID products reaches lower medication blood levels compared to their oral counterparts, but still hold the same package insert warnings related to potential bleeding, heart, stomach, and kidney adverse events.

***Warning:** All Diclofenac products are not recommended as first line analgesics due to an increased risk profile for cardiovascular events (heart attack and stroke) and for increased risk of liver dysfunction (use has resulted in liver failure and death). With the lack of data to support superiority of oral diclofenac over other oral NSAIDs and the possible increased liver and cardiovascular risk associated with its use, alternative analgesics and/or non-pharmacological therapy should be considered.

Intravenous (IV) formulations of the NSAIDs ibuprofen (Caldolor®) and ketorolac (Toradol®) are given most often in the inpatient setting to manage short-term moderate-to-severe pain in adults; ketorolac may also be given intramuscularly (IM). IV ibuprofen is approved also for reduction of fever in adults. In November 2010, IV acetaminophen (Ofirmev®) was FDA approved for the management of mild-to-moderate pain, severe pain with adjunctive opioid analgesics, and reduction of fever in adults and children two or more years old. Similar to the IV NSAIDs, IV acetaminophen is administered in an inpatient setting for short-term pain management and helps reduce the amount of opioid medication needed to manage pain. The FDA has approved dosages of up to 4,000 mg per day of IV acetaminophen. The side effect profile for IV acetaminophen is the same as other acetaminophen dosage forms: headache, agitation, nausea, vomiting, and constipation. Injection site reactions such as redness and swelling may occur with any of the IV non-opioids.



Acetaminophen

Acetaminophen (the ingredient in Tylenol® and a number of other OTC pain and cold remedies) can be toxic to the liver, especially with heavy alcohol use or in those with liver problems, even at fairly low doses. The FDA also issued a warning for rare, but possible skin reactions: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP).

Since acetaminophen is contained in many prescriptions, individuals need to pay close attention to their total daily dose of acetaminophen.

The current recommendations are that self-treating users take only the recommended maximum daily dosage of 3,000 mg. Patients may take a higher daily dosage— up to 4,000 mg—if their health care professional instructs them to do so. The maximum daily dosage may be decreased for patients who consume alcohol or for those with elevations in liver enzymes.

For FDA Acetaminophen Information, go to

<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm>

Acetaminophen is an ingredient in many OTC and prescription medicines. Here are some - *but not all* - of the most common *OTC and prescription drugs* that contain acetaminophen. The amount of acetaminophen varies in combination products and it is important to note the amount of acetaminophen in each tablet so that accurate accounting of daily dosage can be made. Acetaminophen is in more than 600 prescription and over-the-counter medicines. When used as directed it's safe and effective but taking too much can lead to liver damage. Therefore, it is important to know your dose. <http://www.knowyourdose.org/>

Examples of Prescription Drugs with Acetaminophen*

- Acetaminophen and Butalbital (**Axocet®**)
- Acetaminophen and Codeine Phosphate Oral Solution and Tablets (**Tylenol® with Codeine**)
- Acetaminophen, Isometheptene, and Dichloralphenazone Capsules (**Midrin®**)
- Butalbital, Acetaminophen and Caffeine Tablets (**Esgic®**, **Fioricet®**, **Zebutal®**)
- Hydrocodone Bitartrate and Acetaminophen Tablets, Capsules, Elixir (**Lorcet®**, **Lortab®**, **Vicodin®**, **Vicodin ES®**, **Vicodin HP®**, **Norco®**, **Zydone®**, **Hydrocet®**, **Anexsia®**)
- Oxycodone and Acetaminophen Tablets, Capsules, Elixir (**Percocet®**, **Endocet®**, **Roxicet®**, **Tylox®**)
- Tramadol and Acetaminophen Tablets (**Ultracet™**)

Examples of OTC Drugs with Acetaminophen

- **Backaid®** Maximum Strength Backache Relief
- **Benadryl®** Allergy and Sinus Headache Caplets
- **Contac®** Day or Night Cold/Flu Caplets



- **CVS®** 8 Hour Acetaminophen Extended-Release Caplets/Cold and Flu Relief – Day- or Night-time Softgels/Infants’ Non-Aspirin Suspension Drops/Non-Aspirin Children’s Suspension/Non-Aspirin Extra Strength Gelcaps or Caplets/Sinus Headache Decongestant Caplets
- **Duane Reade®** Acetaminophen Tablets, Caplets, or Geltabs/Children’s Acetaminophen Elixir/Extra Strength Acetaminophen Gelcaps, Geltabs, Caplets, or Tablets/Extra Strength Acetaminophen PM Caplets or Gelatin Caplets/Infant’s Acetaminophen Drops
- **Excedrin®** Aspirin-Free Tension Headache/ Quicktabs Fast Dissolving Pain Reliever Tablets
- **FeverAll®** Infants’ or Children’s Acetaminophen Suppositories
- **HealthLine™** Acetaminophen Caplets Extra Strength
- **Inholtra®** Caplets with Acetaminophen
- **Legatrin®** Advanced Formula PM Pain Reliever-Sleep Aid Caplets
- **Pamprin®** Cramp Caplets/Multi-Symptom Caplets Maximum Strength
- **Percogesic®** Analgesic Acetaminophen Caplets Extra Strength/Analgesic Acetaminophen Tablets/Aspirin-Free, Pain Reliever, Fever Reducer Tablets
- **Premysyn®** PMS Maximum Strength Premenstrual Syndrome Relief with Acetaminophen
- **Rite Aid®** Children’s Acetaminophen, Non-Aspirin, Oral Suspension Liquid/Complete Allergy-Sinus-Headache Caplets/Extra Strength Acetaminophen/Extra Strength Acetaminophen PM/Infants’ Acetaminophen, Non-Aspirin, Suspension Drops/Non-Aspirin, Non-Drowsy Sinus Formula Geltabs Pain Reliever Nasal Decongestant
- **Robitussin®** Robitussin Cold, Cough and Flu, Multi-Symptom Cold, Nasal Congestion, Cold+Flu Daytime, Cold+Flu Nighttime
- **Sudafed®** Sinus & Cold Liquid Capsules
- **Theraflu** Packets Severe Cold
- **Triaminic®** Cold, Cough and Fever
- **Tylenol®** 8 Hour Extended Relief/Allergy Sinus - Day or Night; Caplets, Gelcaps or Geltabs/Arthritis Pain Caplets/Chewable Tablets/Children’s Cold Plus Cough Liquid/Children’s Soft-Chews/Cold - Day or Night; Caplets or Gelcaps/Extended Release Caplets or Geltabs/Flu Gelcaps Day and Night/Infant Cold Drops/Junior Strength Soft-Chews or Chewable Tablets/Nighttime Liquid Severe Cold and Flu/PM Extra Strength/Severe Allergy Sinus - Day or Night/Sore Throat Maximum Strength Adult Acetaminophen Liquid
- **Vicks®** DayQuil LiquiCaps Non-Drowsy/DayQuil LiquiCaps or Liquid/NyQuil LiquiCaps or Liquid

Walgreens® Arthritis Pain Relief Extended-Release Caplets/Extra Strength Acetaminophen Caplets, Tablets, Gelcaps or Geltabs/Extra Strength PM Gelcaps or Caplets/Regular Strength Acetaminophen Tablets

Please visit the U.S. National Library of Medicine, MedlinePlus for an in-depth discussion about acetaminophen. This website for a comprehensive list of OTC and prescription medicines that contain acetaminophen: <https://medlineplus.gov/druginfo/meds/a681004.html#brand-name-1>.



NON-OPIOID ANALGESIC DRUGS & THEIR USES

The following chart summarizes the uses and cautions that apply to many of the non-opioid analgesic medications now on the market.

Medications (Generic) and Brand Names*	May Be Useful for	Pros	Cons	Comments
Aspirin Bayer® Bufferin® & other Salicylates	Headache, muscle ache, fever, menstrual cramps, arthritis pain, and inflammation. May reduce the risk of heart attack and stroke.	Anti- inflammatory; inexpensive.	May irritate stomach. Inhibits platelets and can cause prolonged bleeding. Can precipitate asthma in aspirin- sensitive patients.	May cause Reye's syndrome in children and teenagers and should not be used during viral syndromes; may be harmful for women in late pregnancy, people with kidney or liver disease, asthma, high blood pressure, or bleeding disorders.
Acetaminophen FeverALL® Tylenol®	Headache, muscle ache, backache, fever, and arthritis pain (especially osteoarthritis).	Gentler to the stomach than NSAIDs; does not promote bleeding (or protect against heart attack and stroke).	Does not reduce inflammation; may be less effective than aspirin for soft tissue pain.	May be harmful for those who drink alcohol heavily. Long term use or excessive dosing may be harmful for people with kidney or liver disease. May increase bleeding time in individuals receiving anti- coagulation therapy.
Ibuprofen Advil® Motrin®	Headache, muscle ache, fever, sprains, menstrual cramps, backache, and arthritis pain.	Stronger and generally longer lasting than aspirin.	May irritate stomach. Increased risk of serious gastro- intestinal adverse events. Serious risk of cardiovascular events.	May be harmful for people with kidney or liver disease, asthma, bleeding disorders, or those who drink alcohol heavily or are taking cardio- protective aspirin.



Medications (Generic) and Brand Names*	May Be Useful for	Pros	Cons	Comments
Ketoprofen Orudis® Oruvail®	Headache, muscle ache, fever, menstrual cramps, cold or flu aches.	Helps reduce inflammation. Gentler to the stomach than aspirin.	May irritate stomach. Increased risk of serious gastrointestinal adverse events. Serious risk of cardiovascular events.	May be harmful for people with kidney or liver disease or those who drink alcohol heavily. Not recommended for children without a health care professional's supervision.
Naproxen Sodium Aleve® (OTC) Anaprox® Naprelan® Naprosyn®	Headache, muscle ache, fever, menstrual cramps, backache, arthritis pain, and inflammation.	Stronger and generally longer lasting than aspirin for menstrual cramps, toothache, and inflammation.	May irritate stomach. Increased risk of serious gastrointestinal adverse events. Serious risk of cardiovascular events.	Cons and comments are similar to ibuprofen. Not recommended for children without a health care professional's supervision.
Meloxicam Mobic® Vivodex®	Arthritis pain	Associated with less risk of ulcers vs. other NSAIDs.	May irritate stomach. Increased risk of serious gastrointestinal adverse events. Serious risk of cardiovascular events.	Generally well- tolerated but still need to be concerned about GI side effects.
Celecoxib (a COX-2 Inhibitor) Celebrex®	Muscle aches, joint pain, arthritis pain, and inflammation.	Helps reduce inflammation; less stomach irritation vs. other NSAIDs.	May irritate stomach. Increased risk of serious gastrointestinal adverse events. Serious risk of cardiovascular events.	Generally well- tolerated but still need to be concerned about GI side effects. No effect on bleeding time. Use caution with sulfa allergies and celecoxib.

Other NSAIDs include the following:

- Diclofenac (Cataflam®, Voltaren®, Zipsor®, Zorvolex®, others) – see comments below
- Diflunisal (Dolobid®)
- Etodolac (Lodine®, Lodine® XL)
- Fenoprofen (Nalfon®)
- Flurbiprofen (Ansaid®)



- Ibuprofen (Caldolor[®]) - NSAID available intravenous for acute pain and fever
- Indomethacin (Indocin[®], Indocin[®] SR, Tyvorbex[®])
- Ketorolac (Toradol[®], others) – Oral, intranasal and injectable – 5-day use only in adults
- Mefenamic acid (Ponstel[®])
- Nabumetone (Relafen[®])
- Oxaprozin (Daypro[®])
- Piroxicam (Feldene[®])
- Sulindac (Clinoril[®])
- Tolmetin (Tolectin[®])

* Brand names are the trademarked property of the medication's manufacturer.

Diclofenac Warning: All oral diclofenac products are not recommended as first line analgesics due to increased risk profile for cardiovascular events (heart attack and stroke) and for increased risk of liver dysfunction (use has resulted in liver failure and death). With the lack of data to support superiority of diclofenac over other NSAIDs and the possible increased hepatic and cardiovascular risk associated with its use, alternative analgesics (pain medications) and/or non- medication therapy should be considered.

Gastrointestinal (GI) Protective Medications

As mentioned earlier, the NSAID medications can increase the risk of ulcers and other stomach and digestion problems. Often people are prescribed an additional medication to help protect their GI system, sometimes called cytoprotective medications, which are medications that protect cells from noxious chemicals or other harmful stimuli.

Taking antiulcer agents along with an NSAID pain medication is recommended for individuals who will benefit from an NSAID but also have a high GI risk factor profile. Individuals considered being at elevated risk include those with a history of prior GI bleed/uncomplicated ulcer or H. pylori infection, the elderly, diabetics, cigarette smokers, and those with concurrent use of aspirin (including low dose), corticosteroids, or anticoagulants (blood thinners). Long-term NSAID treatment increases the risk among those most susceptible, although anyone can potentially develop an adverse effect at any time.

There are four commonly used antiulcer drug types:

- Proton pump inhibitors (PPIs): esomeprazole (Nexium[®]), lansoprazole (Prevacid[®]), dexlansoprazole (Dexilant[®]), omeprazole (Prilosec[®]), pantoprazole (Protonix[®]), and rabeprazole (Aciphex[®]). PPIs are more effective and longer lasting acid inhibitors than H2 receptor antagonists. There is an increased risk in individuals over 50 years of age of hip, wrist, and spine fractures amongst PPI users. Some scientific studies show evidence linking PPIs with cardiovascular disease. There has been concern expressed regarding increased risk of gastrointestinal infection due to decreased acid production.
- H2 receptor antagonists (H2RAs): famotidine (Pepcid[®]), nizatidine (Axid[®]), ranitidine (Zantac[®]), and cimetidine (Tagamet[®]). They are still used for treatment and maintenance therapy of peptic ulcer disease, treatment of gastroesophageal reflux disease, and management of dyspepsia. However, they achieve less acid suppression than proton pump



inhibitors. Many of the studies on H2 blockers show that they have negligible value in the protection of the gastric mucosa.

- Misoprostol (Cytotec®) - a prostaglandin analog which is effective in preventing NSAID-induced ulcers but has no established role for healing ulcers. Prostaglandins increase the contraction ability in the uterus, so females should not take misoprostol if pregnant or planning to become pregnant. More specifically the FDA states that misoprostol tablets should not be used for reducing the risk of NSAID-induced ulcers in women of childbearing potential unless the patient is at high risk of complications from gastric ulcers associated with use of the NSAID or is at high risk of developing gastric ulceration.
- Antacids containing aluminum and magnesium hydroxide or calcium carbonate (TUMS®) and sucralfate (Carafate®) have not been proven in the treatment of peptic ulcers. Sucralfate (Carafate®) works via interactions with hydrochloric acid found in the stomach and digestive tract. The combination forms a paste-like substance, which forms a protective coating that acts locally to protect the stomach and gastrointestinal tract lining.



Opioid Pain Relievers and Their Safe Use

The Opioid Dilemma

In any acute pain situation, opioids are not always necessary but with severe trauma and immediately post operatively, short-term use of opioid medications (3-5 days) is appropriate although side effects are most problematic when initiating treatment. With that said, some people though are more susceptible to misuse and abuse when started on opioids.

Prolonged use of opioids past a few weeks increases the possibility, over time, of adverse reactions such as dependence or even addiction, gastrointestinal distress including constipation, internal organ problems, balance troubles, hormone problems, sexual dysfunction, and memory and concentration problems. Furthermore, it has been shown that if opioids are used for more than 8 days, 13.5% will be on opioids at 1 year; 30% of persons taking opioids for more than 31 days are on them at 1 year. After prolonged use, an increase in pain sometimes occurs that is thought to be due to opioids causing changes in the peripheral and central nervous systems over time, a phenomenon referred to as opioid-induced hyperalgesia.

Regarding the treatment of chronic pain, considerable controversy exists about the use of opioids for long-term treatment. While there remains a place in the treatment of pain with opioids, **the weight of scientific evidence suggests caution against the widespread use of opioids, noting problems with tolerance, loss of benefit with time, and escalating usage despite decreasing function and increasing side-effects in some individuals, as well as the possibility of developing addiction for others.**

The use of opioids (or for that matter any treatment) for a small and highly selected group of patients; makes sense, when the benefits outweigh the risks and negative side effects. Benefit is suggested when there is an increase in the person's level of functioning, a reduction or elimination of pain complaints, a more positive, hopeful attitude, and when side effects are minimal or controllable.

Opioids are not harmless drugs. The dilemma with the long-term use of opioids is that while opioid treatment may be prescribed to reduce pain and improve function, the treatment may result, at times, in just the opposite. Use of opioids can increase adverse events and drive polypharmacy when medications are added to treat side effects.

A physician who is considering prescribing opioids as well as the person who is deciding whether or not to use this treatment for pain relief, should not just consider the risks vs. benefits of these medications. They should ask themselves whether they are at higher risk (factors include cigarette smoking, misuse with other drugs, strong family history, environmental exposure, history of sexual abuse) for misuse, abuse, or addiction than others. They should look at the bigger picture and compare the risks and benefits of opioids to those of other treatments, many of which are safer and as or more effective for chronic pain.



In the opioid naïve person (someone new to opioid use), the use of opioids may heighten the risk of **accidental death** from respiratory depression. These risks greatly increase with higher doses and when opioids are taken in combination with other drugs (sedative–hypnotics) that also slow breathing, such as benzodiazepines. In fact, current medical evidence suggests that with rare exception, opioids and benzodiazepines (e.g., Valium, Xanax, Klonopin, and others) should not be prescribed at the same time.

The U.S. Centers for Disease Control (CDC) reports that drug overdose deaths and opioid-involved deaths continue to increase in the United States (<https://www.cdc.gov/drugoverdose/index.html>). The majority of drug overdose deaths (more than six out of ten) involve an opioid. Since 1999, the number of overdose deaths involving opioids including prescription opioids and heroin (<https://www.cdc.gov/drugoverdose/opioids/prescribed.html>) quadrupled.

According to the CDC (12/21/18)², The 63,632 drug overdose deaths in the United States in 2016 represented a 21.4% increase from 2015; two thirds of these deaths involved an opioid. In 2017, among 70,237 drug overdose deaths, 47,600 (67.8%) involved opioids, with increases across age groups, racial/ethnic groups, county urbanization levels, and in multiple states. From 2013 to 2017, synthetic opioids contributed to increases in drug overdose death rates in several states. From 2016 to 2017, synthetic opioid-involved overdose death rates increased 45.2%. On average, 130 Americans die every day from an opioid overdose.

The FDA’s approach to reducing the misuse and abuse of opioids is outlined in [FDA’s 2018 Strategic Policy Roadmap](#), which addresses various facets of this complex issue.

The FDA’s web page on Opioid Medications can be found at <https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm>

Further information regarding REMS can be found at:

- **FDA Basics Webinar: A Brief Overview of Risk Evaluation and Mitigation Strategies (REMS)**

<http://www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm>

- **Approved Risk Evaluation and Mitigation Strategies (REMS)**

<http://www.accessdata.fda.gov/scripts/cder/remis/index.cfm>

- **Risk Evaluation and Mitigation Strategy (REMS)**

<http://www.er-la-opioidrems.com/IwgUI/remis/home.action>

The FDA is also working in cooperation with other governmental agencies, state professional licensing boards, and societies of health care professionals to increase prescribers’ knowledge about appropriate prescribing and safe use of opioids. There is renewed emphasis on home storage

² Drug and Opioid-Involved Overdose Deaths — United States, 2013–2017 at https://www.cdc.gov/mmwr/volumes/67/wr/mm675152e1.htm?s_cid=mm675152e1_e



and safe disposal of unused medication to help patients protect their families and others.

The Substance Abuse and Mental Health Services Administration (SAMHSA) provides information about Prescription Drug Misuse and Abuse:

<http://www.samhsa.gov/prescription-drug-misuse-abuse>

General Opioid Adverse Risks & Side Effects

One out of every two patients taking oral opioids experiences at least one adverse event/effect. Approximately one out of five patients taking oral opioids discontinue use because of an adverse event or an associated side effect.

Prolonged use of opioids may result in problems including hyperalgesia (increased pain sensitivity), hormonal effects (decreased testosterone levels, decreased libido and sex drive, irregular menses, etc.), depression, impaired sleep patterns, and suppression of the immune system. The long-term use of opioids may also impair functional improvement in an individual's recovery from surgery or long-standing musculoskeletal disorders. The prolonged use of opioids usually causes tolerance and physical dependence. As a separate issue, the use of opioids may trigger or worsen substance abuse and addiction.

Common opioid side effects, particularly with higher doses, include:

- Nausea
- Vomiting
- Constipation (opioid induced constipation has a different mechanism of disease than general constipation which is why traditional constipation treatments and medications don't always work)
- Thought and memory impairment
- Drowsiness

Many of these side effects can usually be treated with dose adjustments, wane over time (with the exception of constipation) or can be offset by other alternative medications. There is a risk though of too many additional medications being prescribed (also known as polypharmacy) to treat the opioid side-effects when less opioids may be more appropriate.

Although all doses of opioids carry risks, increasing vigilance (concern) is recommended for doses above 50 mg a day morphine milligram equivalent (MME) as the known risk of adverse events rises while the evidence for increased benefit remains weak.

Remember also that taking opioids does not result in being pain-free but rather the goal should be less pain, more function and either manageable or minimal side effects.

Approximately 40 to 81 percent of individuals taking opioid therapy for non-cancer pain experience **constipation** (fewer than three bowel movements per week) secondary to opioid treatment. Most individuals taking opioid medications will not develop tolerance to opioid-induced constipation. Therefore, an effective preventive bowel regimen including diet changes and a stimulant laxative plus a stool softener will have to be maintained throughout the course of opioid treatment. Even individuals that utilize appropriate laxative therapy often still experience constipation that may impede the appropriate use of opioid pain medication and thus result in



higher levels of pain, so attention to and prevention of this side effect is essential.

There are a number of ways to manage constipation through diet. Maximizing fiber intake is critical. Prunes and prune juice can help to overcome constipation because of their high-fiber content. The same is true for pears, peaches, figs, and pineapples. Broccoli, carrots and beans contains a lot of fiber. Another source of fiber is flaxseeds which can be found in bread or added to smoothies. Yogurt contains probiotics which have been shown to help in the digestive process and reduce constipation.

Medications used for constipation include OTC laxatives (pills, suppositories, enemas, etc.) including stimulant laxatives and osmotic laxatives such as polyethylene glycol 3350 (PEG) (MiraLAX).

Bulk forming (fiber) laxatives, such as psyllium, are not recommended for opioid-induced constipation as they can produce colon obstruction.

There are prescription drugs that are utilized for treating opioid induced constipation. These include prescription drugs such as lactulose, lubiprostone (Amitiza®), naloxegol (Movantik™), methylnaltrexone (Relistor®), and naldemedine (Symproic®). For more information on OTC laxatives, please visit Mayo Clinic Site: <http://www.mayoclinic.org/diseases-conditions/constipation/in-depth/laxatives/art-20045906?pg=1>. For more facts about opioid induced constipation: <http://www.theacpa.org/opioid-induced-constipation>.

The American Gastroenterological Association has published a Guideline titled: Medical Management of Opioid-Induced Constipation. [https://www.gastrojournal.org/article/S0016-5085\(18\)34782-6/pdf](https://www.gastrojournal.org/article/S0016-5085(18)34782-6/pdf)

For more information on opioid-induced constipation, see the following from the American Academy of Pain Medicine, Consensus Recommendations on Initiating Prescription Therapies for Opioid-Induced Constipation at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4738423/>.

Considering current opioid guidelines, one method of treating opioid-induced constipation (OIC) is opioid reduction.

Non-pharmacological interventions that can assist with constipation include: 1) increasing fluid intake, 2) increasing physical activity, and 3) encouraging daily bowel movements at the same time, often after a meal.

Mild nausea is also common with opioid therapy. It can be treated with medications, but if it does not resolve within a few days, a trial of an alternate opioid may be appropriate.

Mild sedation and impaired judgment or coordination also should be anticipated, especially at the beginning of opioid therapy and with significant dose increases. Until tolerance or a baseline is reached, the patient and family need to be warned against driving and the potential for falls. Psychostimulants, while not recommended in current guidelines, are covered by insurance plans, are sometimes used in selected patients to treat sedation but can be habit-forming and have serious side effects. Additionally, psychostimulants can have cardiovascular concerns, along with side effects of anxiety and insomnia.



Hormonal Changes: A side effect of long-term opioid use is a decrease in certain hormones, particularly sex hormones. This reduction may cause a loss in “sex drive,” sometimes called libido, and erectile dysfunction along with altered menses and infertility. This tends to be associated with using these medications regularly for many months. Low testosterone levels are associated also with weight gain and mood disturbances/depression. Because of hormonal abnormalities (decreased estrogen levels), bone density may be diminished which may result in the risk of fractures. For this reason, some doctors test bone density periodically in both women and men on long-term opioid medications.

Respiratory Depression: A serious side effect, particularly in opioid-naïve individuals (those who have not been taking opioids regularly), is respiratory depression (slowed rate of breathing or loss of urge to breathe). Tolerance to respiratory depression can occur with regular opioid use, but this has been called into question now and it is even thought that respiratory depression may increase with prolonged use contributing to some postoperative respiratory morbidity in people receiving long-term opioid therapy, especially when combined with benzodiazepines and other sedatives preoperatively. Elderly, cachectic or debilitated individuals as a population are at increased risk for respiratory depression. Individuals with chronic obstructive pulmonary disease (COPD), obstructive sleep apnea and those who smoke also have greater risk for respiratory depression.

A genuine **allergy** to opioids is very rare. If an allergy does occur, opioids from another class should be chosen. For example, morphine, hydromorphone, oxycodone, and oxymorphone belong to the same class of opioid. Fentanyl and meperidine (Demerol) belong to a different class.

Summary of Possible Opioid Side Effects

- Central nervous system (CNS)
 - A sense of emotional well-being and euphoria
 - Drowsiness, sedation, and sleep disturbance
 - Hallucinations
 - Potential for diminished psychomotor performance
 - Dysphoria and agitation
 - Dizziness and seizures
 - Aberrant behavior (see addiction definition below)
 - Delirium
 - Depression
 - Cognitive impairment (i.e., memory, attention, decision-making, motor reaction)
 - Hyperalgesia (see definition below)
- Respiratory system
 - Respiratory depression is the most serious adverse effect and may result from toxicity
 - Risk for slowed breathing and death is greatly increased when opioids are taken with benzodiazepines or other CNS depressant drugs or with alcohol. To minimize risks, do not take opioids with benzodiazepines and never consume alcohol with opioids
- Ocular system
 - Constriction of the pupil of the eye
- Gastrointestinal system
 - Constipation, nausea, and vomiting
 - Delayed gastric emptying



- Genitourinary
 - Urinary retention
- Endocrine
 - Low testosterone in men and low estrogen in women
 - Reduced fertility in reproductive age women
 - Sexual dysfunction resulting from low hormone levels
 - Hypoglycemia – reported with tramadol and methadone
- Cardiovascular
 - Decreased blood pressure
 - Slowed heart rate
 - Peripheral edema (swelling)
- Musculoskeletal system
 - Muscle rigidity and contractions
 - Osteoporosis
- Skin system
 - Itching is common and not an allergic reaction
- Immune system
 - There are data suggesting that long-term administration of opioids suppresses the immune system. Research is being conducted to determine its clinical significance.
- Pregnancy* & Breast Feeding: When at all possible, avoid opioid use during pregnancy to minimize fetal risks
 - All opioids cross the placenta
 - Neonatal central nervous system depression can occur if opioids are used during labor
 - Neonatal abstinence syndrome can occur in infants born to mothers who are taking regular daily doses of opioids
 - Avoid breastfeeding when taking opioids for chronic pain
 - If an opioid is used during breast feeding, use with caution and only under a health care professional's supervision
 - Timing of opioid dose administration is important for safe opioid use during breast feeding
 - Use of opioids during pregnancy and breastfeeding may result in fetal or newborn toxicity including central nervous system and respiratory depression along with life-threatening neonatal opioid withdrawal syndrome.

*FDA Drug Safety Communication: FDA has reviewed possible risks of pain medicine use during pregnancy – see <http://www.fda.gov/Drugs/DrugSafety/ucm429117.htm>.



CONCOMITANT USE OF OPIOIDS AND CNS DEPRESSANTS

The concomitant use of opioids and other CNS depressants including sedatives, hypnotics, tranquilizers, general anesthetics, phenothiazine, marijuana, other opioids and alcohol can increase the risk of respiratory depression, profound sedation, coma, or death. Physicians are instructed to monitor patients receiving CNS depressants and opioids for signs of respiratory depression, sedation and hypotension. When combined therapy with any of the above medications is considered, the dose of one or both agents should be reduced. The CDC, FDA and National Institute on Drug Abuse (NIDA) all strongly warn against combining the use of opioids and benzodiazepines in order to “avoid potential serious health outcomes.”

DEFINITION OF TERMS REGARDING OPIOIDS

Opioid-responsiveness is the ability to achieve pain relief with evidence of improved function without the development of unmanageable or intolerable side effects.

Opioid-induced hyperalgesia (OIH) occurs when continued opioid use causes increased sensitivity to painful stimuli, worsening pain despite increasing doses of opioids, and pain that becomes more diffuse, extending beyond the distribution of pre-existing pain. In other words, opioids can prolong or even increase pain. Research shows that long-term use of large quantities of opioids may interfere with the body’s natural pain relievers: the endorphins. Physical activity is thought to promote release of endorphins; thus, it is also possible that opioids could inhibit the body’s own mechanism of reducing pain by causing a person to be less active. Additionally, long-term opioid use may cause depression in some patients, which may impede their ability to recover. A mechanism called hyperalgesia increases the brain’s sensitivity to pain in some people. An article on this topic, “A Comprehensive Review of Opioid-Induced Hyperalgesia,” may be found by visiting <http://www.integration.samhsa.gov/pbhci-learning-community/Opioid-Induced-Hyperalgesia-Article.pdf>. Under the supervision of a health care professional, weaning and then stopping the opioid reduces this type of pain.

Addiction is one of the primary concerns that limits opioid prescribing. This is a term that requires clarification. Addiction is not the same thing as physical dependence (see below). **Addiction** is a primary, chronic disease of brain reward, motivation, memory, and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations. This is reflected in an individual **pathologically pursuing reward and/or relief** by substance use and other behaviors. In other words, the individual continues to crave and use the drug, despite harm.

Addiction is characterized by (A, B, C, D, E) the inability to consistently Abstain; by impairment in **Behavioral control**; **Craving**; **Diminished** recognition of significant problems with one’s behaviors and interpersonal relationships; and a dysfunctional **Emotional response**. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death. (From the American Society of Addiction Medicine, www.asam.org.)

Opioid Use Disorder is the terminology utilized by the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM 5) from the American Psychiatric Association. It involves mild, moderate and severe forms based on eleven criteria including negative consequences of use, craving and loss of control. Complete list of criteria can be accessed here:



In this book, we will utilize the term “addiction” which is, for the most part, interchangeable with “substance use disorder.”

Drugs capable of producing addiction do so by interacting with the biochemistry of the brain in such a way that the drug begins to seem essential – one feels a “need” for it as one does for food and water. In the case of pain, the “need” and craving may present as the intense desire to relieve the pain. While the media give the impression that the risk of addiction is inherent to the properties of opioids alone, experts in addiction generally recognize that it results from the interaction of the drug and various hereditary, biological, psychological, and situational factors unique to the individual. The effects of opioids on the brain’s reward center are a big part of the problem and shouldn’t be discounted.

Addiction should be distinguished from **physical dependence** (see below). **Any person (or animal) that takes sufficient doses of certain types of drugs for a significant length of time can have withdrawal symptoms if the drug is suddenly stopped or reversed by another medicine. This shows the presence of physical dependence but does not constitute addiction.**

Physical dependence is common among people who take opioids, but it is not synonymous with addiction. A person taking opioids can become physically dependent without being addicted. If someone is physically dependent, the drug's effectiveness decreases, often leading to futile increases in dose to gain relief, resulting in potentially dangerous consequences.

There is a risk that addiction will develop in anyone who takes opioids and some people have more risk of developing addiction than others.

When addiction develops, the pain medication has become a liability rather than an asset to the person. An older description of addiction includes four core elements (the four C’s):

- ☐ **C**ompulsive use and preoccupation with the drug and its supply,
- ☐ Inability to consistently **C**ontrol the quantity used,
- ☐ **C**raving the psychological effects of the drug, and
- ☐ **C**ontinued use despite adverse effects from the drug.

Compulsive use or preoccupation may be demonstrated by taking the drug because it is available (as opposed to taking it exactly as a health care professional has instructed), inappropriate “stocking up,” using several different health care professionals/pharmacists to guarantee a supply, and spending scarce resources on the drug.

Other examples of inappropriate use include selling the drug or changing the drug from pill to powder for injection or snorting.

An example of loss of control with pain medication might involve using up a month’s supply in a week, causing the person to go without the medication for the rest of the month until it is time for a refill, or the person may look elsewhere to increase the available supply (emergency rooms, other doctors or dentists, friends or family, or illegal sources).

Craving is the desire for the drug in the absence of the drug. Craving may present as an intense



desire for a mental effect (“buzz” or “high”) caused by a medicine. It may also include an intense desire to relieve pain “at any expense” even though, in the long run, the medicine is not truly helping much at all.

Examples of use despite adverse consequences may consist of smoking despite emphysema, drinking and driving despite convictions for driving under the influence, or using analgesics and tranquilizers despite experiencing adverse effect or the ability to function, mood, and family relationships.

People should be aware that they may become addicted to their opioid pain medications. Risk for addiction is increased in those who have a personal or family history of problems with drugs or alcohol and those who have a history of anxiety, depression, or other emotional conditions. People with a history of adverse experiences (including sexual abuse) during childhood or adolescence as well as adults who have experienced or witnessed trauma (like veterans, first responders and others) are also at risk. Cigarette smoking is also considered a risk factor. The risk of addiction should be discussed with a health care professional prior to taking an opioid for pain treatment.

Similarly, individuals should let their health care professional know if they are concerned about becoming addicted to opioid pain medications. There are many misconceptions that surround the use of opioids for pain relief, and a knowledgeable health care professional can provide accurate information. Signs of which to be aware during opioid treatment include taking more medication than prescribed without checking with a health care professional first, loss of control over the medication, and feelings of craving the medication or taking the medication for the euphoric (mental) effects rather than for pain relief.

Chemical Copers: Chemical copers use their opioids to cope with stress, fear, depression, anxiety, sleeplessness, etc. Some use pain medications to fall asleep, others to relax, still others to get along better with a spouse. Some individuals demonstrate inappropriate medication use but not to the level of addiction and are not likely to display a severity that rises to the level of compulsivity or loss of control. In addition, they are not likely to display behaviors indicative of drug cravings that would convince a clinician to diagnose addiction. A major hallmark of chemical coping is the overly important place in the person’s life that is occupied by obtaining drugs for pain and a corresponding inflexibility about non-drug components of care. The use of medications becomes central in the chemical coper’s life while other interests become less important. As a result, they often fail to move forward with psychosocial goals and are usually uninterested in or unwilling to treat pain non-pharmacologically; that is, they do not take advantage of other treatment options provided (i.e., functional restoration), including exploring recommendations to exercise or to see psychologists or physical therapists. Further, they remain on the fringe of appropriate use of their medication but are able to comply with their health care professional’s opioid agreement enough to avoid being removed from treatment. Chemical copers often self-escalate their medication dosage when they are faced with stress and need to have their prescriptions refilled early. Opioids in general should be avoided in this category of patients.

Physical dependence is a state of adaptation that is manifested by a withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. In the short-term management of acute pain, physical dependence usually does not develop because of the limited duration of opioid use. *Physical dependence is not addiction but can occur as a part of the process of developing addiction.*

Withdrawal involves developing signs of illness/discomfort when intake of the substance is abruptly



stopped. *Withdrawal is not addiction but can occur in people who are addicted and is characteristic for physical dependence.* Many people who have taken opioids or sedatives for more than a few doses (usually after one or two weeks of steady dosing) will show some tolerance with use and withdrawal on abrupt drug cessation. In addition, numerous drugs can produce tolerance and withdrawal, yet do not produce addiction (e.g., epilepsy medications, some blood pressure drugs). Symptoms of withdrawal to monitor include sweating, goose flesh, runny nose, abdominal cramping, diarrhea, nervousness, agitation, hallucinations, and a fast heartbeat. Tell a health care professional or pharmacist if these or other side effects occur. Obtaining refills on time will prevent withdrawal.

Tolerance is a phenomenon or adaptation of the body, over a period of time, in which one or more effects of a drug diminish with repeated use at the same dose. For example, a person might feel drugged after the first pain pill; but with continued use, a person might require several pills to feel anything including pain relief. With analgesics, the concern is that the individual will build up tolerance to the drug and therefore require more medication to achieve results. Unfortunately, in many cases, increasing doses of medications may lead to increased or intolerable side effects. *Analgesic tolerance is not addiction but does occur in people who are addicted.*

Although questions remain, it is known that tolerance to the different side effects does not develop at the same rate. For example, one rapidly becomes tolerant to the sedating effects of the opioids. It has been shown that people with cancer who take large but stable doses of morphine show little or no sedation. However, if not prevented, they do continue to experience constipation as individuals do not develop tolerance to this side effect.

The real question, of course, is the extent to which tolerance develops to the *analgesic* effects of the drugs; that is, how soon do the drugs lose their ability to reduce pain? This is unclear, and the answer seems to vary in different people and with different types of pain. Some people seem to benefit from the same dose of an opioid for years, while others rapidly require increased doses and still have unsatisfactory relief. Older people with pain may not become tolerant as quickly to the analgesic effects of opioids as younger people with pain. In some patients, a progression of their disease may lead to increased pain signals or to pathology that leads to pain that is not sensitive to opioids. This disease progression can be misinterpreted as opioid tolerance.

Pseudo-tolerance is the need to increase medications such as opioids for pain when other factors are present that may be the underlying cause, such as disease progression, new disease, increased physical activity, prescription of inadequate doses, lack of compliance, change in medication, and drug interactions.

Functional impairment and physical inactivity are additional concerns that make health care professionals reluctant to provide long-term opioid therapy. It is well known that a sedentary life decreases blood flow, impedes healing, decreases muscle tone, and contributes to depression, bone loss, and fatigue. Clearly, some people become inactive and passive on opioids, while others become more active. It may be that some are able to obtain good analgesia without taking enough to produce intoxication, while others are not able to do so.

Drug misuse refers to the intentional or unintentional incorrect use of opioids in a manner other than that prescribed.

Diversion is allowing others to have access to one's prescribed opioids. Diversion can be as simple as sharing one's medications with family members or friends on an occasional basis or can



represent a conscious decision to distribute or sell them to others. Another definition of diversion is the intentional removal of a medication from legitimate distribution and dispensing channels for illicit sale or distribution. It is a federal crime to divert opioids from the person for whom they have been prescribed. Opioid diversion has been a major contributor to the steep rise in opioid-related deaths in the U.S.



What are Opioids?

Opioid Agonists

Opioids are morphine-like substances. Some forms have been available for centuries to relieve pain. The term opioid is derived from opium, which is an extract from the poppy plant.

Opioids come in naturally occurring, synthetic, and semisynthetic forms. In 1975, it was discovered that the body generates its own (internal or endogenous) opioids (called endorphins, enkephalins, and dynorphins).

Most opioids are agonists, a drug that binds to a receptor of a cell and triggers a response by the cell. An agonist produces an action. It is the opposite of an antagonist, which acts against and blocks an action. The body has opioid receptors that, when occupied by an opioid agonist, create the sensation of analgesia (pain relief).

Opioid medications are sometimes also referred to as narcotics. However, this may be considered a misnomer because, by definition, a narcotic can be anything that induces narcosis or a state of stupor or drowsiness. These effects are essentially, unwanted, secondary effects (i.e., adverse drug reactions) of opioid medications. The primary effect is analgesia. For this reason, the preferred designation is opioids or opioid analgesics.

There are numerous opioids available by prescription (see lists below). Examples include morphine, hydromorphone, fentanyl, methadone, and oxycodone.

All opioids have similar clinical effects that vary in degree from one drug to another. The potency, speed of onset, and duration are unique to each drug. Opioids differ in the typical route of administration, whether injection, skin patch, or in pill form. There are both short- and long-acting opioid formulations. Some are used around-the-clock in scheduled doses, while others are used as needed for intermittent or breakthrough pain.

Opioids should be kept in a secure place in the home to prevent diversion/misuse by family members and visitors.

Opioid Mixed Agonists /Antagonists

Early after the discovery of opioids, the side effects and addictive potential of these medications became apparent. This problem served as the impetus to search for synthetic opioids without side effects and addictive properties. This search led to the discovery of drugs that interact differently with the body's opioid receptors. Additionally, it was discovered that there are four separate receptors: mu (μ), kappa (κ), and delta (δ) and nociceptin/orphanin FQ (NOP).

The mu-receptor is the classic morphine-receptor type and the stimulation of which causes analgesia, respiratory depression, euphoria, and physical dependence. The kappa-receptor produces analgesia through alterations of mood. Stimulation of the kappa-receptor also causes dysphoria.

The discovery of these synthetic opioids led to expanded therapeutic options as well as more



understanding of the body's opioid system.

Buprenorphine (e.g., Belbuca™, Buprenex®, Butrans®), is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Buprenorphine has a very strong affinity for the mu-receptor but only partially activates it. For this reason, its effects on analgesia, euphoria, respiratory depression and dependence are lower relative to pure mu-agonist. In fact, partial agonists are known for their ceiling on both respiratory depression and analgesia. The ceiling effect for respiratory depression for buprenorphine has not been confirmed although it has not been a problem in clinical practice. The analgesic ceiling effect has been demonstrated with sublingual buprenorphine.

It is believed that patients with opioid addictions have increased kappa-receptor activity that alter the mu-receptor agonistic effects. For this reason, buprenorphine has found significant utility as a treatment for opioid dependence. However, because of its partial agonist properties, its utility may be limited in addicts who were on very high doses of opioids. At very low doses relative to doses for opioid dependence, buprenorphine can be used for chronic pain. In some circumstances, buprenorphine may be used for as-needed use in treating chronic pain but not in treating addiction.

Nalbuphine, is a partial mu-receptor antagonist and a kappa-receptor agonist. Nalbuphine is only available by injection and indicated for moderate to severe pain or as supplemental analgesia during surgery. At lower doses, nalbuphine is equianalgesic to morphine and produces the same degree of respiratory depression. However, doses beyond 30 mg do not produce further respiratory depression or analgesia.

Butorphanol, is similar to nalbuphine in that it is a mu-receptor antagonist and a kappa-receptor agonist. Butorphanol is available by injection for relief of acute pain generally used inpatient. Butorphanol is not generally used for chronic pain. A nasal spray is available that has become popular for the treatment of migraine headaches. Butorphanol is not specifically approved for migraine and is generally recommended as a last line option due to the risk of side effects and potential for abuse.

Pentazocine (Talwin®), is a weak mu-receptor antagonist and a kappa-receptor agonist. Pentazocine injection is indicated for moderate to severe pain and also preoperatively as a supplement to analgesia. Oral tablets are also available and formulated with naloxone to reduce the potential for abuse by injection.

Given their antagonist nature, these medications can reverse the effects (analgesia and side effects) of full agonist opioids, such as morphine, fentanyl, hydromorphone, and oxycodone, and therefore should be used with caution in those taking a full agonist opioid.

Symptoms of withdrawal include sweating, gooseflesh, or goose bumps (a temporary local change in the skin when it becomes rougher due to erection of little muscles, as from cold, fear, or excitement), runny nose, abdominal cramping, diarrhea, nervousness, agitation, hallucinations, and a fast heartbeat. The health care professional or pharmacist should be informed about these symptoms.



Opioid Delivery

Opioids are commercially available orally (swallowed by mouth), intravenously, by intramuscular injection (although not recommended), by feeding tube, via nasal spray, transdermally (through the skin), oral transmucosally which includes buccally (absorbed between the gum and inside of the cheek) and sublingually (absorbed under the tongue), via suppository, via an epidural (injection of an anesthetic into the space between the spinal cord and the covering membrane call the dura), and intrathecally (injection into the sheath surrounding the spinal cord, also called “spinal injection” – also see discussion on Implanted Targeted Intrathecal Drug Delivery Systems - “Pain Pumps”).

Opioid Dosing

Morphine equivalent dosing, or MED, is a system used to equate different opioids and their varying potencies into a standard morphine equivalent value using a conversion chart created by the Centers for Disease Control and Prevention (CDC). A patient’s cumulative daily morphine equivalent dose is an indicator of potential dose-related risks for adverse drug reactions.

Although all doses of opioids carry risks, increasing vigilance is recommended for doses above 50 mg a day morphine equivalent dose (MED) as the known risk of adverse events rises while the evidence for increased benefit remains weak. For example, the CDC opines a MME factor of 1 for morphine, 1.5 for oxycodone, 3 for oxymorphone, and 10 for 41-60 mg/day of methadone (https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf).

Opioid Weaning/Tapering

The ability for opioids to cause physical dependence means that when withdrawn, discomforting physical symptoms occur. To reduce the severity of withdrawal symptoms (e.g., drug craving, anxiety, vomiting/diarrhea, increased heart rate and blood pressure; sweating; tremors, anxiety), discontinuation of opioid therapy should be done through a gradual dose reduction (i.e., wean/taper).

It is generally recommended to reduce the total daily opioid dose by 10%-20% per week. The rate of reduction should be individualized and is reasonably affected by ancillary or related factors and the length of time the patient has been on opioid therapy.

In theory, the longer a patient has been on opioid therapy, the slower the taper may need to be. Additionally, according to the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain — United States, 2016, tapers may need to be paused and restarted again per patient response and be more gradual once patients reach low dosages.

According to these guidelines, “tapers may be considered successful as long as the patient is making progress”.

The idea behind these guideline statements is to allow patients to drive the process of weaning as much as possible because the decision to wean, after years of use, requires a significant commitment from the patient. It is important to consider that opioid weaning is not a discontinuation of care.



In many ways, opioid weaning requires as much attention, treatment, and care as opioid initiation.

Collaboration among relevant health providers and psychosocial support is needed to ensure success. While acute withdrawal symptoms may subside, depressive-like symptoms may persist for weeks or months. This is referred to as “protracted abstinence syndrome”. Protracted abstinence syndrome presents risk of relapse and continual care may be necessary to manage this risk.

Short-acting, Extended-release and Long-acting Opioid Agonists

Short-acting oral opioids effects only last a short time.

Examples of short-acting opioid and opioid-combination products include:

- codeine
- oxycodone (alone or combined with acetaminophen - Percocet[®]; combined with aspirin - Percodan[®]; combined with ibuprofen - Combunox[®])
- hydrocodone (combined with acetaminophen - Lorcet[®], Lortab[®], Vicodin[®], Norco[®]; combined with ibuprofen - Vicoprofen[®])
- tramadol (alone or combined with acetaminophen - Ultracet[®]) - tramadol is not chemically a true opioid biochemically but works similarly to opioids primarily on the same receptors
- hydromorphone (Dilaudid[®])
- fentanyl (Actiq[®]) - not indicated for non-cancer pain
- oxymorphone (Opana[®])
- tapentadol (Nucynta[®]) – (an agonist of the mu receptor but not truly an opioid biochemically)

Short-acting oral opioids, true to their description, exert a rapid-onset but short-lived therapeutic effect. These agents typically start working 15–30 minutes after administration, with peak analgesic effect within 1–2 hours. Sustained pain relief is maintained for only about 3 to 4 hours. They are a potent option for treating acute pain (e.g., from a serious athletic injury or after a root canal) and are usually prescribed for pain that is anticipated to last only a few days.

Because of their short half-life and rapid clearance from the body, short-acting opioids must be taken every 3 to 4 hours. Therefore, these drugs are not ideal for long-term therapy of chronic pain, and there is little medical evidence to support their use in long-term therapy of chronic non-cancer pain. Short-acting opioids may be effective; however, as an initial “trial” therapy in patients with moderate or severe chronic pain who have not previously received opioid treatment. In this case, short-acting agents are used to establish a patient’s response and tolerance to opioid therapy and lay the groundwork for long-term dosing of long-acting opioid therapy if, and when, that is prescribed and assuming other non-opioid nonpharmacological therapies are not sufficiently improving function and relieving pain.

In addition to their importance in managing acute pain and initiating therapy for chronic pain, short-acting agents are sometimes used with a long-acting agent during long-term therapy as “rescue medication”. Rescue medications are prescribed for addressing flare-ups that occur despite ongoing, long-term analgesic treatment.



Immediate-release (IR) opioids are active immediately. Some contain an opioid as the only active ingredient (e.g., morphine, hydromorphone, oxycodone, tramadol¹ and oxymorphone), while others contain a combination of an opioid and a non-opioid such as acetaminophen or ibuprofen.

Long-acting opioids include extended or controlled release formulations (ER, or CR, respectively). The prolonged effects of these agents are due to their long half-lives or extended delivery into the body via controlled-release opioid preparations.

Medical consideration of long-acting opioids is indicated in the management of pain severe enough to require daily, around-the-clock, long-term treatment for which alternative treatment options are inadequate. These are extended or controlled release formulations (ER, or CR, respectively).

Examples of sustained-release opioids include:

- morphine (oral sustained release, e.g., MS Contin[®], Avinza[®], Kadian[®], and extended-release Morphabond ER[™])
- oxycodone (oral controlled release, e.g., OxyContin[®]; Xtampza[®] ER, oral biphasic release with acetaminophen, e.g., Xartemis[®] ER)
- oxymorphone (oral extended release Opana[®] ER)
- hydrocodone (oral extended release Zohydro[®] ER, Hysingla[®] ER)
- hydromorphone (oral extended release EXALGO[®])
- fentanyl transdermal system (Duragesic[®])
- tapentadol (Nucynta[®] ER)
- buprenorphine transdermal system (Butrans[®])

Examples of long-acting opioids include:

- methadone (oral, e.g., Dolophine[®], Methadose[®])

The prolonged effects of these agents are due to their long half-lives or extended delivery into the body via controlled-release opioid preparations. Because of the extended release of active drug, long-acting opioids can provide prolonged, steady pain relief for 8–12 hours. Long-acting drug preparations are given at regularly scheduled times, such as every 12 hours. For example, hydromorphone EXALGO[®] is a once-daily medication with reported sustained blood levels for 18-24 hours. **Methadone can have some very toxic effects including respiratory depression and death if dose elevations are made too frequently.**

Extended-release tablets should be swallowed whole and are not to be broken, chewed, dissolved, or crushed. Taking broken, chewed, dissolved, or crushed slow-release pills can lead to rapid release and absorption of a potentially fatal dose of the drug.



Examples of Medical Opioid Agonists	
Codeine (with acetaminophen - Tylenol® with codeine No. 2, No. 3, No. 4)	<p>Codeine is metabolized by the liver to morphine. Some individuals do not have the enzyme required to convert codeine to morphine, and therefore the medication is ineffective. Even though they do not receive benefit, they are still at risk for the associated side effects. Codeine often is associated with higher levels of nausea and vomiting and constipation compared to other opioids. Codeine is contraindicated due to potential life-threatening side effects in children under the age of 12 and postoperatively for children under the age of 18. Codeine should not be used for breastfeeding women.</p>
Dihydrocodeine bitartrate, Aspirin, Caffeine (Synalgos-DC®)	<p>This combination drug of dihydrocodeine, aspirin and caffeine is rarely prescribed in chronic pain states.</p>
Hydrocodone <ul style="list-style-type: none"> Hydrocodone alone – Zohydro® ER, Hysingla® ER With acetaminophen – Norco®, Vicodin® With ibuprofen – Reprexain™, Vicoprofen® With aspirin – Lortab ASA, Panasal 	<p>Hydrocodone is a short-acting opioid available alone or in combination with other ingredients, and different combination products are prescribed for different uses.</p> <p>Zohydro® ER (2 X day) and Hysingla® ER (1 X day) are extended-release hydrocodone available for chronic pain, in an acetaminophen-free formulation. Some hydrocodone products are used to relieve moderate to severe pain.</p> <p>Hydrocodone products have been reclassified to schedule II http://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm</p> <p>The concomitant use of hydrocodone with CYP3A4 (an enzyme that metabolizes many drugs) inhibitors may result in an increase in plasma concentrations which could increase to prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuance of a concomitantly used CYP3A4 inducer may result in an increase in plasma concentration.</p>



Examples of Medical Opioid Agonists	
<p>Fentanyl (Actiq[®] lozenge, Fentora[®] buccal tablet and ONSOLIS[™] buccal film, Abstral[®] sublingual tablet, Subsys[®] sublingual spray, Duragesic[®] transdermal patch, Lazanda[®] nasal spray, and also Ionsys iontophoretic transdermal system - only approved for use in hospital settings)</p>	<p>There have been reports of death and other serious side effects from overdoses while on fentanyl transdermal patches. Furthermore, patients that have not been on opioids (opioid naïve) should not be initially started on the fentanyl transdermal patch because of the inherent inaccuracies in dosing which can lead to an overdose. Exposure to heat (hot bath, heating pad, hot sun, etc.) can increase the speed of fentanyl release. The directions for using the fentanyl skin patch must be followed exactly to prevent death or other serious side effects from overdose. Do not cut fentanyl patches. It is extremely important that patches be disposed of properly to avoid harm to children/pets.</p> <p>Oral transmucosal fentanyl is available in multiple formulations for the treatment of breakthrough pain in cancer patients receiving opioid treatment and who have become tolerant to it. The FDA warns that serious adverse events, including deaths, can occur in patients treated with oral fentanyl. The deaths that have occurred were due to respiratory depression as a result of improper patient selection, improper dosing, and/or improper product substitution.</p> <p>Actiq[®] (oral transmucosal fentanyl lozenge on a plastic stick) is absorbed by swabbing the drug-containing lozenge over and under the tongue and between the cheeks and gums. It is contraindicated for acute postoperative pain and migraine headache. Its use should be limited to cancer pain.</p>
<p>Hydromorphone (Dilaudid[®], EXALGO[®])</p>	<p>EXALGO[®] tablets are an extended-release oral formulation.</p>
<p>Levorphanol (Levo-Dromoran[®])</p>	<p>Levorphanol has the same properties as morphine with respect to the potential for habituation, tolerance, physical dependence, and withdrawal syndrome. It is 11 times as potent as morphine and has a longer half-life. It is not used often due to limited availability.</p>
<p>Meperidine (Demerol[®])</p>	<p>Due to its low potency, short duration of action, and unique toxicity (i.e., seizures, delirium, and other neuro-psychological effects) relative to other available opioid analgesics, meperidine has fallen out of favor and is not recommended or typically used in chronic pain states.</p>



Examples of Medical Opioid Agonists	
Methadone (Dolophine [®] , Methadose [®])	Although methadone possesses analgesic properties, it must be used carefully and with a great deal of caution. It has a long half-life and can accumulate in the body, which can lead to an overdose. It interacts with a large number of other medications, including OTC drugs. It is strongly recommended that the individual on methadone not use any OTC or herbal medications without the approval of the prescribing health care professional. The addition of other commonly used pain medications (e.g., antidepressants, anticonvulsants, and NSAIDS) can increase the likelihood of methadone negatively influencing the heart's ability to conduct electrical signals properly. Prior to starting methadone, patients should undergo an electrocardiogram to check for any pre-existing heart abnormalities that may contraindicate its use. Methadone can also be associated with the development of central sleep apnea. Benzodiazepines should be utilized with extreme caution by individuals who take methadone, secondary to the synergistic negative respiratory and cardiac effects.
Morphine (Avinza [®] , Duramorph [®] , Kadian [®] , MS Contin [®] , Oramorph SR [®])	Morphine is considered to be the prototypical opioid and is available in many formulations.



Examples of Medical Opioid Agonists	
<p>Oxycodone (OxyContin[®], Roxicodone[®], Oxecta[®], Xtampa[®] ER</p> <ul style="list-style-type: none"> • Endocet[®] (containing acetaminophen, oxycodone) • Endodan[®] (containing aspirin, oxycodone) • Lynox[®] (containing acetaminophen, oxycodone) • Percocet[®] (containing acetaminophen, oxycodone) • Percodan[®] (containing aspirin, oxycodone) • Primlev[®] (containing acetaminophen, oxycodone) • Roxicet[®] (containing acetaminophen, oxycodone) 	<p>Oxycodone has the same properties as morphine with respect to the potential for habituation, tolerance, physical dependence, and withdrawal syndrome.</p> <p>The concomitant use of oxycodone with CYP3A4 (an enzyme that metabolizes many drugs) inhibitors may result in an increase in plasma concentrations which could increase to prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuance of a concomitantly used CYP3A4 inducer may result in an increase in plasma concentration.</p>
<p>Oxymorphone (Opana[®])</p>	<p>Oxymorphone has the same properties as morphine with respect to the potential for habituation, tolerance, physical dependence, and withdrawal syndrome.</p>
<p>Tapentadol (Nucynta[®], Nucynta[®] ER)</p>	<p>Tapentadol is a dual mechanism drug with both opioid and antidepressant-like activity. The drug is not a true opioid but binds to opioid receptors and also inhibits the reuptake of the neurotransmitter norepinephrine. The short-acting formulation is approved for acute pain treatment, and the extended-release formulation is approved for the management of continuous severe chronic pain. Tapentadol may have an improved GI side effect profile in comparison with other opioids.</p>



Examples of Medical Opioid Agonists

Tramadol* (Ultram®, Ultram® ER)* and tramadol combined with acetaminophen (Ultracet®) is considered a “weak” opioid-like analgesic

*In July 2014, the DEA, citing evidence of possible abuse, dependence and diversion, reclassified all meds containing tramadol as Schedule IV controlled substances (those with a recognized medical use and relatively low potential for abuse & dependence), however there are known cases of addiction to Tramadol, so it should be taken with the same precautions as other opioids.

Tramadol is a weak analgesic that acts on the central nervous system in two ways. It binds modestly to opioid receptors and thus produces some analgesia by the same mechanism as opioids. It also affects certain neurotransmitters in the brain to decrease the perception of pain. Tramadol also carries the risk of excessive serotonin activity especially when combined with other serotonin stimulating drugs (such as antidepressants) leading to a serotonin syndrome. While tramadol is considered a weak opioid-like drug, it is not completely free of the risks associated with opioids and may trigger addiction even in those without a history of drug abuse or previous addiction. Tramadol reduces the respiratory rate to a lesser extent than opioids in overdoses and does not cause the sort of GI irritation produced by NSAIDs. Tramadol reduces the threshold for seizures, which may manifest in overdose. Seizures may also be provoked in those with a history of seizure disorders, head trauma, etc., or in those taking other drugs that reduce the seizure threshold such as certain antidepressants. Tramadol is a centrally acting synthetic analgesic, not an NSAID, and thus it has no anti-inflammatory activity. Unlike NSAIDs, tramadol does not have the potential to compromise the efficacy of certain antihypertensive agents (diuretics and ACE-inhibitors). Tramadol should be used cautiously, if at all, in patients with underlying liver and kidney disease. Tramadol can cause hyperglycemia. Due to increased risks for slowed breathing and death, tramadol should not be prescribed for children <18 years of age or breastfeeding women.



Examples of Medical Opioid Partial Agonists & Mixed Agonists/Antagonists	
<p>Buprenorphine</p> <ul style="list-style-type: none"> • Buprenex[®] injectable (indicated for pain relief/analgesia) • Butrans[®] Transdermal (indicated for pain relief/analgesia) • Belbuca[™] (indicated for pain relief/analgesia) • Sublocade[™] (buprenorphine extended-release) injection, for weekly subcutaneous use (indicated for treatment of adults with moderate to severe addiction (dependence) to opioid drugs (prescription or illegal)) • Probuphine (buprenorphine) implant for subdermal administration lasting six months. <p>Buprenorphine/naloxone</p> <ul style="list-style-type: none"> • BUNAVAIL[®] (buccal film) • Suboxone[®] (sublingual film) • Zubsolv[®] (sublingual tablet) 	<p>In addition to its use for the treatment of chronic pain, buprenorphine is used to help alleviate unpleasant withdrawal symptoms associated with opioid detoxification and to treat addiction. Maintenance dose is generally in the 4–24 milligram range and higher doses have not been demonstrated to provide any clinical advantage. Butrans[®] Transdermal as a 20 mcg/hour maximum dose recommended due to risk of QTc interval prolongation. Higher doses are thought to be ineffective for pain control and are not used due to cardiac concerns regarding prolongation of the QTc interval. Although not scientifically validated, some clinicians believe that the “ceiling effect” with buprenorphine offers advantages when compared to other medications used to manage addiction because there is a lower abuse potential, lower level of both physical dependence and withdrawal, and there is possibly a decreased incidence of dose related side effects (this has not been studied for Butrans[®] Transdermal). If Subutex[®] is swallowed instead of dissolved under the tongue, the patient may experience no effect due to the poor bioavailability and first pass metabolism of buprenorphine.</p> <p>Buprenorphine/naloxone is a combination drug indicated for the treatment of opioid dependence/addiction. Naloxone is a pure opioid antagonist, meaning it blocks the effects that opioid drugs have on the receptors. Naloxone inhibits and reverses opioid-induced respiratory depression, hypotension, sedation, and analgesia. When given sublingually (under tongue), naloxone has no significant effects on buprenorphine. However, if the sublingual tablet is crushed or injected, naloxone will block the effects of buprenorphine. This characteristic discourages misuse of the formulation. If buprenorphine/naloxone products are swallowed instead of dissolved under the tongue or inside the cheek, the patient may experience no effect due to the poor bioavailability and first pass metabolism of buprenorphine.</p>
Butorphanol (Stadol [®] , Stadol NS [®])	Available in injection or nasal spray formulations but not typically used for chronic pain treatment. Sometimes used in migraine treatment.



Clinical Guidelines for the use of Opioids in Noncancer Chronic Pain

Over the last few years, many states as well as the federal government have come out with guidelines for the use of opioids for chronic, non-cancer, pain.

In March 2016, the CDC released a “Guideline for Prescribing Opioids for Chronic Pain.”

<http://www.cdc.gov/drugoverdose/prescribing/guideline.html>

Key Steps to Use Opioids Safely

1. **Only receive opioids from one health care provider.**
2. **Notify all prescribers about your opioid use.** Whenever you receive a new prescription from any health care provider, be sure they are aware of your opioid use. Also, immediately alert your opioid prescriber about any new prescriptions.
3. **Keep the health care professional informed.** Inform the health care professional about any past history of alcohol or substance abuse. All patients treated with opioids for pain require careful monitoring by their health care professional for signs of abuse and addiction and to determine when these analgesics are no longer needed.
4. **Follow directions carefully.** Opioids are associated with significant side effects, including drowsiness, constipation, and depressed breathing depending on the amount taken. Taking more than is prescribed could cause severe respiratory depression or death. Side effects should be reported. Do not crush, break, or dissolve pills. This can alter the rate at which the medication is absorbed and lead to overdose and death. Do not suspend treatment abruptly without talking to your doctor.
5. **Reduce the risk of drug interactions.** Do not mix opioids with alcohol, antihistamines, barbiturates, benzodiazepines and other sedatives including some muscle relaxants (e.g., Soma). All of these substances slow breathing and their combined effects could lead to life-threatening respiratory depression.
6. **Prevent theft, diversion, and child access to your opioids by keeping them in a locked safe.** Remember, one pill can kill. Help keep others safe by never storing opioids in the medicine cabinet or where others have access to the medications. The best strategy is to store medications in a locked box. Do not share medications with anyone else. Although you may feel you are helping someone in need, you may cause harm and even death. Sharing opioids is against the law.
7. **Keep track of when refills are needed** to prevent going without medications which can lead to withdrawal. Discuss refill strategies with the prescriber ahead of time. Some p a i n



clinics will not fill prescriptions without a visit to the clinic. Other clinics will not fill prescriptions on Friday afternoons or weekends/evenings.

8. **People with memory problems may need extra help with their medications.** Avoid unintentional medication overdoses by helping people with memory problems receive assistance in creating a safe plan for taking medication. Such a plan may include help from family members, home care medication reconciliation, or using time-of-day labeled pill boxes (that are also kept in a locked safe).

Opioids and the Goals of Pain Management

There has been disagreement as to whether the goal of pain management should be to reduce pain or to improve the way people function in their daily lives. The consensus of the members of the American Pain Society is that the primary goal in treating people with chronic pain with opioids is to **increase the level of function** rather than just to provide pain relief.

When people are less uncomfortable, they usually resume activities that they had previously avoided. If a person with pain fails to do this, it suggests that symptom relief has not occurred even though the person may believe that the medications “take the edge off”. Clearly, maximizing quality of life entails both factors: minimizing suffering and maximizing function. It is important to understand that the antianxiety and sedative actions of opioids may improve the person’s well-being in the short-term, but these effects rapidly develop tolerance and the opioid dose will need to be escalated to achieve the same level of “Well-being”. Opioids should be used for analgesia alone and when prescribing them the physician should inquire about the goals of opioid treatment and the limitations of opioid therapy. If reducing anxiety or sedation is desired, more appropriate medications and physical, behavioral therapies should be tried before escalating opioid dose. Additionally, opioids work best for constant pain at rest and less well for movement evoked pain. It is important that people using opioids do not try to elevate the dose of opioids to achieve an effect that would be best served by other treatments. While opioids are very useful medications they are not a complete answer to the reduction of pain and restoration of function.

In many respects the primary goal of pain management is essentially rehabilitation. The person experiencing pain and the family must ask to what end they want to be rehabilitated. What does rehabilitation mean to each of them? Webster defines rehabilitation as “*to restore to useful life through education and therapy*”. If a person’s goal is solely to reduce pain at the expense of function, then he or she may overlook the more important (and attainable) goal of rehabilitation. The essence of rehabilitation and maintaining wellness is for the person to take an active part in the recovery process.

It is important to mention that taking opioids precludes certain types of employment, even if one is tolerant and does not have side effects. People should be aware of the rules currently put forth by Federal and State authorities and individual employer drug use policies.

If you use opioids to help manage your pain, it's important to take them, store them, and dispose of them properly. Watch this video to learn more. <https://www.theacpa.org/pain-management-tools/videos/conditiontreatments/>



What is the place of opioid pain medication? There is no question about the usefulness of opioids in acute pain and end-of-life pain. We do not yet know when they are most helpful for chronic non-cancer pain. Benefit is suggested when there is a significant increase in the person's level of functioning, reduction/elimination of pain complaints, a more positive and hopeful attitude, and when the side effects can be managed safely. Those who take opioids should not have the expectation of prolonged opioid use without concomitant side effects.

Monitoring Opioid Medication Use

Health care professionals who prescribe opioids are required to monitor for pain and any unusual drug-related behaviors as part of caring for their patients.

The most relevant areas for monitoring have been termed the **Five A's**:

1. Analgesia (pain relief – often measured by a 10-point rating scale).
2. Affect (what is the patient's mood?).
3. Activities of daily living (physical, psychological, and social functioning).
4. Adverse or side effects.
5. Aberrant or abnormal drug-related behaviors.

Some of the following questions may help clarify how appropriately opioid pain medications are being used and whether they are helping or harming the person's well-being:

- ☐ *Is the person's day centered around taking medication?* If so, consultation with the health care professional may clarify long-term risks and benefits of the medication and identify other treatment options.
- ☐ *Does the person take pain medication only on occasion, perhaps three or four times per day?*
If this is the case, then the likelihood of addiction is low.
- ☐ *Have there been any other chemical (alcohol or drug) abuse problems in the person's life?*
If so, then it is important to inform the health care professional who will need to take that into consideration when prescribing. Often, people with pain with a history of substance use disorders are not ideal candidates for opioid treatment for pain management because the opioids may trigger recurrent addiction.
- ☐ *Does the person in pain spend most of the day resting, avoiding activity, or feeling blue?* If so, that suggests the pain medication is failing to promote rehabilitation. Daily activity is necessary for the body to produce its own pain relievers, to maintain strength and flexibility, and to keep life full and meaningful. Encourage the person with pain to request recommendations from a health care professional for a graduated exercise program.
- ☐ *Is the person in pain able to function (work, household chores, and play) with pain in a way that is clearly better than without?* If so, chances are that the pain medication is contributing to wellness. Most people who are addicted to pain medications or other substances do not function well.



- ❑ *Does the person smoke?* Smoking increases pain and reduces the effectiveness of opioids. Smokers tend to take higher doses of opioids and have greater risks for problems and addiction. Smoking itself is an addictive behavior and; therefore, a clear risk for opioid addiction. ***Opioids should be avoided in smokers.***

The following may be signs that a person is being harmed more than helped by pain medication.

- Sleeping too much or having days and nights confused
- Decrease in appetite
- Inability to concentrate or short attention span
- Mood swings (especially irritability)
- Lack of involvement with others
- Difficulty functioning due to drug effects
- Use of drugs to regress rather than to facilitate involvement in life
- Lack of attention to appearance and hygiene
- Escalation of pain
- Continual dose escalation
- Increasing number of medications prescribed to treat the side effects of opioids

The ACPA Pain Log can be a useful tool for tracking many of the symptoms and impact that pain has on a person. View at

<https://www.theacpa.org/pain-management-tools/videos/conditionstreatments/>

While it is impossible to make generalized guidelines for when to provide opioids on a regular, ongoing basis, the person and his or her family can often help to determine whether these agents are useful. If family members see that the person with pain has lost control of his or her life, is less functional, and is more depressed when taking or increasing the dose of opioids than he or she was before, they should seek help.

Most research suggests that family members over-report their loved one's pain, but they also may be the only ones who can accurately determine whether the person's life, mood, function, attitude, and comfort have changed for the better or worse. The person taking the medication may be so aware of the discomfort produced when they miss doses of pills that they incorrectly conclude that they need the medication. This severe pain may in fact only represent withdrawal due to physical dependence, as opposed to a persistent need for analgesic therapy.

ACPA offers a three-part video series focused on the many challenges that family members experience when living with a person with pain. View at <https://www.theacpa.org/pain-management-tools/videos/support/>.

Opioid Treatment Agreement

Individuals with pain have an important responsibility with respect to opioids to ensure that both they, as well as others, will be able to have access to opioids in the future. When opioids are prescribed, people with pain are usually requested to formally communicate their agreement with the written therapeutic plan (a.k.a., Opioid Treatment Agreement---sometimes termed an Opioid Contract or Opioid Therapy Plan), and in particular, their understanding that the goal of opioid



therapy is not the elimination of pain but rather its reduction to the point where measurable and meaningful increases in function are apparent. This would also include agreeing that they will obtain opioids only from one pharmacy and one medical provider, abstain from using other sedatives without express permission from the health care professional prescribing the opioids, and not engage in activities that would be interpreted as representing misuse or diversion of their medication. The health care professional should clarify what activities would be interpreted as such to ensure a common understanding.

However, violation of an opioid treatment agreement should not be a “zero tolerance policy” where the first violation results in dismissal from care. Instead, it should be the start of a conversation as to why the violation occurred and to offer some counseling. Repeat offenders need to be dealt with – if there are no penalties then it’s a useless tool – but if the violation is treated as an immediate disqualification that does not help the patient.

The majority of persons who abuse opioids obtain the drug from friends or family members, often without the knowledge of the person for whom the medication is prescribed. This use of opioids, or sold or purchased illicitly, is unacceptable and would constitute misuse and abuse that would void the opioid treatment agreement and results in discontinuation of prescribed opioids. Further, it is important to take the opioid exactly as prescribed by the health care professional with respect to dose and to timing between doses and talk with the health care professional if a change in the prescription is thought to be needed.

The discussion of safe storage and disposal not only helps to prevent theft and subsequent abuse but also prevents accidental overdose by children, cognitively impaired family members, and pets. Patients should always be aware of how many refills and how many pills remain in their prescription. The goal of the agreement is to ensure that patients and caregivers have clear communication and safe, effective procedures when opioids are used.

A sample Opioid Treatment Agreement Can Be Found at

http://www.acoem.org/uploadedFiles/Public_Affairs/Policies_And_Position_Statements/Guidelines/Library_and_Reference_Material/OPIOID%20TREATMENT%20-%20Reed%20Group%20Guidelines.pdf

An opioid treatment agreement may include random urine drug testing.

Urine Drug Tests (UDT)/Urine Drug Screening (UDS)

Urine drug testing (UDT) or urine drug screening (UDS) is often ordered by the health care professional prior to starting opioids and at random intervals during treatment. UDT is used to check that the medications prescribed are being taken and that non-prescribed and/or illicit drugs are not used. Typically, urine tests include screening for prescription opioids, benzodiazepines, cocaine, heroin, amphetamines, and marijuana.

The first level of drug testing is screening in the doctor’s office or in a laboratory using a technique called immunoassay. Immunoassays have three important limitations. First, there is a limit to the number and types of drugs that can be detected. Second, there are specificity limitations because, in the case of amphetamines, barbiturates, benzodiazepines, and opiates, the tests are class-specific rather than drug-specific. The final limitation of drug screening methods is sensitivity.



If the screening is positive, the urine is then confirmatory tested under either liquid chromatography (LC) or gas chromatography-mass spectrometry (GC-MS) technology.

Naloxone for Opioid Reversal in Case of Overdose

Opioid overdose is typically reversible through the timely administration of the medication naloxone and the provision of other emergency care. However, access to naloxone and other emergency treatment was historically limited by laws and regulations. In an attempt to reverse the unprecedented increase in preventable overdose deaths, the majority of states have amended those laws to increase access to emergency care and treatment for opioid overdose with naloxone.

In April 2018, the US Surgeon General urged more Americans to individually carry naloxone and be prepared to administer the medication in efforts to prevent future opioid overdoses.³

Naloxone may be administered by medical personnel as an injection, by anyone with the Evzio[®] naloxone auto-injector or Narcan[®] nasal spray, or as an improvised off-label nasal spray that must be assembled from components at the time of use. See the ACPA video: ACPA – Overdose – Aware and Prepared with Naloxone <https://naloxone-be-prepared/>.

It is now recommended that people who are being prescribed opioids should also be co-prescribed Naloxone to have on hand in case of emergency. Consult with your prescriber about having naloxone available to you in the event of possible accidental overdose and make sure your family and friends are aware of its potential life-saving effect.

For more information about Naloxone, go to <https://www.networkforphl.org/asset/qz5pvn/network-naloxone.pdf>; <http://stopoverdose.org/> and <https://www.projectlazarus.org/naloxone>.

³ Surgeon General's Advisory on Naloxone and Opioid Overdose at <https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/naloxone-advisory.html>



Herbal Medicines, Supplements & Vitamins

Herbal supplements come from plants and claim to have medicinal properties that can improve health or aid in managing various medical conditions. They may claim that they can cure, treat, or prevent disease but according to FDA regulations, claims for supplements can only reference supporting healthy function of the body and not management of disease states.

Nutraceuticals are nutrient products such as fish oils and megavitamins.

Even though these products may be billed as “natural” on the label, this does not ensure their efficacy, purity, or safety. Manufacturers of dietary supplements can market their products without receiving approval from the FDA. However, the FDA can remove products from the market if they have been proven to pose serious or unreasonable risk to consumers.

Prior to taking supplements or herbal preparations, it is advisable to discuss with your health care provider to determine potential benefit and any risk of drug interactions with other medications.

While there may be proven health benefits for some herbal and nutraceutical products, potentially harmful effects exist for others. Dietary supplements are not standardized, unlike FDA-approved prescription medications. The same ingredients can be found in different products in varying amounts and this can lead to toxic levels that may cause harmful reactions in the body. Herbal remedies and medicinal agents undergo little oversight of safety, efficacy, sterility of production, bio-equivalency, or stability of product life.

Certification symbols, such as a United States Pharmacopeia (USP) symbol, verifies that the product contains the ingredients in stated amounts and strength, is pure, meets limits for contaminants, and disintegrates quickly. The NSF International verifies products for content and label accuracy, purity, contaminants, and manufacturing processes. ConsumerLab.com independently tests supplements for purity and active ingredients.

Possible Benefit of Herbal Supplements for Pain

There are some herbal remedies for which there is some evidence with regards to the management of acute low back pain and osteoarthritis. White willow bark (*Salix*) extract has been studied in low back pain. A principal ingredient is salicin with salicylic acid as the principal metabolite. This is similar to ingredients in aspirin.

Extract of *Harpagophytum procumbens* (devil’s claw root) has been used in Europe to manage musculoskeletal symptoms with some evidence that it may relieve acute low back pain, acute episodes of chronic low back pain, and osteoarthritis. Mild gastrointestinal upset has been reported at higher doses.

There is some evidence that the antioxidant alpha lipoic acid (ALA) significantly and rapidly reduces the frequency and severity of symptoms of the most common kind of diabetic neuropathy. Symptoms decreased include burning and sharply cutting pain, prickling sensations, and numbness. Unfortunately, studies in people with neuropathy due to cancer chemotherapy revealed no benefit.



There is also evidence that acetyl-L-carnitine (ALC) not only improves the symptoms of diabetic neuropathy, but also helps regenerate nerve fibers and vibration perception. Unfortunately, studies in people with neuropathy due to cancer chemotherapy revealed no benefit and may have caused worsened neuropathy.

Recently, much attention has been given to glucosamine and chondroitin sulfate. Early research suggested that glucosamine and chondroitin sulfate were effective in improving pain and decreasing functional impairment from symptomatic osteoarthritis. The more recent Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) implied that glucosamine and chondroitin sulfate did not reduce pain in individuals with knee osteoarthritis, although a small select group of patients with moderate-to-severe osteoarthritis may benefit from treatment. When using glucosamine and chondroitin sulfate, the recommended daily dose is 1500 mg per day. Currently, a majority of studies do not show medical benefit with this supplement. Glucosamine may also worsen insulin resistance.

Coenzyme Q10, or CoQ10 as it is often called, is commonly taken in supplement form to counteract the muscle pain and weakness associated with cholesterol-lowering statin drugs. Whether it is truly beneficial for this purpose is the subject of current studies.

Low levels of Vitamin D are associated with chronic pain in general and with reduced immunity. Low levels of Vitamin B are thought to affect neuropathic pain. Pain may be reduced by optimizing vitamin levels. Vitamin B and D levels can be checked to decide if supplementation is indicated.

Corydalis Yanhusuo (Chinese poppy plant) has been used for centuries in China to treat different types of pain. Some of its components were found to attach to opioid receptors. There is some evidence that it may be beneficial in treatment of low-grade chronic pain.

Curcumin, a compound found in turmeric and ginger roots and spices, is a potent antioxidant. Multiple studies have provided evidence that it also works as an anti-inflammatory agent.

Many other herbal extracts have been used worldwide for treatment of pain and have anecdotal or low evidence of their effectiveness. Even less is known about their safety alone or in combination with conventional medications.

American Botanical Council website: <http://abc.herbalgram.org> provides a wealth of information to help in making informed decisions on use of medicinal plants.

Consumer Lab is an independent laboratory that tests the quality of nutritional supplements and posts its results at www.consumerlab.com. It is a third-party verification group that provides certification for nutritional products and supplements that meet its quality standards.



WebMD has an article, Can Supplements Help With Pain? At <http://www.webmd.com/a-to-z-guides/prevention-15/vitamins/chronic-pain-relief?page=1> and a Vitamins & Supplements search at <http://www.webmd.com/vitamins-supplements/condition-1452-Pain.aspx?query>.

Cautions regarding the Use of Herbal Preparations, Supplements & Vitamins

All of these OTC products have the potential for toxic side effects and cross reactivity with each other and with prescription medications. Unexpected toxicity or drug interaction from any product or medication may occur due to many variables such as age, gender, nutritional status, other illnesses, and surgery.

Many adverse events from herbal medicines have been reported including hypersensitivity reactions, anaphylaxis (shock), hepatitis, nausea, vomiting, diarrhea, platelet inhibition, lower seizure threshold, elevated digoxin levels, central nervous system depression, skin sensitivity to light, chest pain, electrolyte alterations, low blood pressure, irregular heartbeat, kidney failure, carcinogenicity (may cause cancer), and autoimmune (disease caused by antibodies or lymphocytes produced against substances naturally present in the body) effects. Herbal medicines can affect the ability of blood to clot. Therefore, information on current use of herbal medicines should be provided to the health care professional prior to undergoing any surgery or interventional pain procedure.

The American Society of Anesthesiologists recommends that individuals discontinue or taper off herbal products and nutraceuticals at least two weeks prior to surgery. It is important to carry a list of all medications, including herbals, supplements and vitamins, in your wallet and to consider sharing this list with family members and other caretakers.

Some of the undesirable effects of a few of the more commonly used herbals are shown below.

Possible Adverse Side Effects of Herbal Preparations	
Aloe vera	Nausea, vomiting, diarrhea.
Astragalus	Autoimmune disease.
Belladonna	Atropine side effects of atropine sulfate include dryness of the mouth, blurred vision, sensitivity to light, lack of sweating, dizziness, nausea, loss of balance, and rapid heartbeat.
Chaparral	Hepatitis.
Ephedra – banned in the US due to serious side effects including death	High blood pressure, irregular heartbeat, nervousness, headaches, trouble falling asleep, or even a heart attack or a stroke.
Ginkgo biloba	Excess bleeding.
St. John's wort	Upset stomach, a tired feeling, dizziness, confusion or dry mouth. A sunburn occurs more easily.
Kava products	Sleepiness, a rash, liver injury including hepatitis, cirrhosis and liver failure, or strange movements of the mouth and tongue or other parts of the body.
Garlic	Increased bleeding risk.

The National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine (NCCAM) and the National Library of Medicine (NLM) have partnered to create *CAM on PubMed*, a subset of NLM's PubMed.



More information on the National Center for Complementary and Alternative Medicine can be found at <http://nccam.nih.gov/>.

An article entitled Herbal Remedies: Adverse Effects and Drug Interactions at <http://www.aafp.org/afp/990301ap/1239.html> and a patient handout (Herbal Health Products--What You Should Know at <http://www.aafp.org/afp/990301ap/990301e.html>) on the American Academy of Family Physicians website.

Medical Foods

At the most fundamental level, medical foods can be viewed as dietary supplements that are marketed for the management of a specific disease. By law, dietary supplements are not allowed to be labeled for a specific disease. Drugs, on the other hand, can be labeled for a specific disease because the FDA requires that the drug developer conduct clinical trials to show that it is indeed safe and effective for the said disease. Since dietary supplements are not required to be tested for safety and efficacy, they can only be claimed to support body functions. Dietary supplements (and many medical foods) are essentially vitamins, minerals, or plant extracts. They are naturally occurring in substances humans may consume as food. As science evolved and knowledge is accumulated about the roles or function of these vitamins and minerals in the body, the idea that drove the evolution of the dietary supplement industry was to extract relevant vitamins and minerals and consume them as supplements to food.

For example, CoenzymeQ10 (CoQ10) also known as ubiquinol is naturally occurring in certain meats and vegetables. Once it was discovered that CoQ10 is used by the mitochondria to produce energy and that certain organs, notably the heart, contain high concentrations of mitochondria it was purported that providing the body with extra CoQ10 would help the heart to perform better. Therefore, the only claim that manufacturers of CoQ10 can make is that it helps support heart function.

Pursuant to the Nutritional Labeling and Education Act of 1990, a special category of medical food was created and resides midway between dietary supplement and drugs. For all intents and purposes, this new category allowed manufacturers of dietary supplements to market their products as medical foods, which can be claimed to treat a specific disease. Unfortunately, there is still little oversight over this class of products and for that reason, the field of chronic pain management has seen capitalization by certain manufacturers purporting their medical food product for the management of chronic pain. Some common examples of medical foods targeted for pain management are presented in the table below:

Product Name	Ingredients	Targeted Condition
Metanx®	L-methylfolate, vitamin B6 and B12	Neuropathy
Theramine®	Choline Bitartrate • L-Glutamine • 5-Hydroxytryptophan • L-Serine • L-Arginine • Cinnamon bark • GABA • Grape seed extract • Cocoa • Metabromine.	Pain and inflammation
Limbrel®	Scutellaria Baicalensis extract (baicalin), Acacia catechu extract (catechin) • Zinc (citrate zinc bisglycinate)	Osteoarthritis



For these products' role in chronic pain management, it is important to consider:

- Medical foods have not been approved by the FDA as safe and effective for the conditions for which they are marketed.
- Medical foods are not currently recommended by any nationally recognized pain guideline.
- Despite the composition of “natural” ingredients, safety (especially long-term safety) is largely unknown.

Many of these products are marketed in comparison to the current alternative medications for pain. Since the risk of current alternatives is well recognized (e.g., addiction with opioids, gastrointestinal bleeding, cardiac injury with NSAIDs), it may be tempting to gravitate towards these products as safer and possibly as effective or non-inferior alternatives to current pain medications.

In the case that medical foods are trialed for chronic pain, people with pain should be counseled to immediately report signs or symptoms that may be associated with an adverse reaction. In the case that medical foods are used in combination with other prescription pain medication as a part of a regimen of medications including opioids, NSAIDs, and skeletal muscle relaxants, prescribers should assess the therapeutic value (i.e., the individual contribution of the medical food to the overall therapeutic outcome). Essentially, does the addition of the medical food contribute to lower pain scores, better function, or reduction of other drugs?



OTHER MEDICATIONS

Antidepressants

One of the most common classes of drugs used to treat chronic pain is the antidepressant group. An antidepressant prescribed for pain treatment does not mean that the pain is psychiatric in origin. Antidepressant drugs have been used for many years to relieve pain.

There has been a longstanding association between depression and chronic pain. Not surprisingly, the chemicals (neurotransmitters, such as serotonin and norepinephrine) in the brain and nervous system that play a key role in depression are also believed to be involved in chronic pain.

Some general considerations regarding antidepressants and pain are listed below.

- They do not work for pain only by relieving depression. In fact, they work as well for non-depressed people with pain as for those with depression.
- They do not work equally well for all types of pain. For example, they tend to be helpful for fibromyalgia, headache, and pain due to nerve damage (e.g., diabetic neuropathy) but generally are less helpful for most acute pain, including musculoskeletal sports-type injuries.
- How well they work has little to do with how effective they are as antidepressants. Some very effective antidepressants have virtually no ability to reduce pain.

How Antidepressants May Help

While most people know that pain signals go up the spinal cord to reach the brain, they may not be aware that there are signals coming down the spinal cord that can increase or reduce pain transmission. By increasing levels of chemicals (norepinephrine and serotonin) at nerve endings, antidepressants appear to strengthen the system that inhibits pain transmission.

The antidepressants that increase norepinephrine seem to have better pain-relieving capabilities than those that increase serotonin. This helps to explain why the selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac[®]) and paroxetine (Paxil[®]), work well for depression but do not have the same ability to control pain. There are also dual acting antidepressants that reduce the reuptake of serotonin and norepinephrine such as duloxetine (Cymbalta[®]) - that has shown results in the treatment of neuropathic pain and fibromyalgia.

Some antidepressants may be useful in chronic pain because they effectively reduce anxiety and improve sleep without the risks of habit-forming medications. Some people with chronic pain are depressed and treating the depression may also help reduce the perception of pain. Many people with chronic pain find that antidepressants, along with learning other pain management skills, can help them regain control of their lives and keep their pain under control.



Antidepressant Side Effects & Potential Hazards

The most common side effects of antidepressants are drowsiness, constipation, dry mouth, urinary retention, weight gain, and blurred vision. Some people experience nightmares or an increased heart rate. While some people experience minimal side effects, for others the side effects can be as bad as the pain. It is worth noting that different antidepressants have different side effects and tolerance to these side effects can develop with use.

Some cause more sleepiness while some cause less. Although some lower sex drive, desire may actually increase as pain, sleep, and mood improve. Some may lower blood pressure while others raise it. Some increase appetite while others do not. Several may cause dizziness.

If a person's pain is helped by an antidepressant but the side effects are troublesome, it may be useful to change medications. Doing so may allow the benefit to be retained while reducing the undesirable side effects.

Some antidepressant drugs, especially those within the tricyclic group, such as amitriptyline (Elavil®), nortriptyline (Pamelor®), and desipramine (Norpramin®), can be fatal in overdose and should only be available and prescribed in limited supply.

The FDA has issued the following warning regarding antidepressant prescription use:

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of an antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber.

Concomitant Use of Opioids and CNS Depressants

The concomitant use of opioids and other CNS depressants including sedatives, hypnotics, tranquilizers, general anesthetics, phenothiazine, other opioids and alcohol can increase the risk of respiratory depression, profound sedation, coma, or death. Physicians are instructed to monitor patients receiving CNS depressants and opioids for signs of respiratory depression, sedation and hypotension. When combined therapy with any of the above medications is considered, the dose of one or both agents should be reduced.



Benefits of Antidepressants in Chronic Pain

The optimal role for antidepressants in chronic pain is still being defined as research progresses. The qualities listed below seem clear, however.

- They do not have the potential to cause stomach inflammation and bleeding, as do the anti-inflammatory drugs. The use of antidepressants (e.g., SSRIs) with NSAIDs should occur with caution secondary to a higher risk of GI bleeding.
- They do not seem to interfere with the body's internal pain fighting mechanisms; in that they probably strengthen them by increasing the effects of chemical messengers, such as norepinephrine and serotonin, in the nervous system.
- Many act as sedatives to promote a good night's sleep. Sleep deprivation is often one of the major obstacles in coping with chronic pain. In fact, with severe sleep deprivation, one cannot cope with much of anything.
- They may help to reduce depression.
- They may help to relieve anxiety and panic attacks.
- They may increase the effect of other pain-relieving drugs or analgesics.
- They are non-addictive medications that can be used in pain control and loss of effect tolerance does not occur after the optimal dose for a given person has been determined.
- They have a record of long-term safety and are among the most widely used drugs in medicine.

There is evidence that antidepressants may work at lower doses and blood levels for chronic pain than are required for depression and they may produce responses sooner than the three to five weeks typical for depression treatment. This is not always true, however, and some people require higher doses for maximum pain relief.

Pain States that May Respond to Antidepressants

Postherpetic neuralgia	Migraine & Tension Headache (for prevention)
Diabetic neuropathy	Chemotherapy-induced peripheral neuropathy
Phantom limb pain	Fibromyalgia
Stump / neuroma pain	Irritable Bowel Syndrome
Central pain (following stroke)	Rheumatoid arthritis
Sympathetic dystrophy (CRPS/RSD)	Neuropathic pain
Chronic musculoskeletal pain	Low back pain with radiculopathy



Antidepressants Commonly Use for Chronic Pain

Tricyclic Antidepressants (TCAs)

The first class is the tricyclic antidepressants (TCAs) and includes amitriptyline (Elavil®), doxepin (Sinequan®), imipramine (Tofranil®), desipramine (Norpramin®), nortriptyline (Aventyl®), Pamelor®, protriptyline (Vivactil®), trimipramine (Surmontil®), and clomipramine (Anafranil®). Also included are trazodone (Desyrel®), maprotiline (Ludiomil®), and mirtazapine (Remeron®), which are tetracyclic antidepressants (which are structurally different from TCAs and have different side effects).

The TCAs have been used for many years to treat depression. TCAs and related drugs can be roughly divided into those with additional sedative and relaxing properties and those that are less so. Agitated and anxious patients tend to respond best to antidepressants with sedative properties whereas withdrawn individuals and those with less energy will often obtain the most benefit from less sedating antidepressants. This class of antidepressants has been proven to have pain-relieving effects, typically at lower doses than required to treat depression.

The different tricyclic drugs have varied side effects that may sometimes be used to the patient's advantage. For the overweight patient with lethargy and tiredness, the clinician may choose a TCA with more noradrenergic selectivity (e.g., desipramine), which may be activating and can cause some anorexia. Desipramine is considered to have the lowest side effect profile of the TCAs. For others with poor sleep hygiene, the sedating properties of certain TCAs, such as amitriptyline or doxepin, may be helpful.

Some of these drugs, such as amitriptyline (Elavil®), nortriptyline (Pamelor®), and desipramine (Norpramin®), can be fatal in overdose and should only be available and prescribed in limited supply.

Tricyclic antidepressants (TCAs) can have significant anticholinergic effects, which can include confusion, blurred vision, worsening of glaucoma, constipation, dry mouth, light-headedness, and difficulty with urination or loss of bladder control. In older patients with decreased cognitive abilities, the use of a tricyclic antidepressant can lead to significant confusion. Patients with Alzheimer's disease should not be started on TCAs. The American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults was published in October 2015. They include lists of potentially inappropriate medications to be avoided in older adults. The Internet links is

<http://onlinelibrary.wiley.com/doi/10.1111/jgs.13702/full>.

Also, patients with cardiovascular disease (CVD) should avoid the use of tricyclic antidepressants or be followed closely by a health care professional for cardiac abnormalities that can worsen with their use. In a study published online in December 2010 in the *European Heart Journal*, the authors assessed the association between antidepressant medication use and future risk for CVD. The study suggested TCAs are associated with a 35 percent increased risk for CVD, which is not explained by existing psychiatric illness.

Patients with narrow angle glaucoma should avoid the use of these medications.



They may increase appetite and be associated with weight gain. Go to the following web site for further information about TCA toxicity at <http://www.emedicine.com/emerg/topic616.htm>.

Selective Serotonin and Norepinephrine Reuptake Inhibitors (SNRIS)

The second class includes a number of drugs that are mixed serotonin and norepinephrine reuptake inhibitors or SNRIs. These medications have no cholinergic inhibition and, thus, they are associated with fewer side effects than TCAs. Blood pressure should be monitored in these patients because SNRIs can increase systolic blood pressure.

Duloxetine (Cymbalta®), venlafaxine (Effexor®), desvenlafaxine (Pristiq®), milnacipran (Savella™), and levomilnacipran (Fetzima®) are the SNRIs that are most commonly encountered in association with pain management.

Duloxetine (Cymbalta®) has been approved for management of painful diabetic peripheral neuropathy, fibromyalgia, anxiety disorder, depression, and in 2010 for chronic musculoskeletal pain including osteoarthritis and chronic low back pain.

Milnacipran (Savella™) has been approved for the management of fibromyalgia. Milnacipran more potently inhibits the reuptake of norepinephrine than duloxetine and venlafaxine.

Venlafaxine (Effexor®) has been shown to have therapeutic benefit in the treatment of neuropathic pain. Venlafaxine is available in an extended-release formulation which has a better tolerability profile than the immediate-release formulation.

Some of the side effects associated with SNRIs can include nausea, vomiting, dizziness, sleepiness, trouble sleeping, abnormal dreams, constipation, sweating, dry mouth, yawning, tremor, gas, anxiety, agitation, abnormal vision such as blurred vision or double vision, headache, and sexual dysfunction. Abrupt withdrawal of SNRIs should be avoided (associated with anxiety, vivid dreams and other symptoms).

SNRIs should be used with caution in patients with epilepsy, history of mania, cardiac disease, diabetes, angle-closure glaucoma, concomitant use of drugs that increase risk of bleeding, history of bleeding disorders (especially GI bleeding), disorders of the liver and kidneys, pregnancy, and breast-feeding.

Selective Serotonin Reuptake Inhibitors (SSRIS)

The third class of drugs, the selective serotonin reuptake inhibitors (SSRIs), includes fluoxetine (Prozac®), sertraline (Zoloft®), paroxetine (Paxil®), fluvoxamine (Luvox®), citalopram (Celexa™), escitalopram (Lexapro®), vilazodone (Viibryd®), and vortioxetine (Brintellix®).



The SSRIs have fewer side effects and are less sedating than the tricyclic antidepressants. They are effective antidepressants and can be used for headache prevention, but they are less effective and of questionable benefit for other types of chronic pain.

SSRIs have been disappointing for neuropathic pain. Most studies of the serotonin-selective type (non-tricyclic) antidepressants have shown little or no pain relief.

Some of the side effects associated with SSRIs include dry mouth, stomach distress with nausea and vomiting, diarrhea, sweating, poor appetite, dizziness, tremors, drowsiness, anxiety, nervousness, insomnia, headache, increased blood pressure, increased heart rate, increased cholesterol levels, and sexual problems. Abnormal bleeding can occur especially in individuals currently using an NSAID.

SSRIs should be used with caution in patients with epilepsy, history of mania, cardiac disease, diabetes, angle-closure glaucoma, concomitant use of drugs that increase risk of bleeding, history of bleeding disorders (especially GI bleeding), disorders of the liver and kidneys, pregnancy, and breast-feeding.

Norepinephrine Dopamine Reuptake Inhibitors (NDRIS)

A fourth class of antidepressants includes a number of drugs that are norepinephrine-dopamine reuptake inhibitors or NDRI. They are primarily used in the treatment of depression but are also prescribed for smoking cessation and for the treatment of attention deficit disorder. They are not particularly useful for chronic pain.

The only NDRI that is approved by the Food and Drug Administration for the treatment of depression is bupropion (Wellbutrin®).

Although marketed for different indications, Wellbutrin® (depressant) and Zyban® (smoking cessation) contain the same active ingredient and therefore, should not be taken concurrently without close health care professional supervision.

Other Antidepressants

Trazodone (Desyrel®) was developed for the treatment of depression but is much more frequently used today to alleviate insomnia. It is not commonly used for chronic pain. Some of the most common side effects of trazodone are sedation, dry mouth and dizziness. An extremely rare, but dangerous side effect of trazodone is Priapism – a prolonged painful erection. If it occurs, an admission to emergency department is necessary for a treatment with an antidote.

Mirtazapine (Remeron®) can cause sedation, increased appetite, weight gain, increased cholesterol, dizziness, dry mouth, and constipation.



The monoamine oxidase inhibitors (MAOIs) are very rarely used now days and generally not used to treat chronic pain. Those such as phenelzine (Nardil®), tranylcypromine (Parnate®), isocarboxazid (Marplan®), Rasagiline (Azilect®), Safinamide (Xadago®) and selegiline (Eldepryl®) commonly cause weakness, dizziness, headaches and tremor. While the last three are used to treat Parkinson's disease, the other MAOIs are used as antidepressants. They also have many drug-drug and drug-food interactions further limiting their use.

Stopping Antidepressants: Antidepressants should not be stopped abruptly. It may cause anxiety, headaches, nausea, dizziness and burning and sensory disturbances including shock-like electrical sensations. Always consult your health care provider before discontinuing an antidepressant.

Alert: Mixing Antimigraine Drugs & Certain Antidepressants may cause Serotonin Syndrome

Serotonin is a brain hormone that keeps mood stable and appetite in check, as well as serving other functions. More than 50 commonly prescribed medicines (including certain anti-migraine medications and certain drugs to treat depression) boost the amount or effect of serotonin in the body. When two or more drugs that affect serotonin levels are taken, they can increase the amount of serotonin and may lead to bothersome or dangerous, even life-threatening, symptoms.

Antidepressant medications include:

- Selective serotonin reuptake inhibitors (SSRIs; including citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs; including desvenlafaxine, duloxetine, milnacipran, and venlafaxine)
- Dopamine-norepinephrine reuptake inhibitors (including bupropion)
- Serotonin modulators (including nefazodone, trazodone, and vilazodone)
- Tricyclic antidepressants (TCAs; including amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, and trimipramine)

Antimigraine agents

- Triptans (including sumatriptan, rizatriptan, and others)
- Ergot derivatives (including ergotamine and methylergonovine)

Other agents (the following list is not exhaustive)

- Non-opioid
 - Tryptophan
 - Amphetamines
 - Levodopa, carbidopa-levodopa
 - Metoclopramide
 - Valproate



- Carbamazepine
- Dextromethorphan
- Cyclobenzaprine
- Monoamine oxidase inhibitors
- Lithium
- Opioids
 - Cocaine
 - Pentazocine (Talwin®)
 - Tramadol (Ultram®)
 - Meperidine (Demerol®)
 - Fentanyl (Duragesic®)

Serotonin can cause a variety of symptoms — no one gets all the symptoms at once, but anyone with too much serotonin will have at least a few symptoms. These symptoms can include mental changes such as anxiety, confusion, delirium, hallucinations, headaches, insomnia, mania (constant and sometimes senseless activity without rests), or coma; nerve or muscle symptoms such as tremor (shaking), unsteady coordination, muscle jerks, abnormally jumpy reflexes, jerking eye movements or changes in pupil size, restlessness, or seizures; temperature or vital sign control problems which can include sweating or flushing, fevers, hyperventilation, slowed breathing, a change in heart rhythm, or high or abnormally low blood pressure; and digestive symptoms including abdominal pain, nausea, vomiting, or diarrhea.



Antiepileptic (Anticonvulsant) Drugs

Antiepileptic medications have been found to be widely effective in various neuropathic pain conditions.

Several drugs that were developed for the prevention of epileptic seizures (convulsions) have been found to help certain pain conditions. For example, carbamazepine (Carbatrol[®], Tegretol[®]) is approved by the FDA for relieving the pain of trigeminal neuralgia. Gabapentin (Neurontin[®]) is approved for the management of postherpetic neuralgia (PHN: pain that lasts one to three months after shingles has healed). Pregabalin (Lyrica[®]) is approved for PHN, painful diabetic neuropathic pain, and fibromyalgia. Nevertheless, most use of antiepileptics for pain is “off label”. Some anticonvulsants such as valproic acid and topiramate are indicated migraine prevention.

These medications cause central nervous system sedation and should be used cautiously with opioids.

Although these medications have been thought in the past not to be habit forming, new studies have called this point into question. Regardless, abrupt discontinuation can be hazardous. Antiepileptics should be stopped only after discussing how to do so with a health care professional. Common side effects are drowsiness, peripheral edema (lower extremity swelling), and unsteady gait or poor balance. These symptoms tend to diminish over time.

Gabapentin (Neurontin[®]) is widely utilized and has proven to be effective in many people for nerve injury or neuropathic pain. Decreased mental alertness can occur especially at higher doses, but this is variable and is person specific. Generic gabapentin is available. Gralise[®], a once-a-day gabapentin, is indicated for the management of postherpetic neuralgia (PHN). Gralise[®] is not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration. There is a difference in individual tolerability and experience of adverse effects with each medication.

A similar drug to gabapentin, pregabalin (Lyrica[®]), has been found to be effective in postherpetic neuralgia, fibromyalgia, diabetic neuropathy and in neuropathic pain associated with spinal cord injury. Its primary advantage over gabapentin is thought to be pregabalin’s longer duration of action, allowing a twice daily dosing and improved absorption; however, there is no evidence that this translates to an increased clinical effect. Pregabalin is not associated with significant drug interactions and can be used over a wide dose range (150 to 600 mg/day). Its side effect profile is similar to gabapentin, and it is generally well tolerated. Side effects are mostly mild-to-moderate and transient, with dizziness and somnolence being the most common. Other adverse effects include dry mouth, peripheral edema, blurred vision, weight gain, and concentration or attention difficulties. Often, gabapentin and pregabalin require a period of time before their effectiveness in treating a person with pain is realized because the medications need to be titrated to the appropriate dose.

The FDA issued a warning on the use of antiepileptics and the risks of suicidal thoughts and suicide. Patients utilizing antiepileptics for pain control should be monitored for any signs and



symptoms of suicidal thoughts. There have been scattered reports of misuse of gabapentin and pregabalin for their intoxicating effects.

Decreased mental alertness can be magnified when an antidepressant is taken with an opioid and/or benzodiazepine.

The following table lists antiepileptic (anticonvulsant) but gabapentin and pregabalin are the primary drugs in this class prescribed for chronic pain.

ANTIEPILEPTICS POSSIBLY USEFUL IN CHRONIC PAIN	
Gabapentin* (Neurontin®)	Has proven to be effective in some people for nerve injury or neuropathic pain. Some mental fuzziness possible at higher doses.
Pregabalin* (Lyrica®)	Found to be effective in postherpetic neuralgia, diabetic neuropathy, fibromyalgia, and neuropathic pain from spinal cord injury. Some advantages over gabapentin with twice a day dosing. It is generally well tolerated.
Carbamazepine** (Tegretol®)	Interacts with some other drugs, can affect the liver and white blood cells. Used for trigeminal neuralgia.
Valproic acid** (Depakote®)	Used in headache for prevention or nerve pain. May affect platelets as an adverse effect.
Phenytoin** (Dilantin®)	Stronger evidence supports the use of the above agents over phenytoin. The risk of adverse effects and drug interactions also precludes its regular use.
Lamotrigine (Lamictal®)	May be useful for pain refractory to carbamazepine. Used in trigeminal neuralgia and central pain. Not FDA approved and clinically not recommended for neuropathic pain. May cause dizziness, constipation, nausea, decreased mental awareness, etc.
Tiagabine (Gabitril®)	Used in combination with other anticonvulsant agents in the management of partial seizures. Possibly useful in treating neuropathic pain. Most common side effects include nonspecific dizziness, drowsiness, and difficulty with concentration. Has been associated with new onset seizures and status epilepticus in patients without epilepsy.
Lacosamide (Vimpat®)	Lacosamide is an anticonvulsant. It is not typically used for chronic pain.
Topiramate (Topamax®, Topiragen™)	Generally, well tolerated but sometimes causes confusion, dizziness, fatigue, and problems with coordination and concentration. Minimally useful in treating neuropathic and sympathetically maintained pain. It is also being used as a preventive migraine treatment. Side effects include strange sensations and loss of appetite. May cause secondary angle closure glaucoma and, if left untreated, may lead to permanent vision loss. It may also cause dose-related weight loss and cause or predispose the patient to kidney stones.
Levetiracetam (Keppra®)	Indicated for use as adjunctive therapy in the treatment of partial seizures in adults. It is possibly effective in neuropathic pain.
Oxcarbazepine (Trileptal®)	Indicated for the treatment of partial seizures. Possibly useful in treating neuropathic pain. Probably useful for trigeminal neuralgia.



Zonisamide (Zonegran®)	Indicated for use as adjunctive therapy for treatment of partial seizures (or <i>focal seizures</i>) in adults with epilepsy. Possibly useful in treating neuropathic pain.
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*Only gabapentin and pregabalin are approved by the FDA and have solid evidence of efficacy in general neuropathic pain.

**Carbamazepine, Valproic Acid, and Phenytoin can reach toxic level in blood leading to death and may also cause serious damage to liver, pancreas, and blood cells leading to fatalities. Regular safety blood checks are mandated when taking these three medications, including their blood levels, complete blood count, and liver function test.

Sodium Channel Blocking & Oral Antiarrhythmic Agents

Intravenous lidocaine has strong sodium channel blocking properties and has demonstrated efficacy in several uncontrolled studies on neuropathic pain. Some pain centers use intravenous lidocaine both as a diagnostic tool to assess responsiveness to a subsequent oral sodium channel blocker (e.g., mexiletine, oxcarbazepine, and carbamazepine) as well as a therapeutic tool when delivered in an inpatient setting.

Those anti-arrhythmics with local anesthetic properties are rarely used except in refractory or difficult to treat pain. They are approved for the prevention of disturbances in heart rhythm, but just as they interrupt premature firing of heart fibers, they also diminish premature firing of damaged nerves. This leads to less firing of the nerve and hence less capability of the nerve to trigger pain.

Due to safety concerns, the only anti-arrhythmics that are occasionally used for chronic pain are mexiletine (Mexitil®) and rarely flecainide (Tambocor™) due to possible cardiac side effects. They reduce pain in diabetic neuropathy, post stroke pain, complex regional pain syndrome (CRPS), and traumatic nerve injury.

Mexiletine is chemically similar to lidocaine, an anesthetic. Common side effects of mexiletine include dizziness, anxiety, unsteadiness when walking, heartburn, nausea, and vomiting. Consult a health care professional if pregnant or planning to get pregnant, have a history of heart attack, are a smoker, or take any of the following medications: amiodarone, fluvoxamine, dofetilide (Tikosyn®), bupropion, or sodium bicarbonate. Mexiletine should be taken three times daily with food to lessen stomach irritation. Infrequent adverse reactions include sore throat, fever, mouth sores, blurred vision, confusion, constipation, diarrhea, headache, and numbness or tingling in the hands and feet. Serious symptoms occur with overdose including seizures, convulsions, chest pain, shortness of breath, irregular or fast heartbeat, and cardiac arrest.

Flecainide (Tambocor™) was approved to treat arrhythmias and can slow a fast heart rate. It has also been effective for treating certain painful conditions related to neuropathic pain. Although cardiac side effects with flecainide may be infrequent, they can be catastrophic. An EKG is recommended before treatment is started. This drug should probably not be used for pain management in patients with a history of cardiovascular or heart disease. The health care professional should be made aware of any kidney or liver problems because this may require



monitoring of drug levels or a dosage reduction. Flecainide interacts with amiodarone, several antipsychotic and anti-arrhythmic medications, and ranolazine (Ranexa®). Common side effects, which usually occur within the first two to four weeks of therapy, are nausea or vomiting, constipation, headache, dizziness, visual disturbances, edema, and tremor.

Topical Pain Relievers

Creams, gels, sprays, liquids, patches, or rubs applied on the skin over a painful muscle or joint are called *topical pain relievers* or *topical analgesics*. Topical agents have also gained popularity for use in certain neuropathic pain conditions such as diabetic neuropathy, postherpetic neuralgia (PHN), or neuroma pain. They are also prescribed in CRPS states. Many are available over-the-counter without a prescription. They are not particularly effective for deep neuropathic pain or radicular pain.

Topical agents should be distinguished from transdermal medications, which are also applied directly to the skin. Whereas topical agents work locally and must be applied directly over the painful area, transdermal drugs have effects throughout the body and work when applied away from the area of pain (currently available transdermal drugs include fentanyl, buprenorphine, and clonidine; topical drugs include diclofenac and lidocaine with or without tetracaine and prilocaine). Transdermal medication in a patch is absorbed through the skin by the bloodstream over a period of time.

These products should not be applied on wounds, damaged skin, or the face. Lastly, after application, hands should be washed thoroughly to avoid getting these products in sensitive areas such as the eyes.

Salicylates

Some of the OTC topical agents contain salicylates, a family of drugs that reduce inflammation and pain. They come from the bark of the willow tree and are the pain-relieving substances found in aspirin. Small amounts relieve mild pain. Larger amounts may reduce both pain and inflammation. Salicylates decrease the ability of the nerve endings in the skin to sense pain. Large amounts can be absorbed and lead to similar adverse effects as when given orally. The use of topical medications, which include salicylates or aspirin, should not be used for more than 7 days. Salicylates can be absorbed into the blood stream and cause metabolic acidosis.

Counterirritants

Counterirritants (including salicylates), another group of topical agents, are specifically approved for the topical treatment of minor aches and pains of muscles and joints (simple backache, arthritis pain, strains, bruises, and sprains). They stimulate nerve endings in the skin to cause feelings of cold, warmth, or itching. This produces a paradoxical pain-relieving effect by producing less



severe pain to counter a more intense one. Some topical pain relievers (counterirritants) are methyl salicylate, menthol, camphor, eucalyptus oil, turpentine oil, histamine dihydrochloride, and methyl nicotinate.

Menthol counterirritants come in various forms such as balms, creams, gels, and patches under several brands such as BenGay[®], Icy Hot[®], Salonpas[®], and Thera-Gesic[®] for ease of application. The balms, creams, and gels can be applied to the painful area(s) three to four times a day (usually for up to one week). When using the BenGay[®] patch product, one patch can be applied for up to 8 to 12 hours; if pain is still present, a second patch may be applied for up to 8 to 12 hours (maximum: two patches in 24 hours for no longer than three days of consecutive use). The Salonpas[®] Pain Relief Patch[®] (10% methyl salicylate and 3% menthol) is currently the only FDA-approved OTC topical analgesic patch and can be applied up to three to four times/day for seven days; the patch may remain in place for up to 8 hours. It is approved for temporary relief of mild-to-moderate aches and pains of muscles and joints associated with strains, sprains, simple backache, arthritis, and bruises.

Topical prescription NSAIDs still carry some risk of adverse effects (mostly skin irritation). Topical products containing NSAIDs (e.g., diclofenac) are promoted as carrying less risk of side effects versus the oral NSAIDs (e.g., ibuprofen), but they still must be considered. The FDA warning regarding NSAIDs applies to both oral and topical medications – this would constitute duplicative therapy. Also, these products should not be applied on wounds, damaged skin, or the face. Lastly, after application, hands should be washed thoroughly to avoid getting these products in sensitive areas such as the eyes. When removing and discarding used patches, fold the used patches so that the adhesive side sticks to itself. Safely discard used patches where children and pets cannot get to them.

Prescription NSAID topicals are not recommended on larger “joints” of the body such as the back.

Capsaicin (cap-SAY-sin) is the active ingredient in hot peppers, which produces a characteristic heat sensation when applied to the skin (dermal drug delivery). Several studies have suggested that capsaicin can be an effective analgesic in at least some types of neuropathic pain and arthritic conditions (osteoarthritis and rheumatoid arthritis). An adequate trial of capsaicin usually requires four applications daily, around the clock, for at least three to four weeks. Some individuals may experience a burning sensation, which usually lessens within 72 hours with repeated use. Gloves should be worn during application and hands should be washed with soap and water after application to avoid contact with the eyes or mucous membranes.



Other Agents & Local Anesthetics

Aspirin in chloroform or diethyl ether, capsaicin (Zostrix[®], Zostrix[®]-HP, Qutenza[™]), EMLA[®] (eutectic mixture of local anesthetics; contains lidocaine and prilocaine) cream, and local anesthetics such as the lidocaine patch 5% (Lidoderm[®]) are topical treatments for neuropathic pain. Of these, the topical lidocaine patch 5% and capsaicin patch are the only FDA-approved treatments for neuropathic pain, and they require a prescription.

Topical anesthetics, such as EMLA[®] (Eutectic Mixture of Local Anesthetic; contains lidocaine and prilocaine) cream and L.M.X.4[®] (contains lidocaine 4%), are used primarily prior to painful procedures such as blood draws, lumbar puncture (spinal tap), and wart removal. EMLA[®] cream may be effective in the treatment of postherpetic neuralgia, ischemic (decreased blood supply) neuropathy, and a variety of other neuropathic conditions.

EMLA[®] cream is a combination of the local anesthetics lidocaine and prilocaine. This combination results in a relatively constant release of dissolvable local anesthetics that can diffuse through the skin and soft tissue. A thick layer of EMLA[®] cream is applied to intact skin and covered with an occlusive dressing. The minimal application time to obtain reliable superficial pain relief is one hour. However, the cream may be left on the skin for up to two hours, depending on the degree of the procedure performed. Pain relief can be expected to increase for up to three hours under occlusive dressing and persist for one to two hours after removal of the cream. Side effects to EMLA[®] cream include skin blanching, redness, and swelling. In younger individuals or in cases in which too much has been applied, negative effects can occur to hemoglobin (red blood cells). Therefore, EMLA[®] cream should be avoided in individuals less than one month old and in patients with a predisposition to methemoglobinemia (a problem with the red cell). EMLA[®] cream should also not be applied to broken skin or mucous membranes (e.g., mouth). EMLA[®] requires a prescription in the U.S.

L.M.X.4[®] contains 4% lidocaine and is available without a prescription. It has a shorter application time (30 minutes) and a shorter duration of action (30 minutes) than EMLA. It has not been shown to be effective for chronic pain most likely because of its short duration. L.M.X.4[®] is available OTC in the U.S.

Lidoderm[®] 5% (lidocaine) patches can be cut to fit over the area of pain. The 5% lidocaine patch is FDA approved for the treatment of a neuropathic pain condition, specifically PHN, and requires a prescription. It measures 10 cm x 14 cm and has a clear plastic backing that must be removed before application of the patch to the skin. The manufacturer states that up to three patches can be applied simultaneously to intact skin for up to 12 hours in any 24-hour period. Generic lidocaine is available in multiple forms (e.g., patch, gel, ointment) and can be less expensive.

Side effects of topical local anesthetics are usually minimal and include localized skin irritation and swelling that generally disappear within two to three hours after the local anesthetic is removed from the skin. As a rule, blood concentrations of topical local anesthetics are well below toxic levels.



Potential hazards still exist, however. In 2007, the FDA issued a public health advisory to notify consumers and health care professionals of potential life-threatening side effects associated with the use of topical anesthetics, particularly before cosmetic procedures. At risk are consumers, especially those without the supervision of a health care professional. Issues may arise particularly if the consumer applies large amounts of anesthetics or cover large areas of the skin, leaves these products on for long periods of time, or uses materials, wraps, or dressings to cover the skin after anesthetic application. Application to areas of skin irritation, rash, or broken skin may also increase the risk of systemic absorption. The FDA recommends that if topical anesthetics are needed prior to medical or cosmetic procedures, consumers ask their health care professional for instructions on the safe use of these products, use only FDA-approved products, and use products with the lowest amount of anesthetic while applying the least amount possible to relieve pain.



Compounded Medications

There are additional topical agent combinations, which can be compounded at a local pharmacy. They can be very expensive. These compounded mixtures are prepared uniquely for each individual but have not passed rigorous scientific study. Any benefit from such compounded creams is anecdotal.

Use of these compounded mixtures is controversial and most insurance companies will not pay for these medications. This topic is included here for educational purposes as some physicians prescribe compounded topical agents.

Compounded medications are not commercially available; rather, they are prescribed by a health care professional and prepared by a pharmacist to meet an individual's unique needs. These compounded medications do not go through the same FDA approval process that is required for commercially available prescription drugs. Therefore, trials may or may not be conducted to determine safety and efficacy. Such studies are not a legal requirement for compounded medications.

The most common compounded TOPICAL medications for pain are topical gels, creams and ointments. They typically contain ingredients such as lidocaine, amitriptyline, ibuprofen, gabapentin, and/or ketoprofen. Opioids, such as morphine, are also compounded for topical administration. The benefit to this type of delivery system is that medication is localized to the area of pain. Lidocaine 5% in PLO gel has been shown in studies to be effective in relieving pain with a minimal enough amount of systemic absorption to alleviate fears of approaching toxic levels.

Topical medications, such as the combination of ketamine (a dissociative anesthetic agent with abuse potential) and amitriptyline (a tricyclic antidepressant), have been proposed as an alternative treatment for neuropathic disorders including complex regional pain syndrome (CRPS). These types of topical medications, in general, are so far unproven. There is one study of topical baclofen, amitriptyline, and ketamine that was shown to be effective in relieving chemotherapy induced peripheral neuropathy. The study has been repeated with mixed results but suggesting more effective treatment for the hands than the feet. To justify continued use of these agents beyond the initial prescription, there should be documentation of effectiveness, including functional improvement, and/or decreased use of other pain medications.

Other compounded agents include those injected into the epidural and spinal canal. An outbreak of meningitis in 2012, secondary to epidural steroids that were compounded, produced much more scrutiny of compounding pharmacies and their quality standards by the FDA and state boards of pharmacy.

Many intraspinal or intrathecal (injection into the sheath surrounding the spinal cord) analgesics need to be compounded for improved pain relief and delivered via intraspinal drug delivery systems or pumps. The best recommendation is to work with a compounding pharmacy that has a history of quality care and can answer questions about stability and sterility of their compounding techniques. Many states now regulate and oversee compounding pharmacies under the state's



Board of Pharmacy, thus, compounding pharmacies with active licenses in good standing should be sought out. License standing may be available by searching on the state's Board of Pharmacy website. Prior to using a compounded medication, it is important to know the clear risk vs. benefit and understand whether a commercially available medication might be appropriate.

Medications & Sleep Hygiene

Chronic sleep problems, also known as insomnia, are a significant problem in society and almost a universal issue for persons with persistent or chronic pain. People who have chronic sleep problems may be getting substantially less sleep than is needed for good health.

Sleep problems can be called “chronic” when they last more than three weeks, and these can last for months or years. These sleep disturbances are more serious; sorting them out and restoring good sleep may require the help of a health care professional.

Insomnia is not a disease, but a symptom of a problem; one of which includes pain. Insomnia can be a side effect of many medications. Alcohol and drug abuse or addiction can also interfere with sleep. According to national statistics, at least one half of all instances of insomnia are caused by psychological problems. Waking up too early is common for people who are depressed. Difficulty falling asleep is often caused by anxiety.

Pain is worsened by both the physical and emotional consequences of lack of restful sleep.

When people are deprived of the restful sleep they need:

- They become fatigued and less alert and attentive.
- They are more inclined to irritability and other mood problems that can make relationships with family, friends, and co-workers difficult.
- Their cognitive ability, concentration, and judgment suffer.
- Their ability to perform even simple tasks declines and productivity is sabotaged.
- They can make mistakes resulting in reduced productivity at home and on the job and increasing the opportunity for human error and fatigue-related accidents.

Scientific studies have confirmed that practicing good sleep hygiene is as effective as or more effective than medication treatment in improving the quality and quantity of sleep. It is common for people with persistent pain to believe that they sleep poorly because of pain, which may be true; however, studies demonstrate that it often happens the other way – poor sleep increases pain.

The costs of poor sleep are significant. In addition to the general lack of feeling refreshed both physically and emotionally, there are other consequences of sleep deprivation such as increase in cardiovascular risk. The negative health and economic consequences of poor-quality sleep and sleep deprivation are significant.

Some medications prescribed for chronic pain may disrupt the normal sleep cycle and some may be activating and make quality sleep difficult. Substances, including caffeine, theophylline, and



other stimulants, steroids, and some anti-hypertensive and antidepressant medication can precipitate insomnia.

People who snore or have sleep apnea (a condition in which the flow of air into the lungs is repeatedly blocked during the night resulting in periods when they stop breathing while asleep) are likely to have fitful, low-quality sleep often leading to daytime drowsiness. They half-waken several times a night and wake up unrefreshed. Increased weight and obesity are often associated with chronic pain, probably because of decreased activity, the use of certain medications and even depression that can lead to poor dietary habits. Obesity can cause or worsen sleep apnea and people with chronic pain have a tendency to gain weight due to decreased activity. People with sleep apnea may be at increased risk of respiratory depression when sedatives or opioids are used. These medications should be carefully supervised by medical personnel when used in the presence of sleep apnea.

Here are some sleep hygiene tips:

- Limit consumption of caffeine after early afternoon as well as nicotine and alcohol before sleep.
- Avoid late-afternoon naps (any time after 1 or 2 pm), especially greater than 30 minutes.
- Use the bedroom only for sleep-related activities (or sex!).
- Restrict time in bed to sleep hours.
- Limit strenuous exercise before sleep.
- Turn off electronic devices (phones, tablets, computers) while preparing for bedtime - keep these items out of the bedroom.
- Avoid watching action or violence on TV before bed.
- Develop a bedtime routine—have a regular bedtime and wake time every day.
- Develop a meditation and relaxation therapy program before bed as this can reduce physiologic arousal and promote sleep onset.
- Warm milk or mild tea (herbal or decaffeinated) can be soothing.
- Light can be blocked with an eye mask.
- Resolve emotional distress issues whenever possible before going to sleep.
- Decrease bedroom temperature.
- Use a white noise machine.
- Make sure the bed frame and mattress are adequate.
- In general, avoid naps during the day if they are interfering with getting to sleep at night. If a nap is essential, plan this in the late morning or early afternoon.

The NIH has created a brochure, your Guide to Healthy Sleep at http://www.nhlbi.nih.gov/files/docs/public/sleep/healthy_sleep.pdf.

Information on sleep can be found at <http://www.cci.health.wa.gov.au/docs/Info-sleep%20hygiene.pdf> and <http://www.mayoclinic.org/healthy-living/adult-health/in-depth/sleep/art-20048379>.



Hypnotics (sometimes called sedatives) for Insomnia

Sleep disturbances occur in 50–88 percent of patients experiencing chronic pain. Getting a good night's sleep is critical to the individual with chronic pain and often is hard to obtain. A restful night's sleep provides a number of benefits, including a sanctuary for the pain exhausted brain, extended time for muscle relaxation, and a release of the growth hormone which is necessary for healing damaged tissues of the body and is only released during deep phase of sleep. Not only duration of sleep, but its architecture (going through different phases of sleep throughout the night) is important for overall functioning of the body and reduction of pain. Not only does pain lead to sleep disturbances, though, but disturbed sleep has also been shown to increase pain over both short- and long-term intervals. Additionally, sleep deprivation has been shown to cause enhanced pain sensitivity in healthy individuals, again suggesting a reciprocal relationship between insomnia and pain disorders.

Cognitive behavior therapy (CBT) is recommended for first-line treatment of chronic insomnia. The use of medications (pharmacological therapy) is a reasonable consideration in those who do not respond to CBT.

Various medications may improve sleep. While sleeping pills are commonly prescribed for people with chronic pain, pain specialists rarely, if ever, recommend them for long-term use. Some can be habit-forming and may impair function and memory more than opioid pain relievers. **When combined with opioids, the incidence of adverse-effects, including fatal ones can increase.**

Benzodiazepines: Limitations and dangers of benzodiazepines were discussed above. Medications in this class of sedatives are not recommended as first-line or long-term treatments for chronic insomnia due to their many adverse side effects, including daytime somnolence, cognition and memory impairment, increased risk of falling, respiratory suppression, damaging sleep-architecture, high addiction potentiality, rebound insomnia, and anxiety. All medications in this class are schedule-IV controlled substances. They are, however, useful as short-term insomnia treatments (7-10 days) and include: estazolam (Prosom[®]), flurazepam (Dalmane[®]), triazolam (Halcion[®]) and temazepam (Restoril[®]). Other benzodiazepines commonly used as off-label medications in treating insomnia include lorazepam (Ativan[®]), clonazepam (Klonopin[®]), alprazolam (Xanax[®]), diazepam (Valium[®]), and oxazepam (Serax[®]). The use of these medications in treating insomnia is controversial, and there is no conclusive evidence supporting their use in this context.

Diphenhydramine (Benadryl[®]): Diphenhydramine is not FDA-approved for treatment of insomnia. Its efficacy is controversial; however, in low doses it is widely used and prescribed as an over-the-counter and prescription sleep aide. Adverse side effects include: sedation, dizziness, constipation, nausea, dry mouth, blurred vision, and weight gain. It may have serious side effects including: urine retention, cardiac arrhythmia, confusion, and bowel obstruction. These side effects can be particularly dangerous in older adults.

Zolpidem (Ambien[®]) and Zolpidem CR (controlled release): The difference between these two medications lies primarily in their half-lives. They were two of the most commonly prescribed insomnia medications during the first decade of the present century, yet newer hypnotics have



since been shown to have better safety profiles, making the latter more popular as insomnia treatments of late, but should be avoided for the same reasons as benzodiazepines. Adverse side effects include somnolence, dizziness, ataxia, amnesia, complex sleep-related behavior (such as sleep walking, sleep cooking/eating, sleep driving), and rebound insomnia.

Zaleplon (Sonata®): Although zaleplon was proven effective and safe for treating insomnia, its use among clinical practices has been limited, primarily because of its ultrashort half-life and should be avoided for the same reasons as benzodiazepines. Adverse side effects include: somnolence, dizziness, ataxia, and amnesia.

Eszopiclone (Lunesta®): Eszopiclone is the best-documented agent in terms of safety for long-term use and has little or no suggestion of increased tolerance, dependence, or abuse. This medication should be avoided for the same reasons as benzodiazepines. Adverse side effects may include: somnolence, amnesia, ataxia, dizziness, and dry mouth and unpleasant taste in mouth.

Melatonin is effective at inducing sleep onset, rather than sleep maintenance. In the USA, melatonin is only available as an over-the-counter supplement and is not approved by the FDA for use in treating insomnia. Moreover, its dosage is not always reliable. Nevertheless, it is widely used and often preferred as a first-line treatment for insomnia due to its low side-effect profile. Common side effects include daytime sleepiness and dizziness.

Ramelteon (Rozerem®): Ramelteon is effective at inducing sleep onset, rather than sleep maintenance. Short-term ramelteon use is associated with improved sleep parameters in patients with insomnia, but its clinical impact is deemed small. That said, as it has a relatively low side-effect profile, ramelteon is often preferred over other hypnotics. Adverse side effects include: somnolence, dizziness, and fatigue.

Suvorexant (Belsomra®): It is FDA approved for treating sleep-onset and -maintenance insomnia. Suvorexant does not induce sleepiness but decreases wakefulness. It remains a schedule-IV federally controlled substance and some concerns about abuse potential has been raised. Adverse effects include: somnolence, confusion, complex sleep-related behaviors, and abnormal dreams.

Sedating Antidepressants

Tricyclic Antidepressants: This class of medications was discussed in an earlier section as pain relievers. In addition, in low doses, tricyclic antidepressants have been used as sleep aids for many years.

Doxepin (Silenor®): In low doses, doxepin is the first and only FDA-approved insomnia medication in its class and it is not a controlled substance. While high doses of doxepin can be dangerous, low doses appear to be safe and have proven effective at inducing sleep with few side effects. Adverse side effects include: somnolence and nausea. Doxepin may be preferred over other sleep aids due to its very low side-effect profile and is especially helpful in treating geriatric patients for whom it is the only approved insomnia medication.



Mirtazapine (Remeron®): Mirtazapine is an antidepressant with strong sedating properties, especially in lower doses. It is non-addictive and promotes restoring of sleep architecture. Adverse side effects include: somnolence, increased appetite and weight gain, abnormal dreams, dizziness, dry mouth, constipation, and seizures (rare).

Trazodone (Desyrel®): It is a potent hypnotic and is extensively used among clinical practices in treating insomnia despite its lack of approval from the FDA for use as a sleep medication. As with all antidepressants, it has no addiction potential and restores sleep architecture well. Adverse side effects include: somnolence, dry mouth, orthostatic drop in blood pressure causing dizziness, blurred vision, constipation, priapism (rare), and seizures (rare).

Sedating Antipsychotics

In general, sedating antipsychotics are not recommended for sleep by most guidelines. The FDA Blackbox warning states: 1) increased mortality in elderly patients with dementia-related psychosis and 2) suicidal thoughts and behavior. Warnings: CV events including stroke, neuroleptic malignant syndrome, metabolic changes including hyperglycemia and diabetes, dyslipidemia.

Quetiapine (Seroquel®): Quetiapine is prescribed in low doses as an off-label medication in treating insomnia; however, there are very few studies evaluating its efficacy and safety in this context. Adverse side effects are not commonly reported on low doses of this medication; however, side effects that were mentioned in Antipsychotic section above, like tremors, stiffness, involuntary movements of the body, weight gain, hypertension, elevated cholesterol, and cardiac rhythm alterations cannot be excluded.

Olanzapine (Zyprexa®): Olanzapine has been shown to improve sleep and sleep architecture, however, it is not a commonly prescribed insomnia medication for patients who do not suffer from psychiatric disorders. This is likely due to its notorious metabolic side effects, including weight gain, hypertension, elevated cholesterol and possibility of causing diabetes.

Non-Medication Treatment of Insomnia

Repetitive Transcranial Magnetic Stimulation (rTMS): This procedure uses an electromagnet to generate electric currents that stimulate areas of the brain. It has been used successfully as an adjuvant therapy in treating depression. Promising new research on the use of rTMS in treating insomnia has recently come to light.

Cranial Electrotherapy Stimulation (CES): This has also been shown to yield positive results in the treatment of insomnia. CES uses a small device to send weak electrical pulses to desired areas of the brain. It has been approved by the U.S. Food and Drug Administration for use in treating of anxiety, depression, and insomnia since 1979. It has been shown effective in treating insomnia, with few negative side effects and its use has also been shown to precipitate fast (as little as one week), significant improvements to sleep behaviors.



Psychotherapy: Through the years, multiple psychotherapeutic approaches to improve sleep were used. Cognitive-behavioral therapy for insomnia (CBT-I) is a specially designed insomnia-treatment approach, integrating most of the effective techniques to promote sleep. It consists of effective interventions targeting the various factors that cause insomnia. **As it has proved effective in many clinical trials, the American Academy of Sleep Medicine recommends CBT-I as a standard treatment for chronic insomnia.** CBT-I has proved effective in both individual- and group-treatment settings, improving duration and quality of sleep. Although it can be used as self-help, it works best when facilitated by a trained health care provider, usually a psychologist. One of the important parts of CBT-I is sleep hygiene which can be helpful in relieving insomnia while incorporated in daily life.

Meditation: Mindfulness meditation is a process during which one focuses one's attention on the present moment without judgment. Mindfulness practices are often incorporated in relaxation training, a component of CBT-I. Meditation alone is still considered a helpful technique for treating insomnia.



Muscle Relaxants

Many drugs have been marketed as muscle relaxants, even though most do not seem to have any direct effect on muscle. Perhaps they should be called “brain relaxants,” as they are all sedating, and this may be how they actually work. In the vast majority of cases due to increased sedation, respiratory depression and addiction potential, these medications should not be taken with opioids. If prescribed both classes of medications, be sure to have a discussion with a health care professional about the risks from taking these medications. Also, be sure medications prescribed are from only one health care professional who clearly knows everything being taken.

Sedation is a concern for those who drive, operate machinery, or otherwise are engaged in safety-sensitive jobs. Some also have analgesic (pain reducing) properties. Cyclobenzaprine (Flexeril[®], Amrix[®] extended-release) is chemically similar to the tricyclic antidepressants (TCAs) and may have a similar mechanism. Muscle relaxants have limited efficacy in the treatment of chronic pain but may be used to treat acute flare-ups. There are no studies to support the long-term use of muscle relaxants, especially for low back pain. Also, the long-term use of muscle relaxants for low back pain does not improve functional recovery and can also hinder recovery.

DRUGS USED AS MUSCLE RELAXANTS IN CHRONIC PAIN

Carisoprodol (Soma [®]) (A scheduled IV controlled substance)	Carisoprodol is a centrally acting skeletal muscle relaxant. It is metabolized to Meprobamate which is a barbiturate like drug that can contribute to abuse potential. Prescribers are advised to avoid Carisoprodol especially in patients taking other controlled substances such as opiates. It may cause physical dependence. It should be avoided in kidney or liver disease. <i>Avoid use in chronic pain.</i>
Cyclobenzaprine (Flexeril [®] , Fexmid [®] , Amrix [®])	Skeletal muscle relaxant that is structurally similar to the TCAs. Side effects include dizziness, drowsiness, dry mouth, constipation, confusion, and loss of balance. Avoid long-term regular use in chronic pain.
Methocarbamol (Robaxin [®])	Skeletal muscle relaxant with sedative properties. Side effects include drowsiness and urine discoloration to brown, black, or green.
Metaxalone (Skelaxin [®])	Skeletal muscle relaxant. Use with caution in those with liver disease.
Chlorzoxazone (Parafon Forte [®] DSC, Lorzone [®])	Skeletal muscle relaxant with sedative properties. Use with caution in those with liver disease.
Dantrolene (Dantrium [®])	A true muscle relaxant that acts directly on skeletal muscle and produces fewer central adverse effects. Can have significant liver toxicity. The dose should be increased slowly.
Orphenadrine (Norflex [™])	A skeletal muscle relaxant with analgesic properties.
Tizanidine (Zanaflex [®])	A drug indicated for spasticity associated with multiple sclerosis or spinal cord injury but being used off label for chronic pain. This drug may increase liver enzyme levels. Tizanidine interacts with blood pressure medications and causes low blood pressure.



Baclofen (Lioresal® - oral and injectable), Gablofen® - injectable) - Not technically a muscle relaxant - used for painful spasm from muscle spasticity due to spinal cord or nervous system injury	Withdrawal should not be abrupt and can be life-threatening (mainly with intrathecal therapy). Inhibits transmission at the spinal level and depresses the central nervous system. The dose should be increased slowly to avoid the major side effects of sedation and muscle weakness (other adverse events are uncommon). Baclofen is known to be safer for long-term use. It is not typically recommended for non-neurological muscle spasm.
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Botulinum Toxins

Botulinum toxins, Botox® (onabotulinumtoxinA), Dysport® (abobotulinumtoxinA), Xeomin® (incobotulinumtoxinA), and Myobloc® (rimabotulinumtoxinB) have been found to be effective in decreasing tone in overactive (hypertonic) muscles, which may be present in a number of chronic pain conditions. A recent review article regarding the treatment of refractory pain by Dr. Jabbari summarizes that botulinum toxins have “established efficacy” to control pain of cervical dystonia, chronic migraine, and chronic lateral epicondylitis (tennis elbow).

The review also found a lower level of evidence and classified botulinum toxin as “probably effective and recommended” for post-herpetic neuralgia (PHN), post-traumatic neuralgia, pain of plantar fasciitis, piriformis syndrome, and pain in total knee arthroplasty; “possibly effective, may be used at discretion of clinician” for allodynia of diabetic neuropathy, chronic low back pain, painful knee osteoarthritis, anterior knee pain with vastus lateralis imbalance, pelvic pain, post-operative pain in children with cerebral palsy after adductor hip release surgery, post-operative pain after mastectomy, and sphincter spasms, and pain after hemorrhoidectomy; “efficacy not proven due to diverse class I and II results” for myofascial pain syndrome and chronic daily headaches; and “negative” for episodic migraine and tension headaches (Pain Med 2011; 12:1594-1606). There appears to be additional pain-relieving properties of botulinum toxin irrespective of muscle relaxation.

Botox®, Dysport®, Xeomin®, and Myobloc® are FDA-approved for the treatment of the postural abnormalities and pain associated with cervical dystonia, also known as torticollis (head tilting, neck pain, and neck muscle spasms). Only one botulinum toxin (Botox® onabotulinumtoxinA) is additionally approved by the FDA to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting four or more hours each day in people 18 years or older, and to treat increased muscle stiffness in elbow, wrist, and finger muscles in people 18 years and older with upper limb spasticity.

The efficacy of botulinum toxins in back, neck, and extremity muscle pain has been studied as an off-label use with mixed results. In some studies, on myofascial pain, botulinum toxin has not been found to be more effective than traditional trigger point injections with local anesthetic or saline.

The dosage units for botulinum toxins are unique to each product and are not interchangeable. In addition, the FDA has specified nonproprietary names for each drug to help prevent medication errors. Many physicians are using botulinum toxins off-label for other painful conditions including types of headache other than chronic migraine treated with Botox®



(onabotulinumtoxinA), osteoarthritis of the knee and shoulder and various muscle pain syndromes (myofascial pain), although the evidence for such use is not conclusive.

For treatment of chronic pain conditions, when effective, botulinum toxins typically demonstrate efficacy within 3 to 5 days after intramuscular administration and last for an average of 12 weeks.

Side effects may occur after receiving botulinum toxin (see FDA warning box below). Muscle weakness is one of the most common side effects. Swallowing problems can develop when treating cervical muscle problems, especially with injections into the sternocleidomastoid muscle. Other adverse effects include dry mouth, pain at the injection site, neck pain, headache, and flu-like symptoms. Additionally, adverse effects may include local bruising, generalized fatigue, lethargy, dizziness, and difficulty speaking or hoarseness.

FDA WARNING: DISTANT SPREAD OF BOTULINUM TOXIN EFFECT

Postmarketing reports indicate that botulinum toxin may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses, including spasticity in children, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

NMDA Inhibitors (Including Ketamine)

Numerous compounds that specifically target mechanisms mediating neuropathic pain such as the N-methyl-D-aspartate (NMDA) receptor complex are currently in clinical trials. NMDA inhibitors appear to help prevent sudden acute pain from progressing into chronic pain. These act by blocking receptors of neurotransmitters that are essential for making long-term memories.

The NMDA antagonists also reduce opioid tolerance and may enhance opioid analgesia.

The utility of these agents has been limited by their significant dose-related side effect profile, which includes lightheadedness, dizziness, tiredness, headache, nervous floating sensation, bad dreams, and sensory changes.

Agents that have clinically relevant NMDA blocking properties include ketamine, amantadine (an anti-influenza medication), memantine (an Alzheimer drug; Namenda™ – but not studied for chronic pain), dextromethorphan (an anti-cough medication), and methadone (an opioid).



Memantine and amantadine are weaker NMDA receptor blockers and consequently they are also thought to have fewer CNS side effects.

The basic concept of NMDA antagonism in neuropathic pain remains sound, but there is a strong need for more studies and perhaps development of newer agents with fewer central nervous system side effects.

There has been increasing interest surrounding the use of ketamine in complex regional pain syndrome (CRPS) and pain therapy via the continuous IV infusion of ketamine which has been reported to lead to pain reduction over a number of weeks. However, serious side effects may occur, especially if treatment is repeated including hallucinations, memory defects, panic attacks, nausea/vomiting, somnolence, cardiac stimulation and in a few subjects, liver toxicity. Much of the evidence is anecdotal, but increasing research is suggesting some possible benefit from this therapy although many guidelines do not feel that there is enough evidence to support its use clinically. Reviews of ketamine use for chronic pain and CRPS specifically from 2013 and 2015 concluded that the evidence from available literature is inconclusive and the quality of the research is low with small sample size, lack of blinding or controls and serious methodological flaws.

Because their potential for harm outweighs evidence of limited short-term benefit in patients with CRPS, **NMDA receptor antagonists are not recommended.**

Low-Dose Naltrexone (LDN)

Naltrexone is an opioid antagonist (blocker). Low-dose naltrexone (4.5 mg) is not commercially available, must be purchased from a compounding pharmacy, and its use is off label. While not recommended in most guidelines as studies are inconclusive, it is being prescribed by some pain physicians with anecdotal reports of effectiveness. LDN has a low side effect profile. However, it should never be co-administered with opioids because it is an opioid antagonist.

Antihypertensive & Adrenergic drugs, Bisphosphonates, Thalidomide & Calcitonin

Alpha adrenergic antagonists (e.g., clonidine, lofexidine, phentolamine, phenoxybenzamine, reserpine, dexmedetomidine, and others) have been used clinically for the treatment of CRPS without good evidence from clinical research studies. The rationale for their use is the recognized role of the sympathetic nervous system in CRPS and the theory that blockade will provide pain relief. Oral clonidine has not demonstrated significant efficacy in neuropathic pain and is challenging to use due to its side effect profile. It is more widely utilized in implantable intrathecal (injection into the sheath surrounding the spinal cord) drug pumps for pain.

Clonidine (Catapres[®], Catapres-TTS[®] patch) is a centrally acting alpha-agonist that lowers blood pressure and has also been shown to have pain-relieving properties in sympathetically maintained pain conditions such as complex regional pain syndrome (CRPS). It is available as a tablet for oral



administration, as an injectable solution for administration in an epidural or implanted pump, or as a once-weekly patch. As mentioned previously, clonidine may be helpful controlling withdrawal symptoms from opioids.

Side effects can include dry mouth, drowsiness (sedation and somnolence occurs in over 30% of patients), dizziness, and constipation. Transient localized skin reactions can occur with the patch. Clonidine lowers blood pressure and heart rate, thus, it should be used cautiously in patients who have low blood pressure. Safest usage would suggest measuring blood pressure prior to taking a dose of oral clonidine and not taking it for a blood pressure less than 90/60.

Due to the potential for additive affect, special caution must be taken in individuals taking other central nervous system depressant medications (opioids, sedative hypnotics, and benzodiazepines).

Clonidine should not be discontinued suddenly as this can result in symptoms such as nervousness, agitation, headache, and tremor accompanied or followed by a rapid rise in blood pressure. Some individuals can develop an allergy to clonidine with a generalized rash, itching, or swelling. It should be used with caution in patients with severe heart disease, cerebrovascular disease (stroke), or chronic kidney failure. To avoid hypertensive crisis, clonidine should not be used with tricyclic antidepressants (TCAs).

Lofexidine (Lucemyra™) has recently been approved by the FDA for use to treat opioid withdrawal symptoms and can be used in similar fashion to clonidine. Its efficacy appears to be similar to clonidine for the treatment of opioid withdrawal.

Bisphosphonates are a class of drugs used primarily to increase bone mass and reduce the risk of fractures in patients with osteoporosis. There are seven FDA-approved bisphosphonates: alendronate (Fosamax®, Fosamax Plus D™), etidronate (Didronel®), ibandronate (Boniva®), pamidronate (Aredia®), risedronate (Actonel®, Actonel® with calcium), tiludronate (Skelid®), and zoledronic acid (Reclast®, Zometa®). They are more popularly known for treatment and prevention of osteoporosis. For chronic pain, they have been used in the treatment of CRPS in several studies. While the primary mechanism of these agents has been thought to be reduction in pain by preventing the osteoporosis associated with CRPS, other peripheral and central mechanisms may be responsible and deserve investigation. Adverse effects can include gastritis and erosive esophagitis (stomach and esophagus distress), and rarely, damage of the jaw bone (osteonecrosis). In October 2010, the FDA also issued a special alert on the association between the use of bisphosphonates and the risk of atypical fractures of the thigh. Patients are encouraged to consult their health care professionals for new hip or thigh pain.

There has been interest in the drug **thalidomide** due to its immunomodulatory and anti-inflammatory effects. Thalidomide was first introduced in 1957 as a sleep aid and as a treatment for morning sickness. It was subsequently removed from the market due to severe teratogenic side effects and then returned to the market as a treatment for myelodysplastic syndrome and multiple myeloma. Lenalidomide is an analog of thalidomide with similar efficacy but an improved side effect profile. There are reports and studies of both agents for the treatment of chronic pain, especially CRPS. Recent publications however do not support lenalidomide (a thalidomide derivative) use in unselected CRPS cases.



Calcitonin is the lesser known of the thyroid's two main hormones. It decreases bone resorption and has direct effects on the kidneys and gastrointestinal tract. It is also thought to have anti-pain effects. Recently, the salmon calcitonin formulation that is nasally inhaled has been more commonly used than injectable calcitonin due to ease of administration. Calcitonin has been used to treat the bone pain associated with compression and sacral insufficiency fractures.



Medications for Migraine

Migraine headache treatment typically includes one or a combination of abortive (rescue) and/or prophylactic (preventive) agents. Abortive therapy has been revolutionized with the advent of the triptans (serotonin receptor agonists). Triptans narrow (constrict) [blood](#) vessels in the [brain](#) and relieve swelling. These drugs are used to effectively and quickly relieve headache pain, sensitivity to light and noise, and nausea and vomiting associated with migraines.

Triptans include sumatriptan (Imitrex® – also available by injection or nasal spray, Sumavel® DosePro® – needle-free delivery), zolmitriptan (Zomig® – also available by nasal spray or as orally-disintegrating tablets), naratriptan (Amerge®), rizatriptan (Maxalt® – also available as orally-disintegrating tablets), and almotriptan (Axert™). More recently introduced triptans include frovatriptan (Frova®) and eletriptan (Relpax®).

The most common triptan side effects can include chest pain, feeling a burning sensation, skin tingling, dizziness, nausea and sensation of warmth.

Triptans should not be used by those who have a past history of, or risk factors, for heart disease, high blood pressure, high cholesterol, angina, peripheral vascular disease, impaired liver function, stroke or diabetes.

Preventive agents include beta-blockers, antidepressants, and anti-convulsant medications that are prescribed to be taken on a scheduled basis, whereas abortive therapies are typically used on an as



needed basis and are to be taken at the first onset of a migraine. Because of frequent unpleasant and sometimes debilitating side effects, preventive drugs are only prescribed for those whose quality of life is significantly adversely affected. The drugs are started at a low dose, and gradually increased until therapeutic effects develop, the ceiling dose for the chosen drug is reached, or side effects become intolerable.

In 2018, the FDA approved three CGRP drugs (calcitonin gene related peptides) antagonist drugs for prevention of migraine headache: Erenumab-aooe (Aimovig™), Fremanezumab-vfrm (Ajovy™), and Galcanezumab-gnlm (Emgality™). These drugs appear promising in migraine prevention. These drugs are relatively new and their use is best discussed with your healthcare practitioner. There have been concerns raised about the potential for adverse cardiovascular, pulmonary and psychiatric effects and some experts recommend avoiding them for women who are pregnant or likely to become pregnant.

The key to effective treatment, however, is still a combination of avoidance of migraine triggers, stress management and relaxation techniques, and non-medication symptom relief through the use of locally applied heat or cold, massage, hot showers, and rest in a quiet, darkened room. Some people benefit from complementary or alternative therapies such as relaxation techniques, training in self-hypnosis, biofeedback, yoga, aromatherapy, acupuncture, spinal manipulation, and homeopathic remedies. See ACPA Migraine log now available as a phone app download and communication tool:

[_https://www.theacpa.org/pain-management-tools/communication-tools/phone-apps_](https://www.theacpa.org/pain-management-tools/communication-tools/phone-apps)

Unfortunately, while migraine headaches can now be better controlled, it is unrealistic to expect instant, complete, or permanent pain relief for what is essentially a chronic, recurring disease.

Effective migraine treatment begins with the early recognition that an attack is pending followed by immediate treatment. Migraine sufferers are encouraged to take an active role in managing their headaches by avoiding common triggers, making lifestyle changes, and taking their medication at the first sign of migraine pain.

Botox® was granted approval in 2010 as a preventive treatment option for patients who are diagnosed with Chronic Migraine, a neurological disorder characterized by headaches on 15 or more days per month with headaches lasting four hours a day or longer.

Patients taking certain migraine and antidepressant medications together may be at risk for a dangerous chemical imbalance. Antidepressant medications included in this warning are duloxetine (Cymbalta®), escitalopram (Lexapro™), fluoxetine (Prozac®), paroxetine (Paxil®), sertraline (Zoloft®), and venlafaxine (Effexor®). Migraine drugs include almotriptan (Axert™), naratriptan (Amerge®), sumatriptan (Imitrex®), and zolmitriptan (Zomig®). Serotonin is a brain hormone that keeps our mood stable and our appetite in check, as well as serving other functions. When two or more drugs that affect serotonin levels are taken together, it can increase the amount of serotonin and may lead to bothersome or dangerous symptoms. This is called “serotonin syndrome” in which high levels of the chemical serotonin build up in the brain and cause toxicity.

Please see the discussion about antidepressant medications in this *ACPA Resource Guide to Chronic Pain Management* for more detailed comments about mixing migraine and certain antidepressant medications.



Additionally, the U.S. Food and Drug Administration (FDA) has warned that opioids can interact with antidepressants and migraine medicines to cause serotonin syndrome.

<https://www.fda.gov/Drugs/DrugSafety/ucm489676.htm>

Here are a few web sites about migraine headaches:

- <http://www.mayoclinic.org/diseases-conditions/migraine-headache/home/ovc-20202432>
- <http://www.webmd.com/migraines-headaches/>
- http://my.clevelandclinic.org/disorders/migraine_headache/hic_migraine_headaches.aspx

Treximet® is a combination medication for migraine treatment and contains naproxen 500 mg and sumatriptan 85 mg.

Diclofenac potassium powder for solution (Cambia®) is a NSAID drug indicated for the acute treatment of migraine attacks with or without aura in adults 18 years of age or older. Cambia® is not indicated for the prophylactic therapy of migraine.

NOT RECOMMENDED FOR CHRONIC PAIN

Benzodiazepines

Benzodiazepines are listed here under a separate heading but are mentioned frequently throughout this document. **Benzodiazepines are not recommended for chronic pain. With rare exception, Benzodiazepines should not be used with opioid medications.**

On August 31, 2016, the U.S. Food & Drug Administration (FDA) provided a warning regarding the concomitant risks from use of opioids with benzodiazepines or other central nervous system (CNS) depressants including alcohol may result in profound sedation, respiratory depression, coma and death. The FDA recommends to physicians 1) reserving concomitant prescribing of opioid and benzodiazepines or other CNS depressants presentation room alternative treatment options are inadequate; 2) limit dosages in durations to the minimum required; and 3) follow patient for signs and symptoms are respiratory depression and sedation.

Most people experience anxiety at one time or another in their lives. Anxiety can present as nervousness or sweaty palms, irritability, uneasiness, feelings of apprehension, tight muscles, and difficulty sleeping. Anxiety is often mild, but if it becomes severe, counseling or medications may be needed. The most widely prescribed drugs for anxiety are benzodiazepines like diazepam (Valium®), lorazepam (Ativan®), clonazepam (Klonopin®), flurazepam (Dalmane®), triazolam (Halcion®), temazepam (Restoril®), and alprazolam (Xanax®). They are also used as muscle relaxants and for insomnia (difficulty sleeping). Their use as sleep aids should be limited to only short term as they do not work well when used continuously each night to produce sleep.

Most benzodiazepines are recognized for causing depression and physical dependence when used for long periods. None of them are recommended for long term use.

Side effects are similar to those of alcohol and include sedation, slurred speech, and gait unsteadiness. Other adverse reactions include chest pain and a pounding heartbeat, psychological



changes, headache, nausea, restlessness, vision problems, nightmares, and unexplained fatigue. Alcohol and tobacco should be avoided while taking these drugs. Another major side effect is respiratory depression, particularly when combined with long-acting opioids. Extreme caution should be used when prescribing both opioids and benzodiazepines concomitantly. In fact, this dangerous combination should be avoided. The majority of unintentional overdose occurs when opioids and benzodiazepines are used at the same time.

Because of withdrawal symptoms, these drugs should be discontinued slowly under a health care professional's supervision. Withdrawal reactions may be mistaken for anxiety since many of the symptoms are similar. Without medical supervision, benzodiazepine withdrawal can be associated with seizures or death.



Z-Drugs (see page 126, Hypnotics for Insomnia)

Medicines called zaleplon (Sonata®), zolpidem (Ambien®) and eszopiclone (Lunesta®) are commonly called the Z-drugs. Strictly speaking, Z-drugs are not benzodiazepines but are another class of medicine. However, they act in a similar way to benzodiazepines but there is no evidence of differences in effectiveness and safety.

Antipsychotic Medications

This class of drugs is marketed primarily because of its ability to reduce hallucinations and psychotic thinking, although some members of the class are used to treat mood disorders, including depression, insomnia, nausea and migraine.

Commonly used medications in this class include aripiprazole (Abilify™), brexpiprazole (Rexulti®), haloperidol (Haldol®), olanzapine (Zyprexa®), quetiapine (Seroquel®), risperidone (Risperdal®), paliperidone (Invega®), ziprasidone (Geodon®), lurasidone (Latuda®), azenapine (Saphris®), and iloperidone (Fanapt®).

In general, the prescription of anti-psychotic medications is not recommended for chronic pain.

They are sometimes prescribed off label as anti-anxiety or sleep medications in low doses. They are strong drugs and have the potential to cause Parkinson's-like reactions, e.g., tremors, stiffness, or even a permanent neurological condition called tardive dyskinesia (although sometimes reversible when the antipsychotic drug is stopped). In mild cases, this consists of involuntary movements of the mouth and tongue, which is mostly a cosmetic problem; however, in more severe cases there can be severe muscle activity that interferes with ability to function and even to breathe. For these reasons, they are usually considered "last resort" drugs. Toxicity of anti-psychotics is discussed at <http://www.emedicine.com/EMERG/topic338.htm>.

Central Nervous System (CNS) Stimulants

Side effects from medications prescribed for chronic pain can be bothersome at the least, and if significant enough, may cause the need to discontinue the offending medication. One of these side effects is daytime drowsiness, making it difficult for the individual to function and carry out day to day activities and work.

Rather than give up the benefits of the prescribed medication, some health care professionals will try to treat the side effect of sleepiness and lethargy by prescribing an "activating" medication such as methylphenidate (Ritalin®, Concerta®, and Metadate®), dextroamphetamine (Dexedrine®), modafinil (Provigil®), armodafinil (Nuvigil®), and combination products (Adderall®).

Prescription of these agents is off label. These agents are Class II Controlled Substances which represent a highest addiction potential. While these CNS stimulant drugs may be appropriate for selected individuals, consideration for weaning of the pain medication that is causing the drowsiness is recommended instead of adding a medication to address side



effects.

It should be a rare patient who takes medication (with potential side effects) to control the side effects of another medication rather than discontinuing the offending medication. This combination is generally not considered appropriate therapy, as many patients will show improved functionality when the dose of the sedating drug is reduced or discontinued. Adding additional medications adds more risk for the patient.

Methylphenidate (Ritalin[®], Concerta[®], and Metadate[®]) is a medication prescribed for individuals (usually children) who have an abnormally high level of activity or attention-deficit hyperactivity disorder (ADHD). It is a central nervous system stimulant. It has effects similar to, but more potent than, caffeine and less potent than amphetamines. It is occasionally used off-label as a stimulant when daytime sleepiness from chronic pain medications is a problem. It may be effective when used appropriately, but it does have potential for abuse. Marked anxiety, tension, and agitation are contraindications to methylphenidate since the drug may aggravate these symptoms. Methylphenidate should be given cautiously to emotionally unstable patients and those with a history of drug dependence or alcoholism, as such patients may increase the dose on their own initiative.

The NIH National Institutes of Drug Abuse has published: DrugFacts: Stimulant ADHD Medications - Methylphenidate and Amphetamines which can be found at <http://www.drugabuse.gov/publications/drugfacts/stimulant-adhd-medications-methylphenidate-amphetamines>.

Dextroamphetamine (Dexedrine[®]) is an amphetamine used to treat narcolepsy and attention-deficit hyperactivity disorder in children. In some cases, this drug has been used to treat depression or as an adjunct in the treatment of exogenous obesity.

Modafinil (Provigil[®]) is approved by the FDA to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. While not recommended in current guidelines, it is also being used off-label for persons with chronic pain and excessive daytime sleepiness. It is generally well tolerated, with mild-to-moderate side effects. It reportedly does not affect nighttime sleep. Headaches are the most common reason for discontinuing modafinil. Less frequent side effects include nausea, nervousness, anxiety, insomnia, and cardiovascular adverse reactions including chest pain, palpitations, shortness of breath and transient ischemic EKG changes. Increased monitoring of heart rate and blood pressure may be appropriate when using modafinil. There have been rare cases of serious or life-threatening rash including Stevens-Johnson syndrome and toxic epidermal necrolysis reported in adults and children. Caution should be exercised when Modafinil is given to patients with a history of psychosis, depression, or mania.

Armodafinil (Nuvigil[®]) is a wakefulness-promoting agent for oral administration. It is indicated to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, narcolepsy, and shift work sleep disorder. Headaches are the most common reason for discontinuing armodafinil. This drug carries similar warnings as modafinil (see above).



TAPERING/WEANING OFF PAIN MEDICATIONS (INCLUDING OPIOIDS)

In today's health care system, it is sometimes easier to start taking medications than to stop taking them. This can often lead to a person taking multiple and possibly mechanism-overlapping medications. The questions to discuss with a health care professional are: Are the medications actually making a difference? Are they making the person's life better and improving function? Are the benefits worth any side effects and negative effects? In other words, taking pain medications is a choice that each person must make by weighing the benefits vs. the risks.

When the risks appear to outweigh the benefits of taking a pain medication, reducing the dose and ultimately discontinuing the medication should be considered. This is called weaning or tapering particularly when the individual has become dependent on the medication. The term "detoxification" is sometimes used interchangeably but should be limited to cases with opioid addiction.

The goal of tapering/weaning down the dose is to safely discontinue medications that do not seem helpful in reducing pain while allowing the body to adjust while monitoring for negative effects of withdrawal symptoms. Oftentimes, people discover they feel better taking lower doses, fewer medications, or not taking medications at all.

It is best to check with the health care professional before altering the medication regimen by taking less of the medication or stopping it. It is dangerous to abruptly stop taking some medications (sometimes referred to as going "cold turkey"). Because the body develops physical dependence to some medications when they are taken regularly, abrupt withdrawal or too rapid a reduction in the dose of these medications can be very uncomfortable or even hazardous to one's health. It depends on the type of medication, how much, and for how long the medication has been taken.

Some medications may be safe to stop abruptly:

- A medication that is taken for just a few days or only taken once in a while (weekly).
- Medications that are prescribed and only taken when necessary (as needed, not regularly).
- Some medications that do not produce physical dependence (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs – like aspirin, ibuprofen and others]).

Some medications always require medical supervision when stopped:

- Opioids that have been taken in regular daily doses for several days or longer.
- Benzodiazepines, muscle relaxants, antidepressants, and anticonvulsant medications that have been taken in regular daily doses for several days or longer.
- Barbiturates taken frequently for headache (butalbital).
- Non-benzodiazepine sleeping pills (also referred to as z-drugs) such as zolpidem, zopiclone and eszopiclone.

A sound approach is to talk to a health care professional before making any medication changes or if you have any other questions or concerns. Following are suggestions that can guide the discussion:



- Provide the health care professional with a list that includes the following information about all over-the-counter (OTC) and prescribed medications that are being taken:
 - Name of the medication
 - Dose (e.g., “325 mg”)
 - Directions on the bottle (e.g., “take 2 tablets by mouth every 6-8 hours as needed for pain”)
 - Understanding of why the health care professional prescribed this medication – what it is supposed to do.
 - Actual usage: How often and how much of the medication has the person actually been taking.
 - What has the individual noticed about its effects – the good AND bad effects?
- Take the bottles of all the OTC and prescribed medications to the appointment so the health care professional can see the labels and examine the pills.
- The health care professional should take advantage of every encounter to educate the patients on all their medications. Answer the following questions about each medication, and the person with pain should write down the answers beside the name of each medication during the visit:
 - For what condition is this medication being prescribed?
 - Is the medication essential?
 - If it is essential, how often should it be taken?
 - If the decision is made to stop taking the medication either permanently or for a while, can it be abruptly stopped, or should the dose be gradually weaned down?
 - If the dose should be weaned down:
 - How can this be done safely?
 - How uncomfortable will this process be?
 - What symptoms are danger signs, and which are simply a bother?
 - How long will it take?
 - Are there specific instructions on how to reduce the dose?
 - Will the health care professional help with the weaning process?
 - How often does the person with pain need to see the health care professional during the weaning process?
 - What are the most frequent adverse events that might appear?
 - Which are the interactions one should be aware of (medications, food, etc.)

Weaning off medications may be complicated by the potential for increased levels of pain that may accompany dose reduction but can be done safely under medical supervision. The health care professional determines the rate at which the dose is reduced, and adjustments can be made as necessary. For example, reasonable opioid weaning protocols suggest decreasing pill intake by 10-20 percent per week, as tolerated. Hydration (drinking water), relaxation, and emotional support are all important to enhance the likelihood of success.

Sometimes weaning or discontinuing medication (especially opioids) is most safely accomplished under the close supervision of a specialist (such as a pain or addiction medicine specialist) in a medically-supervised program to prevent complications and severe withdrawal symptoms.

Symptoms of withdrawal from opioids can include:

- worsening of pain
- rapid heart beat
- high blood pressure



- sleeplessness
- agitation and anxiety
- stomach cramps, nausea, vomiting, diarrhea
- body aches (flu-like symptoms) and muscle cramps
- runny nose, sweating, tearing, yawning, goose bumps

Prescription medications recommended by your healthcare provider that can help diminish symptoms of opioid withdrawal include:

- Alternative opioids:
 - methadone
 - buprenorphine
- Other drugs to manage withdrawal symptoms during detoxification
 - naltrexone (Vivitrol) – an extended release non-addictive, once-monthly injection to prevent relapse in opioid dependent patients when used with counseling following detoxification.
 - alpha-2 agonists (clonidine) – blood pressure needs to be monitored
 - anti-nausea medications (e.g., ondansetron, metoclopramide)
 - anti-diarrheal (loperamide)
 - muscle relaxants (e.g., tizanidine, cyclobenzaprine, baclofen)
 - stomach relaxants (dicyclomine)
 - anti-inflammatory pain relievers (e.g., ibuprofen, naproxen, others)
 - sleep aids (e.g., trazodone, amitriptyline)
 - anti-anxiety agents (e.g., diazepam, lorazepam) may be used briefly (5-7 days)

On occasion, alternative detoxification with phenobarbital may be offered.



SELF-MEDICATION: ALCOHOL, TOBACCO, MARIJUANA, AND ILLICIT SUBSTANCES

ALCOHOL & CHRONIC PAIN

Alcohol is also a drug. Alcohol has no place in the treatment of chronic pain, although some individuals turn to alcohol for relief of their pain. It is important to discuss the use of alcohol with your health care provider, including the amount, frequency, and type of alcohol consumed.

Alcohol can enhance the effects of certain prescription drugs as well as markedly increase potential toxic side effects (i.e., liver damage when used in conjunction with acetaminophen or increased sedation and respiratory depression in conjunction with opioids and other sedating medications, like benzodiazepines and other sleeping medications). The mixture of alcohol and opioids along with sedatives or anti-anxiety drugs can cause death.

Alcohol affects the nervous system as a depressant, not as a stimulant. It depresses normal mental activity and normal muscle function. Short-term effects of an average amount of alcohol include relaxation, breakdown of inhibitions, euphoria, and decreased alertness. Short-term effects of large amounts of alcohol include nausea, stupor, hangover, unconsciousness, and even death. Alcohol increases stomach acid and impairs liver function. Chronic alcoholism frequently leads to permanent damage to the liver. Alcohol also affects the heart and blood vessels by decreasing normal function, leading to heart disease. Bleeding from the esophagus and stomach frequently accompany liver disease caused by chronic alcoholism. Many medications cannot be given to patients with abnormal liver function, thus making it more difficult to treat chronic pain.

The early signs of alcoholism include the prominent smell of alcohol on the breath and behavior changes such as aggressiveness, passivity, decreased inhibitions, poor judgment, depression, and outbursts of uncontrolled emotion such as rage or tearfulness. Signs of intoxication with alcohol include unsteady gait, slurred speech, and poor performance of any brain or muscle function. Signs of severe alcohol intoxication include stupor or coma with slow, noisy breathing, cold and clammy skin, and an increased heartbeat.

The long-term effects of alcohol addiction (alcoholism) include craving, compulsive use and continued use despite harm to family, job, health, and safety. When alcohol is unavailable to persons who are severely addicted, withdrawal symptoms will occur and may be life threatening if not treated immediately. Even with successful treatment, individuals addicted to alcohol may at risk for relapse, suggesting the need for ongoing treatment (such as involvement in 12-step programs, counseling, and family support).

Simply put, alcohol and pain medications are dangerous when mixed together.

Additional information is available from the Substance Abuse and Mental Health Services Administration (SAMHSA) at <http://www.samhsa.gov/atod>.



THE EFFECTS OF CIGARETTE SMOKING ON PAIN

Cigarette smoking causes blood vessels to become constricted (due to nicotine); this restricts the amount of oxygen-rich blood flowing to areas of pain. Smoking not only reduces blood flow to your heart but also to other structures such as the skin, bones, and discs. Due to this, the individual may get accelerated aging leading to degenerative conditions. The lack of blood supply caused by cigarette smoke is also responsible for increased healing time after surgery. After back fusion surgery, smoking cigarettes can increase the risk of the fusion not healing properly. Smoking should be avoided both before and after spine surgery. Cigarette smoke triggers the release of pro-inflammatory cytokines, thus increasing inflammation and intensifying pain. Smoking makes the bones weak and increases the prevalence of osteoporosis, spinal degenerative disease, and impaired bone and wound healing. Symptoms of depression are more commonly seen among smokers. Cigarette smoking is also considered a risk factor for misuse of opioid medications and should be considered when prescribing opioids.

Below are some tips to help individuals stop smoking.

Assess readiness to quit smoking and ask a health care professional or pharmacist for help. They will make recommendations, modifications, and develop a treatment plan to optimize success. Even one less cigarette a day is a step in the right direction. Keeping a log may help individuals pinpoint when and why they are smoking. Knowing these triggers can help replace smoking a cigarette with healthier habits.

Smoker's Log:

Cigarettes per day	
Time of each cigarette	
What triggered the craving?	
What were you doing while smoking?	
How did you feel while smoking?	

Nicotine replacement therapy, such as lozenges, gum, or patches, is available.

Some medications can help with the craving of cigarettes that many people experience when they are trying to quit. These medications work by affecting dopamine. Nicotine triggers dopamine release in the brain. Dopamine is a neurotransmitter, a chemical messenger that plays a prominent role in addiction. Dopamine affects movement control, emotional response, and pleasure/pain. It is responsible for the reward pathway and the “feel good” phenomenon experienced when smoking.

Norepinephrine is also a neurotransmitter that sends signals from one neuron to the next. Norepinephrine is similar to noradrenaline and adrenaline and is responsible for constricting and narrowing the blood vessels. It can therefore increase blood pressure. It can also increase blood sugar levels and affect both mood and behavior.



Bupropion is an antidepressant (Wellbutrin®); however, it is also used in the smoking cessation process (Zyban®) – i.e., the same medication and they should never be taken together. Bupropion inhibits the reuptake of both dopamine and norepinephrine, increasing their concentrations within the brain. By increasing dopamine, the frequency and severity of nicotine cravings and urges are reduced. Norepinephrine plays a role in alleviating symptoms associated with nicotine withdrawal. Bupropion effects are not fully seen until one week of treatment is complete. Therefore, it is important for patients to start this medication one to two weeks prior to their “quit-date”. Side-effects include behavior changes, hostility, agitation, and depression. Seizures may occur; however, they are dose dependent. Less severe, more common side effects include dry mouth, headache, nausea, dizziness, sweating, and insomnia.

Varenicline (Chantix®) mimics nicotine at the receptors in order to aid in smoking cessation. Varenicline is similar in structure to cytosine, a natural compound that has aided in smoking cessation since the 1960s. Varenicline works via two different mechanisms. First, varenicline is effective because it provides partial nicotine effects to help with nicotine withdrawal symptoms. Second, varenicline also binds to nicotine receptors to block nicotine’s effect if the person relapses. Duration of therapy is normally 12 weeks. Patients who respond to treatment may receive another 12 weeks of therapy to increase their success rate. Common side effects include nausea, vomiting, insomnia, headache, and abnormal dreams. This is not a benign drug as the FDA warning notes neuropsychiatric adverse events including suicidality. These warnings include changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide. These symptoms can occur with and without pre-existing psychiatric disease. Some neuropsychiatric adverse events, including unusual and sometimes aggressive behavior directed to oneself or others, may have been worsened by concomitant use of alcohol.

MARIJUANA

The use of marijuana for pain is controversial. It is allowed by some states for medicinal and now recreational purposes, but overall it is banned for distribution by the United States federal government. At the time of the writing of this *ACPA Resource Guide to Chronic Pain Management*, marijuana is considered a Schedule I drug (high potential for abuse, no legitimate medical use) by the DEA. However, medicinal use has been independently legalized by 44 states and the District of Columbia. Some states have well defined medical cannabis programs (AK, AR, AZ, CA, CO, CT, DE, FL, HI, IL, LA, MA, MD, ME, MI, MN, MT, ND, NH, NJ, NM, NV, NY, OH, OR, PA, RI, VT, WA, WV) while others have limited access for now (AL, GA, IA, KY, MO, MS, NC, OK, SC, TN, TX, UT, VA, WI). In fact, the only states that have not legalized medical marijuana currently are ID, IN, KS, NE, SD, and WY. In addition, there are now eight states (AK, CA, CO, MA, ME, NV, OR, WA) and the District of Columbia that have legalized recreational marijuana in addition to medical marijuana with several others that will likely vote on the issue in 2018. All of this creates a dissonance between federal and state perspectives on the medicinal use of marijuana (cannabis). This dissonance has also created a conundrum for physicians who are trying to do the right thing for their patients but may find themselves in violation of federal regulation.



In August 2016, the DEA (with input from the FDA and NIDA) reaffirmed that marijuana will remain a Schedule I drug. There is evidence of some analgesic benefits from marijuana, but there is a great deal of research that needs to still be done and this classification impedes that research.

Some of this is related to the change in public opinion in the U.S. about the value and dangers of marijuana, especially when compared to opioids. According to a February 2017 Quinnipiac poll (<https://www.mpp.org/wp-content/uploads/2017/02/Quinnipiac-Poll-Feb-2017.pdf>), 59% say marijuana should be legal, 93% say medical marijuana should be legal, and 71% say federal laws should not be enforced. That can be compared to a Gallup poll in 1969 where only 12% said that marijuana should be legal.

A physician cannot legally prescribe medical marijuana with the exception of FDA-approved formulations such as Marinol since their license to prescribe controlled substances is controlled by a federal agency (DEA) that considers marijuana illegal. Some health care professionals may recommend the use of medical marijuana, some will not provide a recommendation but will not object to a patient's use of marijuana with other pain medicines, and some will refuse to prescribe other medications (especially opioids) to individuals who are using marijuana. Some health care professionals take a "don't ask, don't tell" philosophy and do not check for marijuana when doing urine drug testing. Individuals cannot say they are using marijuana recreationally to deal with a medical problem and expect that to comply with the law as specific medical conditions (e.g., seizures, Parkinson's, glaucoma, cancer, "intractable" pain) and procedures (becoming a registered patient, where/how to purchase, pricing) need to be followed. Nevertheless, the use of any substances should be discussed openly and honestly between the person and his or her health care professional.

If the individual is on opioids and/or pain treatment program, the concurrent use of marijuana should be clearly spelled out in the opioid/pain treatment contract. There are typically consequences if this medication appears in UDS and has not been approved by the pain treating physician.

The most well-known active ingredient found in marijuana (THC) may decrease pain and cause euphoria, but can also lead to dependence and addiction in certain individuals and has significant side effects. The cannabidiol (CBD) component of the marijuana plant is thought to have potential effects to reduce pain without providing the psychoactive high associated with THC. CBD is available in a variety of forms, including oils and salves for topical use. No controlled studies have been carried out to date.

Although some states allow the legal use of marijuana for medicinal purposes, which may or may not include pain, there is no high-level scientific research supporting the long-term use of marijuana for chronic pain. In fact, there is good evidence that excessive smoking of marijuana can be harmful (especially in young people). Oral forms of THC in the forms of candies, energy drinks, juices, etc. are being sold at dispensaries. The potency of THC in these oral preparations is extremely high and has created an over-dosing situation (marijuana taken orally can take up to 20-30 minutes to have an effect because it has to be processed by the digestive system).



However, in January 2017, the National Academies of Sciences, Engineering and Medicine published a paper that concluded after studying 10,000 scientific abstracts published since 1999 that “found evidence to support that patients who were treated with cannabis or cannabinoids were more likely to experience a significant reduction in pain symptoms” (<http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=24625>). That means there is now a disagreement within the federal government whether marijuana can help manage pain (or even be considered medicinal).

More frequent marijuana smoking is associated with an increased risk of severe respiratory illnesses, especially chronic bronchitis. Other potential delivery methods include oils, tinctures, vaporizers, and edibles. Use also leads to reduced workplace productivity, as well as impaired judgment, even hours after use. Marijuana intoxication impairs cognitive and psychomotor performance with complex, demanding tasks. Individuals who have used marijuana over long periods of time demonstrate impaired performance on a variety of neuropsychological tests (e.g., attention, memory, and processing complex information), even when not acutely intoxicated. A recent review of the existing medical literature concluded that the use of marijuana at a young age increased the risk of schizophrenia or a schizophrenia-like psychotic illness by approximately three-fold. Emerging evidence suggests a link between more frequent, or severe, marijuana use and anxiety symptoms and disorders.

Since it is a CNS depressant, marijuana’s use concomitantly with opioids is of concern. Patients using opioids need to be aware of all prescribed and non-prescribed medications that affect the central nervous system, including marijuana and alcohol, because there may be a synergistic effect that may cause respiratory depression and death.

People who are self-medicating with marijuana may not recognize the presence of marijuana withdrawal symptoms. Marijuana causes physical dependence, and withdrawal symptoms can start as early as hours after smoking marijuana and last for up to a month and include sleep disturbances, substantial anxiety (which can worsen pain), discomfort, lack of appetite, and commonly trigger marijuana craving.

Despite some states allowing medicinal marijuana, it is a federal crime for a health care professional to prescribe a scheduled drug to a person known to be using the drug illegally. It is also important to remember that possessing marijuana when traveling through a state where medicinal marijuana is not allowed could result in being charged with possession of an illegal substance, even if the person is using the drug under the supervision of a physician and has the proper home state documentation. Additionally, an individual can be denied employment or fired if the employer or prospective employer conducts drug screenings as a part of the hiring process or has a ‘no-drug tolerance’ policy. Also, individuals can be charged with driving under the influence (DUI) if their driving is impaired and they test positive for marijuana, even in states where medicinal marijuana is allowed.



Illegal Drugs

Regarding chronic pain treatment (excluding cancer and end-of-life care), health care professionals will not prescribe opioids and other medications to individuals who are known to use illegal “street” drugs (heroin, methamphetamines, cocaine, and others) or to be irresponsible with prescription pain medication. Unfortunately, many people suffering from a substance use disorder such as opioid addiction present to pain clinics in search of medication and may need a different form of assistance. If you or a loved one need assistance with an opioid addiction, call [1-877-927-9043](tel:1-877-927-9043) to speak with someone from the **American Addiction Centers** available 24/7 to discuss treatment options. Prescribing Medication Assisted Treatment for addiction (e.g., Methadone, Buprenorphine) requires special training and licensure.

INTERNET PAIN-MANAGEMENT RESOURCES

There are a number of stand-alone and Internet-based programs to help in the management of pain. The American Chronic Pain Association website can be a great source of information (<https://theacpa.org/>). This and other pain management programs include ways to track daily pain and activity and can be a useful vehicle to easily summarize progress over time. They can be especially helpful when starting an exercise routine by tracking progress based on frequency and duration of the exercises. These programs can also suggest warm-up and cool-down stretching routines catered for each individual’s pain problem. They also can be useful for monitoring medication use and giving helpful reminders throughout the day. A daily food diary can help in identifying healthy and unhealthy eating habits. Smart phone applications (apps) are in development specifically for persons with chronic pain. These programs are useful in identifying important information about the pain, summarizing progress for the health care professional, and offering daily tips and recommendations for improving pain management.



Many things can affect your pain. These can include stress, sleep, money worries, and even the weather. This log can help you track the everyday things that have an impact on your pain.

When you understand what makes your pain worse, you can begin to work on ways to reduce or deal with your pain “triggers.”

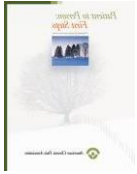
The more you know about how your body reacts, the more you can be in control. Being in better control can help you be less afraid and better able to manage your pain. We encourage you to fill out a chart at the end of each day or several times a week. You also can print out a report and take it to your doctor visits. It can help you talk more openly with your health care provider so that together you can find ways to improve your quality of life. <https://theacpa.org/wp-content/uploads/2017/08/Pain-Log-Rev-2010-V2.pdf>



Back pain can be complex and difficult to describe in the short time you may have with your health care provider. This tool can help you create a detailed picture of your pain---where it is, how it feels, how much it hurts, and what triggers it. Fill it out before your visit, print it, and share it with your provider.

<https://theacpa.org/pain-management-tools/communication-tools/tracking-tools/back-pain-map/>





The beginning journey from patient to person with this workbook is designed to help anyone who has a chronic pain problem gain an understanding of how to cope with the problems that his or her pain creates.

Patient to Person: First Steps

Topics include:

- Understanding Chronic Pain
- Knowing Yourself
- Learning to Live with Others
- Helping Your Body

<http://store.theacpa.org/patient-to-person-first-steps-by-penney-cowan-2004.html>

FINAL COMMENTS

An essential concept in pain management is that each person is different and will respond differently to situations, interventions, surgeries, and medications.

It is important for the person with pain, family members, and others to avoid quick judgments based on what they hear or read about any particular treatment or medication. The best place to get advice about treatments and medications is from the health care professional assisting the person with pain.

Families need to be good reporters—observant, truthful, and honest about what they see in the person who is provided a certain treatment or who is taking medication. Sometimes the person provided the treatment or taking the medication does not realize the changes that are produced. Family member observations will be helpful to the health care professional.

There is no question that there are many treatment approaches (tools) in the “tool chest” of the treating health care professional or therapist, but they should be used judiciously. Benefit should be based on less pain, more function, and return to everyday activities with the least, manageable side effects possible.

This *ACPA Resource Guide to Chronic Pain Management* only deals with certain treatments and medications, but it is important to understand that there are many other treatment approaches to chronic pain that may not be covered in this document. This document is a work in progress and the ACPA welcomes comments and recommendations.

The ACPA once again reminds readers that this *ACPA Resource Guide to Chronic Pain Management* is not meant to serve as medical advice for pain conditions or treatment or medication needs. The best source of information is health care professionals and therapists who understand the treatment and medication options available to people with chronic pain.



REFERENCES: LINKS TO CHRONIC PAIN SITES & RESOURCES

MEDICATION RELATED

1. WebMD: Drugs & Medications A-Z - <http://www.webmd.com/drugs>
2. PDR.net: Drug Information - <http://www.pdr.net>
3. Medscape: Drugs - <http://www.medscape.com/druginfo>
4. FDA: Drugs - <http://www.fda.gov/cder/drug/default.htm>
5. MedLine Plus: Drugs, Herbals, and Supplements - <http://www.nlm.nih.gov/medlineplus/druginformation.html>
6. Drugs.com: Drug Information Online - <http://www.drugs.com/>
7. Drugs and Supplements: <http://www.mayoclinic.com/health/drug-information/DrugHerbIndex>
8. American Society of Health-System Pharmacists: <http://www.safemedication.com/>
9. WebMD: <http://www.webmd.com/pain-management/guide/pain-relievers>

BOOKS

There also are many books on the topic of chronic pain that can be useful. You can go to www.amazon.com and search on chronic pain and a long list of books will come up. There are many good ones, but we can particularly recommend the following:

- Back in Control: A spine surgeon's roadmap out of chronic pain by David Hanscom MD
- The Painful Truth: What Chronic Pain Is Really Like and Why It Matters to Each of Us by Lynn R. Webster MD
- Managing Pain Before It Manages You, Fourth Edition by Margaret A. Caudill MD PhD MPH and MD Herbert Benson
- Living Able and Healthy: Your Guide to Injury and Illness Recovery by Christopher R. Brigham-MD and Henry Bennett
- The Chronic Pain Workbook by Michael Lewandowski, PhD
- Mindfulness Meditation for Pain Relief by Jon Kabat-Zinn PhD



- Conquer Your Chronic Pain by Peter Abaci, MD
- The Pain Antidote: The Proven Program to Help You Stop Suffering from Chronic Pain, Avoid Addiction to Painkillers--and Reclaim Your Life by Mel Pohl and Katherine Ketcham
- Opioid-Free Pain Relief Kit: 10 Simple Steps to Ease Your Pain by Beth Darnall, PhD
- Less Pain, Fewer Pills: Avoid the Dangers of Prescription Opioids and Gain Control over Chronic Pain by Beth Darnall

OTHER REFERENCES

Agency for Healthcare Research and Quality (AHRQ). (2007). *Choosing Nonopioid Analgesics for Osteoarthritis: Clinician Summary Guide*: Available at <http://informahealthcare.com/doi/abs/10.3109/15360280903332237>

American Academy of Family Physicians (AAFP). Herbal Health Products - What You Should Know. Available at <http://www.aafp.org/afp/990301ap/990301e.html>

American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res* (Hoboken). 2012 Apr;64(4):465-74. Available at <http://www.guideline.gov/content.aspx?id=36893>

American Pain Society and American Academy of Pain Medicine (2009). *Evidence Review: APS-AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain*. Available at <http://www.jpain.org/article/PIIS1526590008008316/fulltext>

Food and Drug Administration (FDA). *A Guide to Safe Use of Pain Medicine*. Available at <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm095742.pdf>

Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) maintains a collection of educational materials on topics related to buying and using medicine safely at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm296593.htm>

Food and Drug Administration (FDA). *Buying Prescription Medicine Online: A Consumer Safety Guide*. Available at <http://www.fda.gov/downloads/Drugs/EmergencyPreparedness/BioterrorismAndDrugPreparedness/UCM133237.pdf>

National Center for Complementary and Alternative Medicine (NCCAM). (2010). What is CAM? Available at <http://www.nccam.nih.gov/health/whatiscam/>



PAIN RELATED ORGANIZATIONS, WEB SITES & VIDEOS

The American Chronic Pain Association (The ACPA) at <https://theacpa.org/>

American Society for Pain Management Nurses (ASPMN) at <http://www.aspmn.org/Pages/default.aspx>

American Pain Society at <http://americanpainsociety.org/>

American Academy of Pain Medicine at <http://www.painmed.org/>

American Academy of Integrative Pain Management <http://www.aapainmanage.org/>

Guide to Pain Medication and Treatments <https://theacpa.org/pain-management-tools/resource-guide-to-chronic-pain-treatments/resource-guide-to-chronic-pain-management/>

International Association for the Study of Pain (IASP) at <http://www.iasp-pain.org/>

Opioid Induced Constipation https://theacpa.org/wp-content/uploads/2017/08/ACPA-Opioid_Constipation_Chart-V4.pdf

Understanding Implanted Devices <https://theacpa.org/pain-management-tools/videos/conditionstreatments/>

Understanding NSAIDS <https://theacpa.org/pain-management-tools/videos/conditionstreatments/>

Using Opioids Safely <https://theacpa.org/pain-management-tools/videos/conditionstreatments/>

Youth Living with Pain www.growingpains.org

PainEDU – <http://www.PainEDU.org>

painACTION – <http://www.painaction.com>

Reflex Sympathetic Dystrophy Syndrome Association of America - <https://www.rsds.org/>

Pain Matters - http://painmatters.com/?utm_source=google&utm_medium=cpc&utm_term=chronic%20pains&utm_campaign=Pain%20Education

The Pain Toolkit <http://www.paintoolkit.org/>

Maze-Masters - <http://www.webility.md/maze-masters/>

Take Courage Coaching - <http://www.takecouragecoaching.com/>



Understanding Pain in Less than Five Minutes, and What to Do About It:
https://www.youtube.com/watch?v=C_3phB93rvI

Best Advice for People Taking Opioid Medication
<https://www.youtube.com/watch?v=7Na2m7lx-hU>

American Chronic Pain Association Videos
<https://theacpa.org/pain-management-tools/videos/>

Retrain Pain Foundation
<https://www.retrainpain.org/>

Dr. David Hanscom's website and book:
Back In Control or
www.backincontrol.com

Dr. Howard Schubiner's book and
website: Unlearn Your Pain
<https://www.unlearnyourpain.com>

Dr. Beth Darnall's Books and website:
<https://bethdarnall.com/>

Video & website: Tame the Beast
<https://www.tamethebeast.org/>

Sleepwell Recommends:
<https://mysleepwell.ca/cbti/sleepwell-recommends/>

