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Breakthrough Pain

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Breakthrough Pain Management: The Interface of Pain and Addiction Related Issues
Interview with Dr. Steve Passik

Steven D. Passik, PhD, is Director of Symptom Management and Palliative Care at the Markey Cancer Center of the University of Kentucky in Lexington and Associate Professor of Medicine and Behavioral Sciences at the University of Kentucky. Dr Passik is a member of the American Society of Clinical Oncology, American Society of Psychiatric Oncology/AIDS, American Pain Society, American Psychological Association, International Association for the Study of Pain, and the International Psycho-Oncology Society. In 1999, Dr Passik was a Faculty Scholar for the SOROS Foundation's Project on Death in America, and in 1992-1993 he received a National Research Service Award from the National Cancer Institute. Dr Passik has served on the editorial board of the Journal of Pain and Symptom Management and has been a reviewer for the Journal of Pharmaceutical Care in Pain and Symptom Control, Journal of Pain and Symptom Management, Psycho-Oncology, Agency for Health Care Policy and Research Cancer Pain Guidelines, Cancer Investigation, and Oncology. Dr. Passik has served as the President of the Indiana Cancer and AIDS Pain Initiative and as Editor in Chief of the National Cancer Institute's PDQ Supportive Care Editorial Board. He is the author of more than 62 journal articles, 33 book chapters, and 50 abstracts. Dr Passik received his doctorate in clinical psychology from the New School for Social Research, New York, NY, and was a chief fellow, Psychiatry Service at Memorial Sloan-Kettering Cancer Center in New York.

Pain.com: How does breakthrough pain treatment in non-malignant pain interface with addiction related issues?

Dr. Passik: This is a general and overriding question. In fact, they interface in multiple ways. On the one hand, breakthrough pain usually requires the use of short acting opioids and rapid onset opioid formulations - either of which may interface with the high-risk patient in some complicated ways. While we certainly know that addicts prefer short acting drugs due to their psychological and mental effects i.e. "to get high," it is also well known that they prefer drugs that come on quickly and come off quickly as opposed to drugs that take a long time to reach their peak effect. In many cases, addicts, when presented with a system that delivers drugs in a delayed fashion, will alter those delivery systems in an attempt to make them deliver drugs more quickly. Thus, we have a very broad kind of interface. Currently, we now have a class of drug that can be delivered more and more rapidly while requiring no alteration by those who are inclined to use these drugs for their psychological effects or to get high. Physicians are challenged with the complication of dealing with a certain subset of the population who have chronic pain and who are also at risk of addiction. Consequently, physicians, at the very least, are forced to consider the level of risk of addiction in the particular individual while deciding on their options for treating breakthrough pain. Consider, for example, if one were treating a very high-risk patient with chronic non-cancer pain with a long acting opioid but there was still incident pain, pain-on-motion, end-of-dose failure or any other varieties of breakthrough pain. They need to ask themselves: What is the benefit-risk ratio for that particular patient where, on the one hand, you are providing the treatment that has the potential of improving coverage of pain during those breakthrough moments and, on the other hand, you need to measure that against the potential risk of exposing that high-risk patient to a drug that could trigger cravings? The consequence of not considering the benefit-risk ratio could be setting the patient up on a kind of roller coaster of blood levels that could in fact lead to more use and more aberrant use. This certainly does not pertain to patients with no history of drug addiction. However, it is incumbent upon the clinician then to try to identify whom those patients are and tailor treatment accordingly. Under certain circumstances, even in high-risk patients, the pain may be so hard to cover with a long-acting agent, especially if it is titrated up and toxicities begin to accumulate, that some degree of very carefully measured help with breakthrough pain might require the use of short acting or rapid onset opioids. In this situation the clinician would need to be skillful in controlling how those medicines are dispensed, how they are monitored, how the patients thought process is guided on how to use them in a limited fashion and also how to keep tabs on whether or not cravings are set in motion by the new agent. The interface in general terms between the treatments of breakthrough pain and the whole set of addiction related screening issues, management issues and monitoring are complex and requires a certain level of expertise in addiction medicine when it comes to understanding who are the at risk patients and figuring out how to best manage breakthrough pain in those individuals.

Pain.com: Are short acting opioids more prone to abuse?

Dr. Passik: As mentioned previously, there is no question that in both laboratory studies and in general observation rapid onset drugs are the ones most sought after for recreational use and abuse. The prevailing question is: Does that then translate in any meaningful way to the clinical breakthrough pain management paradigm? As mentioned in my previous answer, I think these drugs might be avoided at least at first in high-risk patients. Breakthrough pain might be approached through raising the dose of the longer acting agents in an effort to cover breakthroughs in patients who are considered too high-risk to be able to safely utilize the short acting opioids. To date there aren't any definitive studies that show the high-risk patients with careful monitoring of adherence can't use some of these agents in some selected situations with appropriate psychological counseling, monitoring, pill counting, etc. if necessary. There is one study in cancer pain that has shown that raising the dose of the long acting agent can decrease both the frequency and intensity of breakthrough episodes. This, however, may come hand in hand with some additional toxicity. Subsequently, the clinician managing the high-risk patient may have to decide if this toxicity is a reasonable tradeoff with the risk of abuse of the rapid onset formulations by the high-risk population. Nevertheless, there are no definitive studies, just extrapolation from experiences with addicted people, that indicate short acting or rapid onset opioids do seem to be preferred. This is supported by the fact that they are willing to pay more for them. Certainly, those effects, the rapid peaks and troughs, are the ones that seem to feed into the rapid development of tolerance and escalation of use. Though, as mentioned previously, this is not clearly demonstrated in the pain management context. With the low risk patient, here again, there is not a single study that shows that a patient with no history of addiction is at any increased risk if they are managed with shorter acting agents. An older patient with arthritis for example, who has never abused drugs or alcohol, is not likely to be exposed to any greater risk if their pain is managed by short acting, or rapid onset opioids as opposed to long acting agents. Careful screening to ascertain that the patient is at the lowest level of risk would liberate the clinician's use of virtually any formulation that they felt best covered the particular pattern of pain in that individual without the worry of abuse potentials with these agents.

Pain.com: How can I screen patients for risk of aberrant behavior and how does this interface with breakthrough pain treatment?

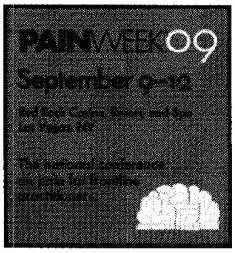
Dr. Passik: Had I been doing this interview five years ago, I would be bemoaning the lack of usable screening tools designed for the pain management context. Fortunately, in that period we have seen a rapid development of these instruments. Many of them have tremendous utility and very impressive psychometric qualities. Some of them involve paper and pencil, some are interview based, etc. My particular favorites are the ORT (The Opioid Risk Tool was developed by Webster and Webster and published in Pain Medicine). [LINK:] http://www.pain.com/sections/categories_of_pain/breakthrough/resources/expert_interviews/interview_webster.cfm. This is a five-item tool weighted differentially for men and women that can be given to the patient to fill out. The other one that I like is SOAPP® [LINK:a target="_blank" href http://www.painedu.org/soap.asp>]http://www.painedu.org/soap.asp (The Screener and Opioid Assessment for Patients in Pain from Steve Butler and colleagues is a tool to facilitate assessment and planning for chronic pain patients being considered for a long-term opioid treatment). Although this is a longer tool, the authors have been working on shortening it. Both of these tools show that clinicians are doing their due diligence for risk of aberrant behavior as they can physically be incorporated into the medical record. These tools also help triage patients while doing a good job of identifying low, medium and high-risk patient groups. There is no direct study that links screening on these tools, ascertainment of risk level or any particular abuse pattern that pertains to the short acting or rapid onset opioid formulations although Dr. Lynn Webster's study clearly showed a much higher likelihood of aberrant behavior with opioids in general with his tool. It stands to reason, of course, that if you take patients who are at risk for aberrant behavior with opioids and give them a formulation that may be preferred by people who abuse drugs for their psychological qualities then Dr. Webster's tool can be used to predict who shouldn't be provided, at least not on first pass, with the rapid onset or short acting formulations. Though this particular connection has never be empirically demonstrated and seems quite commonsensical, it stands to reason that if there are certain situations in which those high-risk patients absolutely have to be given access to these drugs then they would have to be done quite cautiously and with concurrent use of psychological services and heavy doses of monitoring of adherence. As previously noted but worthy of re-emphasis, there is no data to suggest that in the lowest risk group of patients that the rapid onset opioids as compared to the short acting opioids convey any additional risk to the lowest risk group of patients.

Pain.com: Are there non-medication approaches that are viable ways to treat breakthrough pain and chronic non-malignant pain?

Dr. Passik: Absolutely. If we all had in an ideal world the amount of time it would take to do the cognitive behavioral therapy of pain that would be part and parcel of anybody's chronic pain treatment, we would probably address breakthrough flare with a program and a thought process whereby the patient might go through a sort of hierarchy of things they can do to try to relieve the pain. If the pain is particularly short in duration the patient might simply take a time out and wait for the pain to pass. If exacerbations are sometimes helped by heat or taking a bath or distraction, we might train patients to utilize those kinds of techniques. If catastrophizing is set in motion by an acute exacerbation of pain, we might teach patients cognitive behavioral techniques to help them correct those kinds of negative thoughts and help make those episodes a little bit more bearable and possibly less distressing. And, finally, in the case where one or two of these techniques is tried and proves inadequate, we may suggest to the patient that rather than take a medication and they might give some thought to the possible outcome of 'Will this pass before the medicine would even work?" So the goal for the patient would be to use their breakthrough medicine in a thoughtful way as part of an armamentarium and not have automated drug taking take on a life of its own. Besides, in some instances, short acting opioids might be ineffectual anyway. As in the case where a pain crisis or breakthrough will come on and be over with in 20 minutes and the pain medicine itself doesn't even begin to work until 20 minutes or more, then, the patient has to deal with increased sedation and side effects that could last 6 hours. And, so we would want our patients to be thoughtful. We would want them to be open to use a variety of techniques, so that their pain is optimally managed, their side effects are controlled and the lowest possible risk of addiction is conveyed in the ways in which they chose to manage their breakthrough episodes.

Pain.com: How does chemical coping and breakthrough pain management interface?

Dr. Passik: Chemical coping is a term that Dr. Eduardo Bruera originally coined and interestingly was using in a palliative care context with substance abusers with end stages of cancer. My research group along with Ken Kirsh, Dan Bennett and Jim Hagen and others actually have been working on an inventory to assess tendency towards chemical coping so that patients with these qualities can get the psychological and other kinds of interventions that will help them use their medicines in as safe as possible way and also afford them access to techniques that will help them enhance their coping with their chronic pain that goes beyond automated drug taking. Our definition of chemical coping is, "patients who use medicines for a variety of psychological effects, who use drugs to the exclusion of alternatives, who are inflexible and unwilling to try other kinds of techniques that will help them augment their coping." Patients, who are somewhat alexithymic or have a difficult time labeling affective states and tend to feel globally good or bad and their drug taking, can sometimes be influenced when they feel globally bad as opposed teasing out whether they are feeling sad, anxious, angry or are, in fact, in pain with related characteristics. Clearly these are the kind of patients who if we had a good screening tool and could identify them, not only would we want to present them with other kinds of interventions but we would classify the use of the rapid onset opioids for this group who's prone to automated use and poor coping, as a particularly poor fit. For these kinds of patients we might want to teach them a whole range of psychological and other techniques. We may want to manage their pain in general and their breakthrough pain in particular with longer acting agents titrated upwards as opposed to giving them access to too much medicine that could in fact spiral out of their control at some point. Again this is not to say that patients that might score high for example on a chemical coping inventory would be absolutely contraindicated for the short acting or rapid onset opioids. But one would think that short acting or rapid onset opioids would have to be administered with a lot of adherence monitoring and concurrent psychological techniques and so that patient's use of short acting or rapid onset opioids remains controlled, thoughtful and beneficial to that patient while conveying as little risk as possible.



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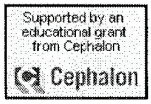

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Persistent Pain in Older Patients
Interview with Perry G. Fine, MD

Dr. Perry Fine completed medical school in 1981 at the Medical College of Virginia in Richmond. He served an internship in 1982 at the Community Hospital of Sonoma County in California and completed his residency in 1984 at the University of Utah Medical Center. In addition, Dr. Fine completed a fellowship in 1985 at the Smythe Pain Clinic at the University of Toronto in Canada.

Dr. Fine is a Professor in the Department of Anesthesiology in the School of Medicine at the University of Utah, where he serves on the faculty in the Pain Research Center and is an attending physician in the Pain Management Center. He teaches the first and second year medical school courses in Social Medicine and the fourth year medical school course in Medical Ethics. Dr. Fine serves as Senior Fellow for Medical Leadership for the National Hospice and Palliative Care Organization, where he has served on the Board of Directors, and chaired both the Ethics Committee and Research Committee.

Dr. Fine was a founding member, and served on the Board of Directors, VistaCare Hospice Foundation (including as Chair), for ten years. He currently holds several Board of Directors positions, including: VistaCare, Inc., a national leader in hospice care, based in Scottsdale, Arizona; the American Academy of Pain Medicine (Treasurer); the Society for Arts in Healthcare. He is a consultant to the Center for Advanced Illness Coordinated Care, based in Albany, NY, developing and educationally supporting self-sustaining models of pre-hospice palliative care in community settings, as an integrative component of disease management and advanced illness coordinated care. He has served as the Chair of the National Initiative on Pain Control since 2003, an educational endeavor of CME offerings in pain management that has engaged several hundred thousand physicians during this time.

Dr. Fine is widely published in the fields of pain management and end of life care. He serves on the editorial boards of several peer review medical journals. As a medical avocation, he has worked as a team physician for the University of Utah football team for the last 16 years, and was a medical officer for the 2002 Winter Olympics in Salt Lake City. He was awarded The Josefina Magno Distinguished Hospice Physician Award by the American Academy of Hospice and Palliative Medicine in 2007.

Pain.com: How common is persistent pain in older patients?

Dr. Fine: The prevalence of persistent pain in older persons has been reported to be between 20 and 50% in community dwelling-adults, and up to 84% of nursing home patients report daily pain. Despite the high incidence of pain in older persons, studies have revealed that older patients are less likely to be adequately treated for pain compared with younger individuals.

Pain.com: What are the consequences of persistent pain in the geriatric age group?

Dr. Fine: Poor pain control in older persons has been shown to contribute to an overall diminished quality of life and impaired physical functioning. It also has been associated with impaired cognition and mood and sleep disorders, impaired ambulation and gait disturbances. Poorly controlled pain is associated with decreased self-rated overall health assessments which have been shown to be an independent predictor of age-matched life expectancy. Needless to say, the link between persistent pain, independent of its cause, and the risk of premature mortality to persistent pain as a public health issue needs to be taken seriously and addressed accordingly.

Pain.com: What are the common pain-producing conditions that affect older patients?

Dr. Fine: Similar to younger adult populations, low back pain is a leading cause of pain and debility in older patients, with combinations of nociceptive and neuropathic pain arising from degenerative changes in spinal structures, including intervetebral discs and facet joints with resultant spondylosis, neuroforaminal encroachment and spinal canal stenosis. Osteoarthritis and osteoporosis are very common with advanced age, and older individuals are at risk for developing polymyalgia rheumatica, peripheral neuropathies, post-stroke central pain, postherpetic and trigeminal neuralgia, as well as vascular diseases with concomitant ischemic pain. Therefore, because pain-producing conditions are increasingly common with aging, a brief screening assessment for pain should be considered a routine part of geriatric care.

Pain.com: How can physicians and other healthcare professionals determine if patients are in pain if they are unable to self-report due to cognitive impairment from a dementing illness such as Alzheimer's Disease or other causes? Link to PAINAD is http://www.coh.org/prc/Review%20of%20Tools%20for%20Pain%20Assessment/PAINAD.htm Link to DOLOPLUS-2 is http://www doloplus.com/versiongb/rubechelle/intro.htm

Dr. Fine: Pain assessment in patients who are not able to provide a verbal report themselves is an important issue in this patient population. Caregivers and clinicians must observe behaviors as "proxies" for verbal self-report. Changes in usual activity, facial expressions, vocalizations, lack of interest in previously pleasurable events such as eating or grooming, stiff or rigid body postures or guarding, restlessness and spontaneous movements, and so forth, represent the types of behavioral indicators that suggest pain may be present.

Pain.com: What are the affects of aging on drug disposition?

Dr. Fine: Reduced muscle mass, decreases in serum proteins, and decreased renal clearance are the most common changes that account for alterations in pharmacokinetics, such as volume of distribution and clearance. Drugs such as the opioids that are highly protein bound may lead to seemingly more potent effects due to more free drug available to cross the blood-brain barrier. Drugs with active metabolites, such as morphine, that depend upon renal clearance must be used with much greater caution in older patients with predictably elevated creatinine clearance.

Pain.com: What is new and different within the last year or two with regard to pharmacologic agents used to treat pain that may have applicability to older patients in particular?

Dr. Fine: With the withdrawal of two of the three previously available COX-2 inhibitors from the analgesic formulary, and the most recent FDA advisory group recommendation not to approve etoricoxib for osteoarthritis due to concerns about cardiac and cerebrovascular risks, as well as the new warning labels for over-the-counter NSAIDs, clinicians are faced with the challenge of reduced treatment options for their older patients with chronic pain. There has been the addition of a low-dose transdermal fentanyl patch, that releases 12 mcg fentanyl per hour, which may be of benefit to older patients with continuous moderate-to-severe pain from a variety of causes, including cancer, Osteoarthritis (OA) or degenerative joint or spine disease and painful neuropathies not responsive to other treatment modalities. Similarly, tramadol is now available in an extended release formulation for around-the-clock coverage of continuous pain. Oxymorphone has recently been approved for oral administration and is available both as immediate release and extended release formulations, adding to the expanding pharmacopoiea of opioids available for the treatment of moderate or greater pain. One other opioid preparation, the fentanyl buccal tablet, is a rapid-onset agent approved by the FDA for the treatment of cancer-related breakthrough pain in opioid tolerant patients.
In the realm of neuropathic pain, duloxetine, a mixed norepinephrine and serotonin re-uptake inhibitor and pregabalin, an anti-convulsant drug, have been approved for the treatment of painful diabetic peripheral neuropathy. These drugs may be less likely to produce less adverse effects and be better tolerated in older patients than the tricyclic antidepressants, due to less anticholinergic effects. Although not quite as new, it is worth reminding readers that the lidocaine 5% patch is approved for the treatment of post-herpetic neuralgia, but clinical trials have also shown efficacy in a variety of other localized pain states. Since it is extremely safe, its use should be considered as a stand-alone agent or adjunct to systemic therapies.
Lastly, I would like to add that there has been an increased usage of methadone for the treatment of chronic pain conditions, probably due to anecdotally-reported heightened efficacy compared with other opioid analgesics coupled with its relatively low cost. However, there has also been an alarming rise in methadone-related morbidity and mortality in adults being treated for persistent pain. It needs to be emphasized that methadone has a highly variable elimination half-life, making dose accumulation a very real potential problem. As well, methadone has been shown to have a dose-dependent effect on the cardiac QT interval, which can lead to ventricular arrhythmias. Although it can be a very valuable agent, all due caution needs to be exercised in prescribing, titrating and monitoring its use, and those without ample experience should consult with clinicians who are highly experienced with this agent in order to minimize risks in their patients.

Pain.com: Other than the concerns you have raised about methadone, how does opioid therapy in elderly patients differ from younger adults?

Dr. Fine: It must be remembered that pharmacodynamic and pharmacokinetic alterations occur with aging. Most commonly, drug sensitivity is increased leading to more potential cognitive, balance and bowel-related side effects in the older patient. Although not inevitable, a more slow and cautious approach to initiating therapy, dose titration, and opioid rotation are required. Similarly, drug absorption, distribution, metabolism and clearance are likely to be altered, due to progressive changes in body tissue composition, cardiac function and consequent tissue perfusion, bowel motility, hepatic and renal function, and protein binding capacity. All told, this requires more awareness of each individual's physiologic state, potential for drug-drug and drug-disease interactions, and likely consequences of metabolite-related adverse effects. For example, morphine's metabolites, morphine-3 and morphine-6 glucuronide, depend upon renal excretion. In older patients with reduced creatinine clearance, these potentially toxic metabolites may accumulate and lead to excessive sedation or CNS irritability, depending upon the relative ratios of these metabolites. An alternative opioid might be preferred in patients with incipient renal insufficiency. Also, since opioid-related bowel dysfunction is so common, and older patients are especially vulnerable, instituting a bowel regimen that includes a motility agent such as senna or bisacodyl is advised when initiating opioid therapy. It may well be that in the future there will be peripherally-acting opioid antagonists that will counteract opioid-agonist bowel dysfunction, but until then, the more conventional prophylactic approaches need to be remembered and reinforced continually.
Other than this, when opioids are indicated for the control of moderate or greater intensity pain, assessment and subsequent treatment for both components of persistent pain, continuous and breakthrough pain, is required in order to optimize functional outcomes. A risk assessment and management plan should be part and parcel of routine care in order to ensure that therapeutic intent is realized, while toxicity, untoward side effects, misuse, abuse and purposeful or unintended diversion are minimized and rapidly detected. Since older patients, and especially those with cognitive impairment, may be dependent on caregivers, the risk management plan must take this into account. Treatment goals such as reduced pain intensity, reduced pain behaviors, improved functional capacities, improved sleep and mood, or improved social interactions should be documented in order to justify ongoing pharmacologic therapy.

Pain.com: Is breakthrough pain more or less of a problem in older patients?

Dr. Fine: This is a rather new area of inquiry, but surveys to date suggest that breakthrough pain is very common in all patients with advanced cancer. Patients with a variety of non-cancer chronic pain disorders appear to have increasingly frequent episodes of breakthrough pain as their chronic condition progresses to end-stage. Since breakthrough pain erodes quality of life, this is an important component of persistent pain to assess and treat, especially when comfort is a chief objective in end-of-life care.

Pain.com: Are there any additional or concluding comments you would like to share?

Dr. Fine: Additional treatment challenges in the provision of effective pharmacological pain management for older patients include an increased risk of drug-drug and drug-disease interactions due to the commonality of multiple comorbidities and medications in this population. Pharmacokinetic and pharmacodynamic differences in older persons can contribute to increased sensitivity to adverse drug reactions and noncompliance due to concerns about adverse drug reactions and fears of addiction, side effects, or dependence with opioids. With this segment of our population growing quite rapidly, it is increasingly incumbent upon clinicians who are involved in adult medicine to continually update their core knowledge, assessment and management skills in this clinical area. This discussion is a good beginning and on behalf of this vulnerable group of patients, I am grateful for the readers' interest in pursuing this area of inquiry.

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Use of opioids in chronic pain.
Interview with Charles E. Argoff, MD

Charles E. Argoff, MD, is director of the North Shore University Hospital, Cohn Pain Management Center, located on Long Island, New York, and is an assistant professor of neurology at New York University School of Medicine, New York, New York.

Dr Argoff is a member of the American Academy of Neurology, American Association for the Study of Headache, the International Association for the Study of Pain, the National Headache Foundation, and the American Pain Society. His clinical and research interests include the evaluation and treatment of pain, and headache and stroke rehabilitation.

He has contributed to articles in peer-reviewed publications and has been the author or coauthor of book chapters on metabolic and neurologic diseases. A graduate of Northwestern University Medical School, Chicago, Illinois, he completed a residency in neurology at the State University of New York at Stony Brook Medical School and a fellowship in developmental and metabolic neurology at the National Institute of Neurological Disorders and Stroke of the National Institutes of Health, Bethesda, Maryland.

Pain.com: WHAT IS BREAKTHROUGH PAIN AND HOW DOES IT RELATE TO CHRONIC PAIN?

Dr. Argoff: Chronic pain consists of two components: stable, persistent, baseline pain and a transient exacerbation of pain, or breakthrough pain (Portenoy, Hagen 1990; Fine, Busch 1998). Although the duration of baseline pain varies among patients and pain types, it typically lasts months or years (Portenoy 2006c). Breakthrough pain, found in patients with chronic baseline pain who are undergoing analgesic drug therapy on most days, is transitory pain that lasts seconds to hours, is more severe than the background pain, and has a negative effect on function or quality of life (Consensus definition 2006). Both components of chronic pain—baseline persistent and breakthrough pain— need to be independently assessed and treated.

Pain.com: HOW DO OPIOIDS WORK?

Dr. Argoff: Several major classes of opioid receptors in both the peripheral and central nervous system have been identified. These include the mu opioid receptor (typical agonist- morphine), the kappa receptor (typical agonist- butorphanol) and the delta opioid receptor. Endogenous opioids such as endorphins, enkephalins and dynorphins as well as exogenous opioids have multiple sites of action including within the peripheral nerve, the dorsal horn of the spinal cord as well as at higher levels of the central nervous system. Multiple subtypes of these opioid receptors exist and these polymorphisms may be important in ultimately understanding why some patients respond better to opioids than others as well as why some patients respond better to particular opioids and not others.

Pain.com: IS THERE ANY EVIDENCE THAT OPIOIDS ARE EFFECTIVE IN CHRONIC PAIN?

Dr. Argoff: Numerous randomized controlled studies have been completed which demonstrate that compared to placebo the studied opioid offered greater pain relief for patients with osteoarthritis, post-herpetic neuralgia, painful diabetic neuropathy, chronic low back pain, and cancer related pain. A non-controlled study has suggested that a subset of patients with chronic headache may respond favorably long term when treated with opioids. The important point made by this study was that only a relatively small subset of patients (less than 25%) continued to do well on opioids for the three-year period. Most of the other reported studies were of a much shorter duration. While opioids have been shown to provide analgesic benefits, which are superior to placebo treated patients, there are insufficient data to predict how durable this response will be for a given patient. The opioid medications, which were studied included codeine, oxycodone, morphine, fentanyl, methadone, and levorphanol among others.

Pain.com: WHO SHOULD BE TREATED WITH OPIOIDS?

Dr. Argoff: Patients with chronic pain who continue to suffer despite treatment with non-pharmacotherpeutic approaches, or a reasonable number of trials of non- opioid analgesics including neuromodulating agents as well as patients whose unique situation would contraindicate their use of other analgesics may be considered candidates for a TRIAL of opioid therapy. The key at this point is to emphasize the word, TRIAL- while many people may ultimately benefit from and tolerate treatment with an opioid, many others do not and the patient to be treated must hear emphatically from the treating health care provider that the use of opioids will be continued only if the patient experiences meaningful pain relief with acceptable side effects and without any other issues occurring that would contraindicate their continued use (such as misuse or abuse of the medication). Opioids, of course, are used in acute painful states including acute exacerbations of chronic pain when the severity of the pain warrants rapid relief.

Pain.com: WHAT TYPE OF ASSESSMENT IS REQUIRED BEFORE INITIATING OPIOID THERAPY?

Dr. Argoff: The treatment provider must be able to document the pain syndrome that is being treated with opioid therapy. This may require further diagnostic testing in some instances. Do not confuse WNL for within normal limits as this often may mean we never looked! The specific characteristics of the pain, provocative as well as palliative factors and the variability of the pain must be noted. Various assessment tools are available to help to document the intensity of the pain (numerical pain intensity scale) as well as the interference of the pain on the patient's activities (brief pain inventory). The results of prior treatments and their results, the patient's history of addiction (if any) and psychosocial history needs to be explored and documented as well. A number of tools including SOAPP (Screener and Opioid Assessment for Patient s with Pain) are now available to help predict the likelihood that a given patient will use opioids long term without any aberrant behaviors. These should be considered during the initial evaluation, not after a problem has arisen. Unless the treatment provider is

appropriately trained to do so, patients who may be considered otherwise as appropriate candidates for opioid therapy but who have a history of substance abuse or significant psychosocial issues may be referred to a specialized pain treatment facility which may have more experience with and may be more comfortable with treating such patients. Any relevant family history of substance abuse or addictions should be noted and the treatment provider should document that upon considering the benefits and risks of an opioid trial that the benefits appear to outweigh the risks. The rationale for opioid therapy must be clearly documented. This assessment is subject however to ongoing reassessment of the patient and the need and appropriateness of continuing opioid therapy.

Pain.com: WHAT OTHER TYPES OF TREATMENT MIGHT BE CONSIDERED CONCURRENTLY WITH OPIOID THERAPY?

Dr. Argoff: The use of opioids in the management of chronic pain should be considered as one tool in the overall management of the patient. Appropriate use of other medications, interventional pain management, physical rehabilitation alternative medical approaches and behavioral pain management strategies must be considered and implemented to the fullest extent possible.

Pain.com: WHAT IS A TRIAL OF OPIOID THERAPY?

Dr. Argoff: A trial of opioid therapy involves the documentation of realistic treatment goals. These may include sufficient pain reduction, improvement in function and possibly if relevant return to work. The patient must be informed of the potential benefits and risks of opioid therapy and any other relevant information you deem to be important related to their use of opioids. This can be accomplished in part by having the patient review and sign a treatment agreement prior to the initiation of the trial. Your policy regarding refills and medication dose adjustments as well as your policies regarding emergency issues can be discussed in such an agreement. Side effects must be discussed as well as the need for regular follow up for ongoing assessment and reassessment off this therapy. Guidelines for continuing treatment as well as for discontinuing treatment, eg. often called, "exit strategy," needs to be discussed with the patient at the initiation of the opioid treatment trial. Patients need to be aware that it may be necessary to titrate the opioid dose to the desired analgesic effect, and that no pharmacologic agent is likely to completely relieve chronic pain. An exit strategy, eg. failure of the therapy and discontinuation of such may occur if there is a lack of significant pain reduction, lack of functional improvement, intolerable side effects or patient non-compliance with the treatment.

Pain.com: WHAT OPIOID SHOULD YOU USE?

Dr. Argoff: Numerous short-acting and longer-acting opioids are currently available. The treatment provider's choice of a particular opioid may be based upon the patient's past experiences, the patient's diagnosis and current evidence regarding treatment of such with specific opioids (if available) as well as the treatment provider's own personal experience with and comfort with the various agents currently available. Most pain specialists would advocate the use of a longer acting opioid for patients with chronic pain (around-the clock). Short acting opioids may be used to help titrate to an effective dose of a long acting agent as well as for breakthrough pain. Not all longer acting agents are equal with respect to their duration of action. For example, extended release oxycodone has a release mechanism which allows for approximately 40% of the dose to be immediately released and only 60% of it released over a more extended period of time (12 hours); contrast that with the fentanyl patch which may provide analgesia to a patient for up to72 hours. One must be familiar with the various agents and their relative strengths and limitations before prescribing. Certain opioids such as methadone have unique pharmacokinetic issues and/or drug-drug interactions, which the prescriber must be aware of when prescribing these!

Pain.com: WHAT SHOULD BE CONSIDERED AT PATIENT REASSESSMENT?

Dr. Argoff: Patient reassessment involves noting the presence or absence of analgesia, noting functional improvement or lack of such, noting the presence or absence of adverse effects (and treating them) as well as noting the presence or absence of aberrant drug-taking behaviors. If there is insufficient pain relief, then the opioid dose can be increased or the opioid itself rotated to a different one due to incomplete cross-tolerance among various opioids. Adverse effects must be aggressively managed. The treatment provider must be aware of the difference among physical dependence, tolerance, pseudotolerance, addiction and pseudoaddiction when screening the patient for aberrant behaviors.

Urine drug testing must be considered as well. Ultimately, the treatment provider needs to determine at the end of the reassessment visit whether the opioid therapy should be continued or if an exit strategy should be implemented.

Breakthrough Pain

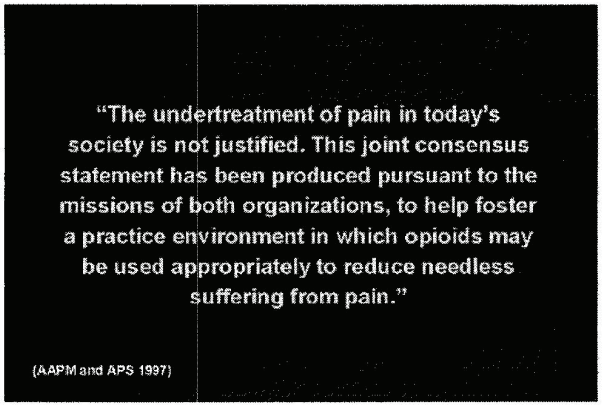
Pain.com routinely interviews pain specialists on a variety of topics so that our healthcare professionals can receive up-to-date information on medications, therapies, procedures, and other medical news. Please note that the opinions expressed in these interviews are specific to the interviewees.

Advances in the Management of Breakthrough Pain
Interview with Gerald M. Aronoff, M.D.

Gerald M. Aronoff, M.D. is Board Certified by the American Board of Pain Medicine and in Psychiatry by the American Board of Psychiatry and Neurology. He has been practicing in the field of pain medicine for more than 25 years and is one of the founding members of the American Academy of Pain Medicine. Throughout his career, Dr. Aronoff has emphasized the importance of interdisciplinary pain management with the goal of functional restoration. Dr. Aronoff is a graduate of the New Jersey College of Medicine and did his residency training at the Harvard Medical School's, McLean Hospital. He did fellowship training at the Boston University School of Medicine and spent the first part of his career as Medical Director of the Boston Pain Center before relocating to Charlotte, North Carolina to become the Medical Director of the Presbyterian Center for Pain Medicine. From 2001 to 2005, he was Chairman of the Department of Pain Medicine at Presbyterian Hospital and Presbyterian Orthopedic Hospital in Charlotte, North Carolina. He continues in the full-time practice of pain medicine and is involved in patient care as well as clinical research on the pharmacological management of chronic pain as well as preventing disability from chronic pain. He is the author of *The Evaluation and Treatment of Chronic Pain* (3rd Ed, 1999) and his most recent book is *The Handbook on The Pharmacological Management of Chronic Pain* (2005). Dr. Aronoff is currently Adjunct Associate Professor, Department of Psychiatry, Duke University School of Medicine. Dr. Aronoff is the Consultant Editor for the Pain.com category, Breakthrough Pain

Pain.com: Good morning Dr. Aronoff, and welcome to the continuing series of expert interviews on breakthrough pain. You wrote the 1st Edition of your text *Evaluation and Treatment of Chronic Pain* in 1985, and you did not advocate the use of maintenance opioids for the treatment of non-cancer pain except in rare circumstances. I understand that your position on this topic has changed dramatically over the years. Could you please discuss why your position changed and tell us about your current views on the use of opioids for severe non-cancer pain management?

Dr. Aronoff: Much of my career has been spent working in the context of a multidisciplinary pain management center (MPC). In the 1970s and 1980s, one of the outcome measures for a successful MPC was the percentage of patients "successfully" tapered from opioids during the treatment program and maintained off of opioids during follow-up. Studies from MPCs often provided conflicting data. Much of this was uncontrolled data, anecdotal and inadequate to reach any definitive conclusions. For example, patients were queried about their opioid use. Most often, this involved short-acting opioids with an analgesic half-life of 3 to 4 hr. Yet often they were being prescribed every 6 to 8 hr. Patients were asked whether they had sustained benefit, significant functional improvement or a greater ability to cope with pain. Generally the responses were not affirmative, and it was concluded that opioids were ineffective for chronic pain. I now suggest that the conclusions were unfounded and misleading. They often reflected inadequate or inappropriate opioid prescribing without enough attention to pharmacodynamics or pharmacokinetics. As many of the patients responded to an MPC treatment approach, this further reinforced the conclusion that opioids should not be used in chronic pain. In retrospect, I can say that many of these patients had not done well prior to their admission to the MPC when they were on opioids and, therefore, justification of the medication taper was not difficult. But with 2006 knowledge and hindsight, I suspect that many of us inadvertently did a disservice to a group of patients who were "detoxified" or treated for "drug dependence." These patients might have benefited from long-term opioid treatment, but we dogmatically refused to prescribe opioids. Some of the patients lost to follow up might have changed physicians and were treated more aggressively elsewhere for ongoing pain. Over the years, I have been grateful to multiple colleagues who urged me to revisit this issue. Much has been learned about opioid use in chronic non-cancer pain, especially from clinical studies and treatment of cancer pain. Insights from the cancer population include the following: · Unrelieved pain is associated with increased morbidity and psychosocial distress. · Effective analgesia can reverse these and improve quality of life. · Management problems related to tolerance or physical dependency are rare. · Addiction is rare without a prior history of substance abuse. Multiple studies over the last 20 years, suggest that these same findings apply to the non-cancer pain population. We now know that in appropriately selected non-cancer pain patients, opioids have a low morbidity (often less than NSAIDs), and a low addiction potential. Although tolerance may occur in some cases, generally patients become tolerant to bothersome side effects (other than constipation) more so than to analgesic effects. In 1997, the American Academy of Pain Medicine (AAPM) and the American Pain Society (APS) issued a joint consensus statement (figure 1)



Pain.com: In view of these comments, why do some medical practitioners still feel uncomfortable treating non-cancer pain more aggressively, since many studies suggest that the problem is often quite disabling.

Dr. Aronoff: It has become clear that chronic non-cancer pain is a major public health problem causing enormous suffering as well as being a major economic drain on society as a result of direct and indirect medical costs and associated lost productivity. The three most prevalent, nonmalignant diseases associated with significant pain include back pain with a prevalence of more than 50 million, arthritis 43 million and chronic headache with more than 40 million sufferers in the United States alone. Estimates indicate that on any given day in America, up to 30% of our population can be suffering from chronic pain. When the physician considers the use of opioids in chronic pain patients with moderate-to-severe pain, the use of sustained-acting (or long-acting) opioid preparations has improved the likelihood of getting good analgesia for around-the-clock pain. The side-effect profile of these medications is significantly lower than repeated dosing with short-acting opioids. Chronic pain is generally subdivided into persistent (e.g., around-the-clock) pain and breakthrough pain. Most pain practitioners think of persistent pain as the baseline pain that chronic pain patients experience. As noted above, when this pain is severe it is generally managed with the use of sustained-action, time-released opioids, at times in conjunction with peripherally acting non-opioid analgesics and adjuvant analgesics. In 1990, Portenoy and Hagen (1) described breakthrough pain in cancer patients as a flare up or acute exacerbation of moderate-to-severe pain in otherwise controlled baseline pain. They distinguished breakthrough pain from poorly controlled persistent pain, as well as from acute episodic pain. Breakthrough pain is further subdivided into *incident pain*, associated with movement or activities (that may be predictable, or unpredictable such as pain related to coughing or sneezing, or bladder spasms); *idiopathic or spontaneous pain*, not having a definable pattern; and *end-of-dose failure* that occurs because the analgesic action of the around-the-clock medication is inadequate to contain the pain until the next scheduled dose. End-of-dose failure generally is not considered actual breakthrough pain and often is best managed by an adjustment in the dose of around-the-clock medication. Multiple surveys and studies have documented that more than half of chronic cancer pain patients experience significant breakthrough pain (2), with some studies indicating a prevalence of breakthrough pain as high as 89% (3). It is generally of rapid onset, brief and in > 40 % of cancer patients begins in less than 4 minutes (2). It is now well established that uncontrolled breakthrough pain often predicts a poor patient outcome associated with patient dissatisfaction with treatment, decreased levels of function and increased levels of anxiety and depression. Unrelieved breakthrough pain increases the economic burden placed on patients and the healthcare system because of increased hospitalizations and more medical and emergency room visits (4). Most patients who have persistent pain and breakthrough pain are able to acknowledge that there are multiple factors influencing their pain, and these range from the disease itself to their activity level or other physical and psychological factors. Clinicians are advised to take a very detailed history in an attempt to define the factors that influence the baseline persistent pain, as well as the episodes of breakthrough pain. There is no justification for withholding treatment for patients with severe, non-cancer breakthrough pain if they meet the criteria for treatment. Despite concerns regarding scrutiny from regulatory agencies, pain management within the guidelines of the various regulatory agencies is appropriate and should be viewed as the standard of care.

Pain.com: Conventional management of breakthrough pain involves the use of immediate release opioids or short-acting opioids and most physicians have developed a certain level of comfort prescribing these. Why is there a need for new agents to manage breakthrough pain?

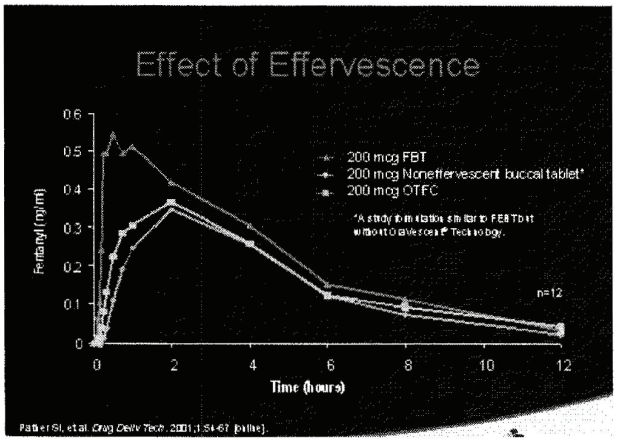
Dr. Aronoff: In a recent article, *Prevalence and Characteristics of Breakthrough Pain in Opioid Treated Patients with Chronic Non-Cancer Pain*, Portenoy et al. (5) surveyed 228 patients with diverse types of chronic non-cancer pain all of whom had controlled baseline pain. They noted that 74% experienced severe to excruciating breakthrough pain, (exceeding the prevalence of 64% and 51% in some cancer surveys) although they found that the median number of episodes per day was less (2 for the non-cancer pain group versus 4-6 for the cancer population). They also found that in the non-cancer pain population, the time to peak pain intensity was 10 minutes or less and the median duration was one hour. Although oral agents are most commonly used to treat breakthrough pain, GI absorption prevents rapid absorption for most agents and therefore is often inadequate for rapid-onset breakthrough pain. Other possibilities include rectal and transdermal routes, as well as multiple invasive techniques such as intramuscular, subcutaneous, intravenous, epidural, and spinal. Invasive techniques such as IV administration and patient-controlled analgesia (PCA) provide rapid onset of action but are expensive and require technical expertise.

Pain.com: In a 2005 article, you and several colleagues discuss some of the advantages of using oral transmucosal fentanyl citrate (OTFC, Actiq®) for rapid onset breakthrough pain. Can you discuss some of your conclusions with our readers?

Dr. Aronoff: Oral transmucosal fentanyl OTFC (Actiq®) was developed to provide rapid-onset and relatively short duration of action via a convenient and noninvasive delivery system (6-9). It is FDA approved for the treatment of breakthrough pain in opioid tolerant cancer patients, but because it is so well tolerated, increasingly has been used for severe rapid-onset breakthrough pain in noncancer patients. Advantages of the oral transmucosal route relate to the physiology of the oral mucosa and pharmacology of fentanyl. The oral mucosa is highly permeable, well vascularized, and lipophilic allowing for rapid drug delivery through the mucosa into the bloodstream. The oral cavity has a relatively uniform temperature and a large surface area, further optimizing this delivery route. The pharmacodynamics of OTFC are comparable to intravenous administration of hydrophilic opioids such as morphine (10,11) but because intravenous access is not necessary, OTFC has the advantages of convenience in terms of portability and ease-of-use that are similar to pills and liquids. Many drugs are not suitable for oral transmucosal administration. Overall, lipophilic drugs are better absorbed in hydrophilic drugs. Morphine, hydrocodone, and oxycodone are poorly absorbed across the oral mucosa due to their low lipid solubility and extensive ionization at the pH of the mouth. Each OTFC unit consists of a fentanyl-containing lozenge attached to a handle. As the lozenge dissolves during the OTFC administration, approximately 25% of the total fentanyl dose is rapidly absorbed across the oral mucosa and become systemically available. The remaining 75% of the total dose is swallowed, and approximately one-third of that amount (25% of the total dose) escapes hepatic and intestinal first pass metabolism and is absorbed more slowly in the intestine. The rapid oral transmucosal absorption of fentanyl combined with fast diffusion across the blood-brain barrier contributes to its swift onset of effect. In our study (12), we noted that the most serious adverse effects associated with all opioids are respiratory depression, circulatory depression, hypotension, and shock. These are extremely rare in appropriately selected patients who take their medication as directed. Patients who are regularly receiving opioid analgesic drugs are typically less susceptible to the serious adverse effects then opioid-naïve patients. In particular, caution should be used when titrating OTFC in patients with medical conditions that predispose them to respiratory depression. We specifically indicated that patients at highest risk for adverse side effects include: · The elderly · Patients with significant pulmonary disease · Patients who indicate that even low doses of most medications cause considerable adverse side effects. We advised increased caution in the titration of these higher risk individuals. We concluded that the unique pharmacodynamic properties of OTFC combined with its non-invasive delivery form offered advantages over current medications then available for the treatment of rapid onset breakthrough pain and that in appropriately selected patients, OTFC was safe and effective.

Pain.com: I understand that there is a next-generation fentanyl product that has recently been FDA-approved for cancer breakthrough pain. Can you discuss this and its advantages over existing breakthrough pain medication.

Dr. Aronoff: The newest transmucosal delivery system utilizes OraVescent® technology that relies on an effervescent reaction to improve the efficiency of the buccal fentanyl absorption. The effervescent reaction causes the production and dissipation of carbon dioxide, causing a dynamic shift in pH as the tablet dissolves. The initial low pH favors dissolution of fentanyl citrate in saliva. The subsequent increase in pH favors the buccal absorption of non-ionized fentanyl across the buccal mucosa and increases the permeation of fentanyl into and through the buccal mucosa. Pharmacokinetic data suggest that the effervescence reaction employed in the fentanyl effervescent buccal tablet (FBT, Fentora®) increases the total amount of fentanyl absorbed, increases peak blood concentration, and decreases the time it takes to achieve peak blood concentration when compared with buccal delivery systems without effervescence (13, 14) Research data is compelling at indicating that the rate and extent of fentanyl absorption is greater with FBT Fentora when compared to non-effervescent fentanyl formulations. (Fig 2) as a result of the effervescent reaction.



Perhaps the most important clinical advantage in the use of the fentanyl effervescent buccal tablet is the significant increase in fentanyl bioavailability. The enhanced bioavailability via the oral transmucosal route allows for more of the fentanyl to be rapidly absorbed into the systemic circulation and CNS (48% vs 22% for OTFC), and less absorbed via GI metabolism. The absolute bioavailability for FBT Fentora® is about 65% (vs 47% for OTFC). This has favorable implications for the significant population of chronic pain patients with rapid onset breakthrough pain. In my clinical experience, many such patients limit their activity level and are far more sedentary than they need to be because of a fear of breakthrough pain. As noted above in this article, although some of breakthrough pain is predictable, frequently it is not and comes on very rapidly without warning. Some patients are fearful that if they are out alone, or with family or friends, they will have an episode of breakthrough pain severe enough that they will need to be taken to an emergency room or be taken home. This fear contributes to many patients remaining homebound. For them, the reassurance of getting more rapid analgesia allows them to increase their functional daily activities and helps them improve their quality-of-life. FBT's Fentora® clinical indication is similar to that of OTFC Actiq® that is, the management of breakthrough pain in patients with cancer who are opioid tolerant. This degree of tolerance is described as patients who are taking · At least 60 mg of oral morphine a day · At least 25 µg transdermal fentanyl per hour · At least 30 mg of oxycodone a day · At least 8 mg oral Hydro morphine a day · An equianalgesic dose of another opioid for a week or longer. Guidelines from Cephalon, Inc. (package insert) indicate that Fentora® FBT should not be used in opioid non-tolerant patients. Multi-center cancer pain studies (15) document the clinical efficacy and safety of using FBT Fentora® for rapid onset chronic breakthrough pain and conclude that most patients (91%) found an effective dose of FBT Fentora® or were managed at the 800 µg dose with a low incidence of treatment-related adverse side effects and without any reports of respiratory depression.

Pain.com: You emphasized earlier that FBT Fentora® is FDA-approved only for breakthrough pain in cancer patients who are opioid tolerant. You also indicated that OTFC Actiq® had a similar indication. We understand from the clinical experience with OTFC Actiq® that many of the pain physicians who use OTFC Actiq® do so in patients who have moderate to severe non-cancer breakthrough pain. Can you comment on this and the implications for FBT Fentora®?

Dr. Aronoff: I believe that my clinical experience is similar to many of my pain medicine colleagues in that much of what we do in pharmacological management with chronic pain patients is "off label" for non-FDA-approved indications. Common examples include the use of tricyclic antidepressants for neuropathic pain. This class of medication is FDA-approved for the management of depression and is not FDA approved for any specific pain process. However, it has been used over the last 30 years for the management of many types of neuropathic pain and other pain states because it has been found to be clinically effective. Other examples of common off label prescribing include the use of gabapentin (Neurontin®) and many other antiepileptics drugs for many types of neuropathic pain. Until recent years, gabapentin was not FDA approved for any pain condition. Prior to its approval for postherpetic neuralgia, In recent years, it became FDA-approved for postherpetic neuralgia gabapentin For years it had been used off label because it was found to be safe and clinically effective. Pregabalin (Lyrica®) has more recently been developed released as an anti-epileptic drug that is FDA-approved for postherpetic neuralgia and for painful diabetic neuropathy. However, many studies are emerging to suggest clinical efficacy in other neuropathic and non-neuropathic pain conditions justifying, in my opinion off label usage. The Lidoderm 5% Patch® is FDA-approved for postherpetic neuralgia and in recent years has been used off label successfully in many neuropathic and nociceptive pain conditions. These are just a few of the many examples of appropriate off label prescribing in the field of pain medicine. Physicians who limit their pharmacological choices to only FDA-approved clinical indications are putting themselves and their patients at a serious disadvantage by not considering treatment options supported by evidence based medicine and good clinical studies to support off label usage. Having said that, I strongly believe that as a physician it is my responsibility to inform my patients when I am using a medication off label. I discuss with them the FDA-approved indications and also share with them my belief that there is adequate clinical evidence to support trying the proposed medication to assist them in their pain management. I document this discussion in my progress note. I have had a great deal of experience using OTFC Actiq® for rapid onset breakthrough pain in non-cancer patients as well as cancer patients. Available data suggests that the overwhelming use of OTFC Actiq® is off label for non-cancer breakthrough pain. Clinical reports support its efficacy and safety in appropriate carefully selected patients. A recent open-label multicenter study of fentanyl effervescent buccal tablets in opioid tolerant patients with chronic non-cancer pain and breakthrough pain (16) evaluated patient's preference regarding use of FBT FEBT® compared with previous supplemental opioids after approximately 4 weeks of use. The primary pain condition treated most often was chronic low back pain (65%) and the pathophysiology of the breakthrough pain was predominantly nociceptive (40%), mixed (37%) and predominantly neuropathic (22%). The most common previous supplemental opioids prior to entering the study were oxycodone (23%), hydrocodone/APAP (22%), and oxycodone/APAP (14%). The study concluded that: · The majority of patients (91%) with chronic non-cancer pain conditions were able to identify an effective dose of FBT FEBT to adequately treat their breakthrough pain. · The results of the interim analysis suggested that a majority of patients with chronic non-cancer pain and breakthrough pain prefer FBT FEBT (100 µg to 800 µg) over previous supplemental opioids.

Pain.com: Dr. Aronoff, do you have any concluding comments you would like to share with our readers?

Dr. Aronoff: In my book, *Handbook on the Pharmacological Management of Chronic Pain*, I emphasize what I believe to be basic principles in the management of all chronic pain patients. These include a treatment approach that addresses the patient's: · Pain · Suffering (emotional distress) · Functional activity level (ADL) · Quality-of-life Chronic pain is woefully under treated and as I noted above, is now recognized as being a major public health problem. Those of us involved in treating this population need to recognize that clinically effective pharmacotherapeutics may play a major role in the care of many patients who might otherwise be incapacitated by their pain. Patients should be carefully evaluated with a comprehensive history and physical examination. Every treatment offered to a patient should be selected only after consideration of the risks and potential benefits of the treatment. I strongly believe that pharmacotherapy is but one aspect of a more comprehensive treatment approach that many patients require. However, effective treatment of breakthrough pain episodes may improve physical and emotional well-being, as well as vocational and recreational functionality for many patients. Additionally, it may decrease patient's reliance upon and use of the healthcare system, particularly the emergency room. The rapid onset of analgesia from the latest effervescent fentanyl buccal tablets acts as oral from new formulations of fentanyl may act as oral PCA and gives outpatients the same type of control that parenteral PCA gives hospital patients.

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