




e-Briefing

Access to Clinical News, Information, Research, and Education

In This Issue

- **EDITOR'S NOTEBOOK...**
Can Pain Medicine Research Be Trusted? 1
- **UPDATE ON NEWS/RESEARCH UPDATES...**
Opioid-Analgesic Abuse & Addiction Prevalence Uncertain 6
- **PAIN-TOPICS RESEARCH ROUNDUP...**
Special Reports
 - » Aches? Pains? An Extra Dose of Vitamin D May Help 11
 - » Safety Stressed in Updated Guidance on Methadone 12*Current Comments*
 - » Do Opioid Analgesics Sometimes Make Pain Worse? 14
 - » Discharging Patients for Opioid-Analgesic Abuse/Addiction? 15
 - » Telltale Signs Identify Patients with Uncontrolled Pain 16
 - » Sexual Dysfunction – Common with Opioid Analgesics 17
- **RECENT CHANGES at Pain-Topics.org** – Certifications & Awards 19

Links in this PDF document – indicated by [blue lettering](#) – are activated for easier navigation. To follow a link...

-  1. Select the Hand tool (located on the Adobe menu bar).
-  2. Position the hand over the linked area until it changes to a hand with a pointing finger (and a boxed 'W'). Then click on the link.
-  3. To return to this document, click the browser back button.



Can Pain Medicine Research Be Trusted?

Research Reporting Run Amok

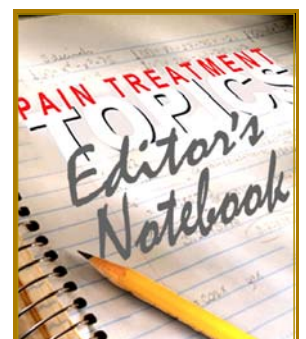
As we began developing this edition of our *e-Briefing* newsletter highlighting some of the research reported at Pain-Topics.org during 2008, we recognized two basic tenets: 1) all medical research is imperfect, and 2) how that research is reported via journal articles, conference presentations, video programs on the Internet, or other media can make matters worse.

This was brought to mind by a recent editorial in the *British Medical Journal (BMJ)* stating that they “continue to be dismayed by submissions that describe poorly conducted studies and by reports of apparently adequate studies that are so incomplete and confusingly written that they are impossible to appraise” [Groves 2008]. We understand and share their disappointment.

An important mission of *Pain Treatment Topics* is to be a “resource-of-resources” in the pain management field. Therefore, one of our roles is to ferret out the best-of-the-best research that is available for access via the Internet by our audience .

Within the 80 section-pages at the Pain-Topics.org website, there are nearly 2700 URL links to resources of various types: guidelines, systematic reviews, reports, articles, books/booklets/brochures, CME courses, etc. To arrive at this number we examine thousands of such resources during the course of a year – rejecting most of them.

(Continued on page 2)



All medical research is imperfect. How it is reported can make matters worse.

(From Editor... continued from page 1)

Frankly, the task is daunting. The medical communications industry is out of control, and resources within the pain management field are growing exponentially at an alarming rate to feed the many journals and websites. We have observed that many documents and programs of all types are often redundant or poorly conceived, and/or sometimes contain errors or portray biased interpretations of the literature.

Our focus is on clinical pain medicine – practical guidance for healthcare providers in treating patients – but a large proportion of the literature is written by researchers for other researchers. Another segment is authored by academicians who may be motivated by archaic “publish or perish” policies in order to assure their career advancement. Furthermore, whether in print or other media, depictions of accepted or common medical practices are not necessarily the same thing as evidence-based practices.

Caveat Lector, Caveat Auditor

We have always contended that there is typically bias of one sort or another in medical research, and the reporting of findings is essentially a form of persuasive communication. As in other disciplines, this is true in the pain management field.

It cannot be assumed that everything appearing in print is worthwhile or valid. So, readers must beware (*caveat lector*) of writing based more on opinion than solid evidence. The same should be said about lectures at conferences and video presentations on the Internet. These communications are generally not peer reviewed, they often rely upon literature that has not been critically assessed, and they focus on the opinions and perspectives of the lecturers – usually without warning notices to that effect. Listener beware (*caveat auditor*).

Observers of the medical communications industry have proposed that many wrong, or at least unreliable, therapeutic answers are being generated due to biased studies, representing small numbers of patients, and using inappropriate analyses [Altman 2002]. Investigations of reputable medical journals, spanning many years, have found a surprising number of faults:

- Abstracts accompanying journal articles often receive the greatest attention by readers. Yet, a review of articles chosen randomly from 6 major medical journals found that up to 68% of the abstracts examined contained data that were inconsistent with or absent from the main body of the articles [Pitkin et al. 1999].
- An epidemiologist at Tufts University School of Medicine, John P.A. Ioannidis [2005], found that nearly one-third (14/45) of the original research studies he randomly examined portrayed either exaggerated or false claims. Among the problems he detected were small study size, design flaws, publication biases (failure to recognize negative results or duplicate positive findings), and disregarding or downplaying the probable role of mere chance in the outcomes.
- In various other investigations, from 25% to 90% of all articles in the journals examined contained errors ranging from omissions of crucial information to significant design flaws affecting validity [Altman 2002; Glantz 1997; McGuigan 1995].
- In one investigation, 80% (40/50) of systematic reviews and meta-analyses randomly selected for examination were judged to have serious and extensive flaws [Jadad et al. 2000].

(Continued on page 3)

The medical communications industry is out of control, and resources within the pain management field are growing exponentially at an alarming rate to feed the many journals and websites.

Abstracts of journal articles often receive the greatest attention, yet one review found that up to 68% of abstracts contain data that are inconsistent with or absent from the main articles.

(From Editor... continued from page 2)

While the above claims themselves might be subjected to critical review, they do point toward the need for very cautious examinations of medical literature. However, the overabundance of medical publications combined with the lack of time by healthcare providers to critically assess what is presented to them poses a serious problem. Plus, most practitioners are not trained to be critical evaluators of medical literature in the first place.

Unfortunately, the scrutiny of medical editors and the peer-review process often cannot be relied upon to act as a filter, separating the wheat from the chaff of medical research. Marcia Angell, former editor-in-chief of the *New England Journal of Medicine*, has conceded the following [in Lenzer 2008]:

“Let me tell you the dirty secret of medical journals: It is very hard to find enough articles to publish. With a rejection rate of 90 percent for original research, we were hard pressed to find 10 percent that were worth publishing. So you end up publishing weak studies because there is so much bad work out there. Doctors are not skeptical enough about what they read in top journals.”

If a top-tier publication like *NEJM* has problems filling its pages with worthwhile articles, one can only imagine what happens at the many journals of lesser quality. In some cases, perhaps they provide a haven for articles and studies that have been rejected by or were never submitted to the scrutiny of more demanding editors and peer reviewers.

Unattainable “Gold Standards”

Ioannidis [2005], mentioned above, asserted that research studies can be designed and/or interpreted in ways that make essentially ineffective therapies look like lifesavers and, conversely, underrate genuinely helpful treatments as being only marginally beneficial. He went so far as to claim that for most research study designs and settings it is more likely for findings and subsequent efficacy claims to be false rather than true.

Ioannidis further observed that, for many published studies, outcomes proposed as evidence for some effect or lack of effect may be simply reflecting prevailing biases. Even worse, highly prejudiced stakeholders (ie, prominent researchers or public agencies) can create barriers to deter efforts at obtaining and disseminating results or viewpoints that oppose their own research findings and/or perspectives.

Yet, for any research question (hypothesis) it is impossible to know with 100% certainty what the truth is – by its nature, research does not “prove” anything. “In this regard,” Ioannidis affirms, “the pure ‘gold standard’ is unattainable.” He reminds us that any single investigation, no matter how comprehensive or statistically significant, provides only a partial picture of what has been discovered or is yet to be revealed in a field of study.

“Lake Wobegon Effect”

A principle doctrine proposed by Ioannidis [2005] is that the greater the financial and other interests or prejudices in a scientific field, the less likely research findings are to be true. Indeed, an investigation published in *JAMA* found that financial relationships among industry, researchers, and academic institutions strongly influence the reporting of outcomes to favor the drug or therapy being promoted [Bekelman et al. 2003]. Therefore, it is always wise to consider who is ultimately



The scrutiny of medical editors and the peer-review process often cannot be relied upon to act as a filter, separating the wheat from the chaff of medical research.

(Continued on page 4)

(From Editor... continued from page 3)

paying the tab for the presentation that one is examining – whether in written or oral form, and whether it is in a journal, at a conference, or on a website.

Along these lines, an interesting phenomenon is the *Lake Wobegon Effect* [in Lenzer 2008]. Researchers, medical institutions, their industry sponsors, and publishers often have overly enthusiastic and optimistic views of the validity, importance, and value of their work. This effect is named for the fictional town of Lake Wobegon where, according to storyteller Garrison Keillor, "all the women are strong, all the men are good-looking, and all the children are above average."

In reality, even the most genuinely "above average" therapies would suffer a progressive dilution of impact during their travels from success in clinical trials (efficacy) to benefits in everyday practice (effectiveness) [see Leavitt 2007]. For example, it has been calculated that a therapy demonstrated as 100% *efficacious* in controlled trials would most likely only be adopted by some practitioners, work only in a subpopulation of real-world patients, and only some patients would adhere to the prescribed treatment regimen. The ultimate clinical *effectiveness* may be surprisingly less than 1% [Carr 2008].

In many respects, healthcare providers need to understand that, despite how straightforward and positive the research literature may portray outcomes for a particular therapy, from bench to bedside there is a layering-on of complexities so that any therapy may or may not confer beneficial effects for individual patients. And, this is particularly the case when it comes to the practice of pain medicine.

Developing a Healthy Skepticism

Clinical research, as reported in the literature, reflects the potential for treatments to have certain outcome effects within specified limitations – but it does not necessarily characterize the realities of everyday pain management practice. To be useful for healthcare providers, medical reporting must satisfy essential questions of relevance:

- Overall, does the study or presentation reflect high quality, valid evidence?
- Do the questions (hypotheses) addressed by the study/presentation pertain to your needs?
- Are the patients being examined or discussed similar to your own patients?
- Is the research gathering and analysis process free of bias and clearly explained?
- Are the results understandable and statistically significant?
- Do conclusions make sense from patient-benefit perspectives (clinically significant)?

Above all, clinical research reports should satisfy the last question by helping to define best practices, with important benefits for patients outweighing any disadvantages. However, keep in mind that simple and clear questions do not always have simple clear answers [Carr 2008].

At the very least, pain management practitioners need to develop a healthy skepticism and become more critical in their reading of research literature (*caveat lector*) or acceptance of oral

Even most "above average" therapies would suffer a progressive dilution of impact during their travels from success in clinical trials (efficacy) to benefits in everyday practice (effectiveness)

To be useful for everyday practice, clinical research reports should help define best practices, with benefits for patients outweighing disadvantages.

(Continued on page 5)

(From Editor... continued from page 4)

presentations at conferences or in video programs at websites (*caveat auditor*). Being aware of the potential for biases, flawed study designs or analyses, and inappropriate reporting methods can help in avoiding untrustworthy data and conclusions.

As if in response to the concerns expressed above, the *British Medical Journal (BMJ)* very recently announced that it is starting a separate section in its publication to address the nuts and bolts of conducting research and writing up results in ways that are valid, readable, and actionable [Groves 2008]. Their series should be worthy of attention and hopefully will benefit the entire medical community, including pain management.

What Else Can You Do?

You can help to promote better pain research by supporting and subscribing to only those publications offering the highest quality articles presenting clearly stated and valid research evidence. Attend those conferences that adhere to the highest standards of evidence-based medicine. And, become a frequent visitor only at those websites certified by the Health on the Net Foundation Code of Conduct (HONcode), which helps to insure unbiased reporting, including full disclosures of authorship, information sources, and funding. Take the time to read the policy statements and disclaimers of those websites you rely on most often for clinical information and guidance. (Pain-Topics.org policies are at: http://pain-topics.org/site_policies/.)

Stewart B. Leavitt, MA, PhD; Publisher/Editor-in-Chief

November 2008

References:

- Altman DG. Poor-quality medical research: what can journals do? *JAMA*. 2002;287(21):2765-2767.
- Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research. *JAMA*. 2003;289(4):454-465.
- Carr DB. When bad evidence happens to good treatments. *Regional Anesth Pain Med*. 2008;33(3):229-240.
- Glantz SA. *Primer of Bio-Statistics*. 4th ed. New York, NY: McGraw-Hill, Health Professional Division; 1997.
- Groves T. Research methods and reporting: a new section of the *BMJ* about how to do and write up research. *BMJ*. 2008;337:946.
- Ioannidis JPA. Why most published research findings are false. *PLoS Med*. 2005;8(2):696-701. Available online at: <http://dx.doi.org/10.1371/journal.pmed.0020124>. Accessed 10/28/08.
- Jadad AR, Moher M, Browman GP, et al. Systematic reviews and meta-analyses on the treatment of asthma: critical evaluation. *BMJ*. 2000;320:537-540.
- Leavitt SB. "Efficacious" treatments are not always "effective." *Pain-Topics e-Briefing*. 2007;2(2). Available online at: <http://pain-topics.org/pdf/e-Briefing-Vol2-No2-2007.pdf>. Access checked 10/30/08.
- Lenzer J. Wonder drugs that can kill. *Discover*. 2008(Jun 20). Available online at: <http://discovermagazine.com/2008/jul/20-wonder-drugs-that-can-kill/> (Access checked 10/28/08.)
- McGuigan SM. The use of statistics in the *British Journal of Psychiatry*. *Br J Psychiatry*. 1995;167:683-688.
- Pitkin RM, Branagan MA, Burmeister LF. Accuracy of data in abstracts of published research articles. *JAMA*. 1999;281(12):1110-1111.

Become a frequent visitor only at those websites certified by the Health on the Net Foundation Code of Conduct.

Look for the HONcode seal.



Stewart B. Leavitt, MA, PhD is the founding Publisher/Editor of *Pain Treatment Topics* and has more than 25 years of experience in healthcare education and medical communications. He also was the founding Editor of *Addiction Treatment Forum*, in 1992, and worked on that project for 15 years. Leavitt was educated in biomedical communications at the University of Illinois College of Medicine and served as an Officer in the US Public Health Service. His advanced degrees focusing on health and medical education are from Northwestern University.



Reader feedback is always welcome and might be shared in a future e-Briefing edition.

Send e-mail to the Editor: Stew.Leavitt@Pain-Topics.org.

Also, be sure to register for e-Notifications of when Pain-Topics.org is updated and to be informed when e-Briefing newsletters are published. Go to: <http://pain-topics.org/register.php>.

Opioid-Analgesic Abuse & Addiction Prevalence Still Uncertain Update on News/Research **UPDATES**

During the past 12 months, we featured 85 items in our bimonthly UPDATES of news and research for healthcare providers interested in pain management. To arrive at that number, we examined hundreds of articles, news releases, and other sources to select those that a) are clinically oriented, and b) focus on treatments that are available today (rather than being purely experimental). Furthermore, reports that appear to be invalid, inaccurate, or confusing for any reason – which unfortunately applies to most of those that we review – are rejected.

One subject we have been closely following and reporting on in the *News/Research Updates* is concerns regarding the abuse and addiction potential of long-term opioid analgesics in patients with chronic pain. Although there has been considerable research, the actual prevalence of these substance-use disorders in this population of patients has yet to be firmly established. And, all indications are that these problems may not be as common as many practitioners, regulators, and the public seem to believe.



Opioid-analgesic abuse and addiction may be less prevalent than is commonly believed.

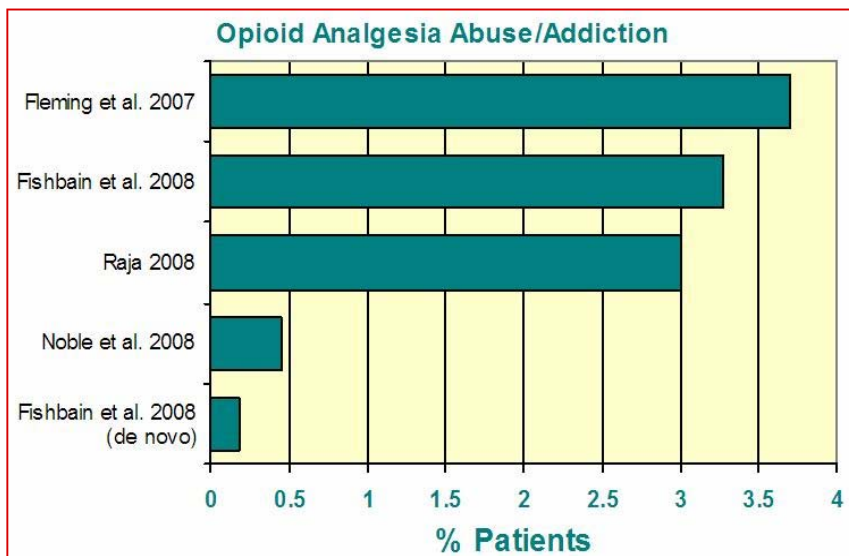
Relatively Low Prevalence of Problems

In the September/October 2008 edition of the Pain-Topics *News/Research Updates* we reported that Fishbain et al. [2008] from the Miller School of Medicine at the University of Miami, Florida, conducted a structured evidence-based review of all available studies as of year 2006 relevant for assessing the development of abuse/addiction and aberrant drug-related behaviors in patients with chronic noncancer pain exposed to long-term opioid analgesic therapy.

Among 2507 patients included in 24 studies qualifying for analysis, the opioid analgesic abuse/addiction rate was 3.27%. However, in patients specifically with *de novo* abuse/addiction (without a previous or current history of substance-use problems) the rate was only 0.19% (see **Graph**).

These authors also reviewed studies that assessed urine toxicology as a surrogate marker for abuse/addiction. In 5 studies, encompassing 15,442 subjects, 20.4% of the patients had either no opioid at all or an illicit opioid in their urine. In another 5 studies (1965 subjects total) various illicit drugs were reported in 14.5% of patients. In these analyses, no distinctions were made between patients with or without a prior history of substance-use problems.

At the annual meeting of the American Pain Society last May, Srinivasa Raja [2008] from Johns Hopkins University School of Medicine observed in his plenary session address that less



(Continued on page 7)

(Opioid Abuse/Addiction... continued from page 6)

than 3% of patients without a prior history of drug abuse who are prescribed opioids for chronic pain will show signs of possible opioid abuse or addiction. He suggested that mass media accusations of increased pain medication abuse by patients being due to increased opioid prescribing for chronic pain management were unfounded. Raja did not cite the source of his data, but this observation coincides closely with the findings of Fishbain et al.

In another systematic review, reported in our *News/Research Updates* last January/February, Noble and colleagues [2008], at the ECRI Institute (a nonprofit organization dedicated to applied sciences research), evaluated 115 clinical trials of long-term opioid therapy in patients with chronic noncancer pain (CNCP). In their final analyses there were 17 qualifying studies that had enrolled patients with moderate-to-severe CNCP who were treated with opioid analgesics for a minimum of 6 months.

Surprisingly, opioid abuse was reported in only 3 of 685 (0.4%) patients assessed for this problem, and signs of opioid addiction were evident in only 1 case out of 2042 (0.05%) subjects evaluated. However, there was no indication if these extremely low rates were in the overall subject population or solely in patients without prior substance-use problems.

Interestingly, Fishbain et al. noted that many studies they examined did not report any opioid abuse or addiction at all. They stated that, if it is assumed that this represents zero incidence rather than a reporting oversight by the researchers, and these studies are combined with the others, then the already low rate of abuse/addiction without prior history of such problems might have been merely 0.07%. However, this would be a risky approach – it cannot be assumed in this case that a lack of reported data means no incidents occurred.

In an earlier clinical investigation, Fleming et al. [2007] examined the rate of substance-use disorders in a population of patients receiving daily opioid therapy for chronic noncancer pain prescribed by primary-care physicians. Their analysis of 801 adult patients found that 3.7% met DSM-IV clinical criteria for an opioid-use disorder, either abuse (0.6%) or dependence/addiction (3.1%).

This 3.7% overall rate, using validated criteria from the “Diagnostic and Statistical Manual of Mental Disorders” (DSM) for defining abuse and addiction, is strikingly close to the 3.27% rate of abuse/addiction reported by Fishbain et al. This might suggest that previous studies actually used definitions of abuse and addiction that have some validity. Unfortunately, the study by Fleming and colleagues did not also distinguish between patients with or without a prior history of substance-use problems.

Marijuana Confounds Illicit-Drug-Use Data

As for illicit drug use in patients with chronic pain, the rates noted by researchers reporting on these problems – Fishbain et al. 2008 (14.5%); Fleming et al. 2007 (24%) – are considerably high and of concern. As we observed earlier in our May/June 2006 *News/Research Updates*, other researchers similarly found illicit-drug use rates of 16% to 22% in patients with pain [Manchikanti et al. 2005, 2006].

In some analyses, significant differences in patients with pain have been observed based on age: 26% of patients under 45 years of age, 13% of those between 45 and 64 years, and no patients over age 65 were illicit-drug abusers [Manchikanti et al. 2006]. Therefore, demographics

Mass media accusations of increased pain medication abuse by patients being due to increased opioid prescribing for chronic pain management may be unfounded.

(Continued on page 8)

(Opioid Abuse/Addiction... continued from page 7)

could strongly bias the observed prevalence rates in some studies that have larger proportions of subjects in certain age groups.

Among all the illicit drugs used in the United States, marijuana has been the most common for several decades [Manchikanti and Singh 2008]. Consequently, data reflecting illicit drug use in patients with pain are inflated by a high prevalence specifically of marijuana use. Fleming et al. [2007] reported that 20% of all patients with chronic pain tested for illicit substances were using marijuana. Manchikanti et al. [2005] found that up to a third of such patients used marijuana.

Although researchers specify “nonmedical use” of illicit agents in their data, in the case of marijuana it is actually not known whether patients were using this drug for expected medicinal effects or strictly nonmedical (recreational) purposes – this is not examined in the research. Marijuana use probably should be evaluated as a problem distinct from the abuse of either non-prescribed (hence, illicit) opioids or illegal drugs, such as cocaine, heroin, phencyclidine, and others.

Medicinal marijuana has been a complicated issue surrounded by legal and political controversies. As we reported in our September/October 2008 *News/Research Updates*, new evidence suggests that smoking marijuana may help relieve neuropathic pain. In a randomized, controlled trial, Ellis and colleagues [2008], at the University of California, San Diego, School of Medicine, compared medical marijuana with placebo in patients with HIV-related neuropathic pain that was not adequately managed by analgesics, including opioids. Clinically significant pain relief – varying from moderate to strong – was provided in 46% of marijuana smokers compared with only 18% of those smoking the placebo product.

This was a small study enrolling only 28 patients in a hospital setting; however, the researchers believe their results demonstrated that medical marijuana can significantly reduce neuropathic pain when added to a patient's already-prescribed pain management regimen. It is noteworthy that the cannabis and identical placebo cigarettes were provided by the National Institute on Drug Abuse (NIDA), suggesting that there continues to be some government-sanctioned scientific interest in the analgesic potential of this agent.

Overall, however, there is general opposition to medicinal marijuana by the federal government in the US. Despite this, during the recent national election on November 4, 2008, Michigan became the 13th state to approve medical marijuana. The new law will permit terminally and seriously ill patients to use marijuana for medical purposes with a physicians' approval, allow such patients to legally grow and possess certain amounts of the drug for their personal medical use, and create an ID-card system for medical use.

There appears to be a growing body of evidence suggesting that medical marijuana may be helpful for patients with chronic pain conditions. However, there have been no large-scale, prospective, controlled clinical trials, and the substance can have a negative impact on certain mental skills and can cause lung problems. Therefore, a body of sufficiently high-quality evidence is lacking to make informed risk-benefit decisions regarding marijuana as an analgesic adjunct.

Still, combining marijuana-use rates with other data reporting substance abuse problems in patients with pain may be inappropriately inflating the prevalence of such problems. This is unhelpful for understanding the extent of illicit drug use in these patients and how it may affect pain management practice.



Medicinal marijuana has been a complicated issue surrounded by legal and political controversies. However, if the research is valid, the drug may offer certain analgesic benefits.

(Continued on page 9)

The Jury is Still Out

Based on their comprehensive review, Fishbain and colleagues [2008] concluded that clinicians can be reasonably certain that only a relatively small percentage of all patients with chronic pain will exhibit abuse/addiction when receiving long-term opioid analgesics. Furthermore, the chance of iatrogenic abuse/addiction development is probably quite rare in patients not having a prior history of substance-use disorders.

However, Fishbain et al. conceded that this sort of research can be confounded by unclear or inconsistent definitions of opioid “addiction,” “abuse,” and “aberrant behaviors” used across studies. In fact, due to imprecise definitions in so many studies they had to combine abuse and addiction data into a single category for their overall analyses. They believed that the 3.27% prevalence of abuse/addiction could have been lower if standardized and accurate criteria had been used; although, the 3.7% rate found by Fleming et al. [2007] using validated DSM definitions was quite similar. (The Fleming et al. study was published after the cut-off date for the Fishbain et al. analysis and was not included in their report.)

Another problem is found with the quality of available research evidence. In their extensive analysis of clinical trials investigating long-term opioid therapy, Noble and colleagues [2008] noted that *all* of the 117 studies they initially considered were of low quality due to methodological and/or reporting deficiencies. There were no randomized placebo-controlled trials (RCTs) available for analysis and there was only one long-term controlled trial, which compared 2 opioids rather than opioid versus non-opioid therapy.

Only a small proportion of the studies selected as qualifying for review by Noble et al. included assessments of opioid abuse or addiction, although a relatively large number of patients overall were evaluated for these problems. The studies used very broad and inclusive definitions of abuse/addiction and still found extremely low incidences of substance-use disorders. These were curiously in sharp contrast to the higher, but still quite low, overall rates reported by Fishbain et al. and Fleming et al.

There was no doubt some overlap in the studies examined by Noble et al. and Fishbain et al. in their respective comprehensive reviews, and this needs further examination to determine if there was a selection bias in one or both of them. It is not unusual for two groups of investigators to approach identical bodies of evidence selectively or from different perspectives to arrive at disparate results.

Some question remains as to how rates of substance abuse/addiction in patients with chronic pain compare with the general population. Fishbain et al. [2008] noted that the prevalence of opioid-use disorders in the general population is approximately 10%; whereas, Fleming and colleagues [2007] claimed the frequency is merely 0.9%. This suggests that the rate of opioid-use problems in patients with pain may be either about two-thirds less or 4 times greater than in the general public – quite a disparity. However, neither group of authors provided reference sources for these data, and the veracity of the 0.9% figure in particular is questionable.

More verifiable sources have noted that about 8% of all Americans aged 12 and older use illicit substances. And, depending on the medical population examined, rates of substance-use disorders have ranged from 5% to as high as 67% [Savage et al. 2008]. The exact percentages of those disorders involving only opioids has been poorly delineated. Therefore, any conclusions

The chance of iatrogenic opioid abuse/addiction development is probably quite rare in patients not having a prior history of substance-use disorders.

It is not unusual for two groups of investigators to approach identical bodies of evidence selectively or from different perspectives to arrive at disparate results.

(Continued on page 10)

(Opioid Abuse/Addiction... continued from page 9)

about how rates of these disorders in patients with pain compare with the overall population would be meaningless without much more extensive scrutiny of the data and/or further research.

In sum, this entire area of investigation has been burdened by small studies, imprecise definitions of terms, inconsistencies in research designs, and a lack of repetitive and comparable studies to assess reliability of results. Therefore, the jury is still out when it comes to reaching a judgment based on current evidence regarding opioid abuse and addiction, as well as illicit-drug use, during long-term opioid analgesia for chronic noncancer pain.

Meanwhile, establishing policies or medical practices in pain management based on a presumption of certain rates of opioid-analgesic abuse or addiction in patients could be misguided, resulting in added costs for healthcare delivery and the undertreatment of pain. This area is worthy of further investigation and debate, but if preliminary indications hold true after further scrutiny, this problem may be of much smaller proportions than has been portrayed in the past.

References:

- Ellis RJ, Toperoff W, Vaida F, et al. Smoked medicinal cannabis for neuropathic pain in HIV: A randomized, crossover clinical trial. *Neuropsychopharmacology*. Advance online publication, August 6, 2008; doi: 10.1038/npp.2008.120. See News/Research Update: Pot Provides Neuropathic Pain Relief, Study Says. Available at: http://pain-topics.org/news_research_updates/issue16.php#Pot
- Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med*. 2008;9(4):444-459. See News/Research Update: Evidence Review: Opioid Analgesic Abuse & Addiction Uncommon in Patients with Chronic Pain. Available at: http://pain-topics.org/news_research_updates/issue17.php#AnalgesicAbuse
- Fleming MF, Balousek SL, Klessig CL, et al. Substance use disorders in a primary care sample receiving daily opioid therapy. *The Journal of Pain*. 2007;8(7):573-582. See News/Research Update: Abuse of Opioid Analgesics in Primary Care Studied. Available at: http://pain-topics.org/news_research_updates/issue10.php#abuse
- Manchikanti L, Fellows B, Damron KS, et al. Prevalence of illicit drug use among individuals with chronic pain in the Commonwealth of Kentucky: an evaluation of patterns and trends. *J Ky Med Assoc*. 2005(Feb):103(2):55-62.
- Manchikanti L, Manchukonda R, Pampati V, et al. Does random urine drug testing reduce illicit drug use in chronic pain patients receiving opioids? *Pain Physician*. 2006(Apr);9(2):123-129. See News/Research Update: Random Testing Reduces Illicit-Drug Use in Patients With Pain. Available at: http://pain-topics.org/news_research_updates/index3.php#random
- Manchikanti L, Singh A. Therapeutic opioids: A ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician*. 2008;11:S63-S88.
- Noble M, Tregear SJ, Treadwell JR, et al. Long-term opioid therapy for chronic noncancer pain: a systematic review and meta-analysis of efficacy and safety. *J Pain Symptom Manage*. 2008(Feb);35(2):214-228. See News/Research Update: Long-Term Opioids in Chronic Noncancer Pain Reviewed – Lack of Abuse/Addiction. Available at: http://pain-topics.org/news_research_updates/issue13.php#Noncancer
- Raja S. From poppies to pill popping: Is there a middle way? American Pain Society Annual Meeting Plenary Session, May 10, 2008, Tampa, Florida. See News/Research Update: Opioid Pain-Relief Benefits Outweigh Risks of Abuse. Available at: http://pain-topics.org/news_research_updates/issue15.php#Outweigh
- Savage SR, Kirsh KL, Passik SD. Challenges in using opioids to treat pain in persons with substance use disorders. *Addict Sci Clin Prac*. 2008;4(2):4-25. Available at: http://pain-topics.org/opioid_rx/addiction.php#NIDA
- ** For earlier commentary on this subject, see “Iatrogenic Opioid-Use Problems; What’s the Risk” in the Pain-Topics.org e-Briefing newsletter, Vol. 2, No. 1, 2007. Available at: <http://www.pain-topics.org/pdf/e-Briefing-Vol2-No1-2007.pdf>

Establishing policies or medical practices in pain management based on a presumption of certain rates of opioid analgesic abuse or addiction in patients could be misguided

*Researcher/Writer –
Stewart B. Leavitt, MA, PhD
November 2008*

Pain-Topics.org *Special Reports* for 2008

Special Reports from Pain Treatment Topics are designed to address specific questions or more thoroughly discuss topics of concern that are inadequately covered or neglected by other literature in the pain management field. These reports are based on current best evidence, with complete reference sources cited, and they undergo extensive peer review prior to publication and posting at Pain-Topics.org.

Aches? Pains? An Extra Dose of Vitamin D May Help

Pain is the most common complaint leading patients to seek medical care and much of it is chronic, lasting 3 months or longer. According to an extensive review of clinical research in a report from *Pain Treatment Topics* introduced last June 2008, inadequate vitamin D intake has been linked to a long list of chronic painful maladies, including bone and joint pain of various types, muscle pain, fibromyalgia syndrome, rheumatic disorders, osteoarthritis, and other complaints. Lack of vitamin D also has been implicated in the mood disturbances of chronic fatigue syndrome and seasonal affective disorder.

According to Stewart B. Leavitt, MA, PhD, editor of *Pain Treatment Topics* and author of the report, "our examination of the research, including 22 clinical investigations of patients with various chronic pain and fatigue syndromes, found that these persons almost always had inadequate levels of vitamin D. When sufficient vitamin D supplementation was provided, the aches, pains, weakness, and related problems in most of them either vanished or were at least helped to a significant extent."

The report, "Vitamin D – A Neglected 'Analgesic' for Chronic Musculoskeletal Pain," was peer-reviewed by a panel of 8 experts and includes the following important points:

- Vitamin D is a complex nutrient that functions as a hormone to benefit numerous body tissues and organs, including bones, muscles, and nerves.
- A surprising majority of persons in many parts of the world, including the United States, do not get adequate vitamin D from sun exposure or foods. Why such deficiencies are associated with pain in some persons but not others is not always known.
- The currently recommended adequate intake of vitamin D – up to 600 IU per day – is outdated and too low. According to the research, most children and adults need at least 1000 IU per day, and persons with chronic musculoskeletal pain would benefit from 2000 IU or more per day of supplemental vitamin D₃ (also called cholecalciferol).
- Vitamin D supplements have a highly favorable safety profile. They interact with very few drugs or other agents, and are usually not harmful unless extremely high doses – such as, 50,000 IU or more – are taken daily for an extended period of time.
- Vitamin D supplements are easy for patients to self-administer, are well tolerated, and typically cost as little as 7 to 10 cents per day.



Helping patients to overcome their chronic muscle, bone, or joint aches and pains may be as simple, safe, and inexpensive as an extra daily supplement of vitamin D.

(Continued on page 12)

Vitamin D Supplementation for Chronic Pain — Conservative Dosing Protocol

1. In patients with chronic, nonspecific musculoskeletal pain and fatigue syndromes, it usually can be expected that vitamin D intake from combined sources is inadequate and concentrations of serum 25(OH)D are insufficient or deficient.
2. All patients should take a multivitamin to ensure at least minimal daily values of essential nutrients, including calcium and 400 IU to 800 IU of vitamin D.
3. Recommend a daily 2000 IU vitamin D₃ supplement, bringing total supplement intake to 2400 to 2800 IU/day (incl. from multivitamin). *Extra calcium may not be necessary unless diet is insufficient and/or there are concerns about osteoporosis (eg, in postmenopausal women or the elderly).*
4. Monitor patient compliance and results for up to 3 months. *Other therapies for pain already in progress do not necessarily need to be discontinued.*
5. If results are still lacking after 3 months, or persistent 25(OH)D deficiency or osteomalacia are verified, consider a brief course of prescribed high-dose vitamin D₃ with or without added calcium as appropriate, followed by ongoing supplementation as maintenance.

(Special Reports... continued from page 11)

Leavitt stresses that vitamin D should not be viewed as a cure for all pain conditions and in all patients. It also is not necessarily a replacement for other pain treatments. “While further research would be helpful,” he says, “current best evidence indicates that recommending supplemental vitamin D for patients with chronic musculoskeletal pain and fatigue disorders would do no harm and could do much good at little cost. It should be considered by healthcare providers for their patients early in the course of pain management” (See **Table** above.)

Besides the comprehensive **Research Report* (50-pages, 170 references), there is available a shorter **Practitioner Briefing* (7-pages) that summarizes the report and provides guidance for healthcare providers. Additionally, a special **Patient Brochure* (6-pages) explains what vitamin D is, how it works, and how it may help in relieving pain.

***All 3 documents are available for free access at:** <Click on the blue URL link>



<http://www.Pain-Topics.org/VitaminD>

Safety Stressed in Updated Guidance on Methadone for the Relief of Chronic Pain

Methadone is an effective and economical opioid analgesic for the management of cancer pain and chronic noncancer pain, both as a first line medication and as a replacement opioid. However, methadone-associated emergencies, overdoses, and deaths have increased, so there is a critical need for the proper prescribing and use of this medication.

Two documents, updated in March 2008 and available exclusively from *Pain Treatment Topics*, help teach healthcare providers how to best prescribe methadone, and provide special instructions for patients on how to safely use it.

“Oral Methadone Dosing for Chronic Pain: A Practitioner’s Guide”

In this 12-page guidance report, author James D. Toombs, MD, cautions that methadone works differently than other opioid pain relievers. It is much more powerful than morphine, but there are significant differences in how patients respond to methadone. Further-

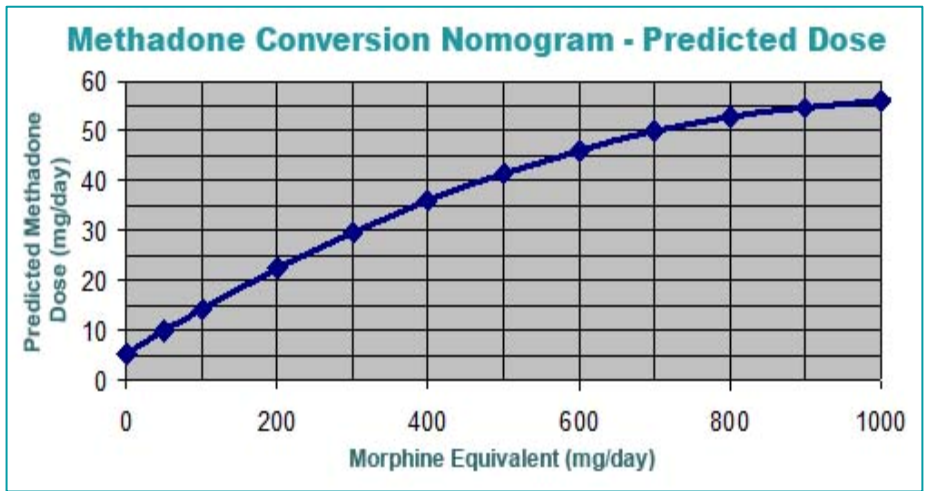


(Continued on page 13)

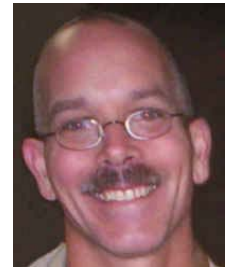
(Special Reports... continued from page 12)

more, methadone can interact with a large number of other medications, so harmful drug interactions must be considered. At the same time, compared with other opioids, methadone is generally much less expensive, making effective pain relief affordable for all patients. Toombs' paper discusses these vital issues and provides specific guidance on how oral methadone should be dosed daily for best results and , importantly, with the least risks of adverse reactions or overdose.


Toombs also provides a helpful nomogram (above) for calculating conversions from other opioids (in morphine equivalents) to methadone. The nomogram is used by locating the current morphine oral equivalent dose along the X-axis, moving up to the curve, and reading the corresponding methadone-dose value along the vertical Y-axis.



James D. Toombs, MD, is a Staff Physician in the Division of Primary Care/ Pain Medicine at the Harry S. Truman Memorial Veterans' Hospital in Columbia, Missouri. He is a Diplomate of the American Board of Family Practice and holds a Subspecialty Certification in Pain Medicine from the American Board of Physical Medicine and Rehabilitation. Dr. Toombs has published several papers focusing on pain management. He is a Senior Flight Surgeon in the Missouri Army National Guard and served two tours of active duty as a Field Surgeon in Iraq during Operation Iraqi Freedom. He currently serves as a medical advisor to Pain Treatment Topics.




This document is available for free access at: <Click on the blue URL link>

 http://pain-topics.org/opioid_rx/methadone.php#methchropain

“Methadone Safety Handout for Patients” (in English and Spanish)

Stewart B. Leavitt, MA, PhD, editor of *Pain Treatment Topics*, has developed these special 2-page handouts for patients and their families or caregivers. They offer vital instructions for methadone treatment compliance and safety, and can be freely copied and provided to patients at the time they receive their methadone prescription from the healthcare provider. These easy-to-understand instructions warn patients that misuse or abuse of this strong opioid can have dire consequences including overdose and death, and guidance is provided for how to avoid these hazards.

This document is available for free access at: <Click on the blue URL link>

 http://pain-topics.org/opioid_rx/methadone.php#handout

Patient Instructions
Safely Taking Methadone for Pain

Please read the following carefully and share it with family members or caregivers. It does not take the place of your healthcare provider's guidance or the methadone package insert.

Your healthcare provider has prescribed methadone to help control pain. Methadone (methu-ahn-don) is a strong pain reliever that has been used successfully for more than 50 years in millions of persons worldwide. It is a man-made, or synthetic, opioid (oh-pee-oid) drug with actions similar to natural opioids like morphine or codeine that come from the opium poppy; except, methadone is more potent.

Methadone is a very effective and economical medication. When used properly, it can help safely relieve pain even when other medications fail. However, since it is a long-acting and powerful drug, its improper use or abuse can be harmful and even fatal (causing death). Therefore, it is very important that you read, understand, and follow all of the safety instructions below.

- Always take methadone exactly as directed.
 - Taking extra methadone or combining it with other drugs, alcohol, or over-the-counter products, unless approved by your healthcare provider, can be harmful or fatal.
 - Make sure the methadone prescriber knows of all healthcare products and drugs (prescribed or not) that you are using and your complete medical history.
 - You must take only the prescribed amount of methadone and at the specified time intervals, such as every 6 or 8 hours (that is 4 or 3 times per day).
 - If you were told to split methadone tablets for the proper dose, ask your healthcare provider or pharmacist how to do so accurately.
 - Methadone builds up in the body over time, often taking a week or longer to achieve full effect. During that time, pain relief may be incomplete. However, unless told to do so by your healthcare provider, never take extra methadone doses or other pain relievers, as this could be harmful or fatal.
 - If you forget to take your usual methadone dose on time, you can take it very soon afterward. Otherwise, wait until it is time for the next dose and take only that; do not take extra methadone to make up for what was missed.
 - To help avoid missing doses or taking extra ones, use a dosing chart or medication log to keep track of when you take each dose of methadone.
 - If you are forgetful, have someone else give you each dose of methadone and keep a record of it.
 - Do not take methadone with grapefruit or grapefruit juice. It can block digestion of methadone, causing a harmful excessive amount to accumulate.
 - Tell all of your healthcare providers that you are taking methadone. Unless they know of this they might prescribe medications that alter methadone's effects. They should contact the methadone prescriber if there are questions.

Taking extra methadone, more often, or with other drugs or alcohol can be harmful or even fatal.

Keep careful track of when you take your methadone.

Since the last edition of this *e-Briefings* Newsletter several new “Current Comments” essays have been published and posted at Pain-Topics.org. These address concerns about achieving effective pain treatment while managing inherent risks of analgesia, primarily relating to opioids. The papers are briefly summarized below, and instructions for accessing the full article follows each synopsis.

Opinions and perspectives expressed in Current Comments essays/reports are those of the authors and are not peer-reviewed. Pain Treatment Topics and its advisors, sponsors, or affiliates do not necessarily endorse any viewpoints, medications, or treatments discussed. Nor are any representations made concerning their effectiveness, appropriateness, or suitability.

Do Opioid Analgesics Sometimes Make Pain Worse?

Opioid medications are essential for helping to relieve all types of serious pain. However, relatively recent evidence suggests that in some patients they can paradoxically worsen the pain.

“Actually, this possible negative effect of opioids, such as morphine, to cause increased sensitivity to pain was observed in the 19th Century,” says Peggy Compton, RN, PhD. “Today, we call this opioid-induced hyperalgesia, or OIH.”

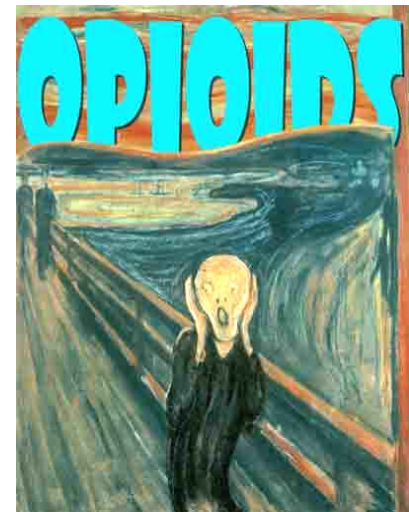
Her extensive review of the clinical evidence on OIH, exclusively for *Pain Treatment Topics* and published at the Pain-Topics.org website, is titled, “The OIH Paradox: Can Opioids Make Pain Worse?”

Fortunately, it seems that OIH *does not arise in the majority of patients* taking opioid analgesics, but when it does occur it can be difficult to manage. In addition to OIH, pain increasing during opioid therapy can indicate several other conditions that must be considered, including: 1) worsening pain-causing disease, 2) tolerance to opioid effects, 3) opioid withdrawal symptoms, or 4) pseudoaddiction (opioid-seeking due to unrelieved pain). For these conditions, increasing the opioid dose usually helps relieve pain.

A patient who is addicted to opioids may complain of worsening pain but may not be helped by increasing the opioid dose. In fact, signs of addiction may emerge further, such as difficulty controlling opioid use, a preoccupation with obtaining opioids, or other misbehavior.

In the case of OIH, increasing the opioid dose will actually make the pain worse. Often, the pain is difficult for the patient to describe and can spread beyond the original point of pain. According to Compton’s review, several strategies may help prevent OIH or to deal with OIH if it occurs:

- The opioid dose should be kept as low as is clinically effective for managing pain.
- Additional medications can be used to help minimize the need for opioids, such as COX-2 inhibitors, dextromethorphan, adjuvant agents (eg, antidepressants), and others.
- Long-acting opioids are preferred over shorter-acting formulations for chronic pain.
- If a particular opioid becomes ineffective, it is often helpful to rotate to a completely different opioid drug (methadone is especially useful for opioid rotation).
- New research suggests combining low-doses of opioid antagonists (eg, naltrexone) with opioid therapy to counteract development of OIH.



As new evidence becomes available, healthcare providers are becoming increasingly aware that ongoing opioid therapy for chronic pain might actually worsen the pain in some patients – a condition called Opioid-Induced Hyperalgesia or OIH.

(Continued on page 15)


(Current Comments... continued from page 14)

Compton observes that there are still many unanswered questions about OIH, and research investigations are ongoing. Meanwhile, it is essential for healthcare providers to carefully monitor patients' responses to opioid therapy and recognize that several opioid-related responses other than OIH can lessen opioid-analgesic effectiveness (see **Table**). In some cases, higher dosing is needed; however, if OIH occurs, other strategies should be employed to provide patients the pain relief they need and deserve.

In some cases, higher opioid dosing is needed; however, if OIH occurs, other strategies should be employed to provide patients the pain relief that they need and deserve.

Differential Assessment of OIH vs Other Conditions			
Condition	Nature of Pain	Presentation or Onset of Pain	Response to Opioid Administration
Opioid-Induced Hyperalgesia (OIH)	Increased sensitivity to pain; diffuse pain, extending beyond the distribution of pre-existing pain; allodynia may be present.	Abrupt onset with rapid opioid escalation or high-dose opioid administration.	Pain worsens.
Worsening Pain Pathology	Localized to site of pre-existing pain or new site of pathology.	Variable, depending on source of pain.	Pain improves.
Opioid Tolerance	Localized to site of pre-existing pain.	Gradual onset.	Pain improves.
Opioid Withdrawal	Increased sensitivity to pain; diffuse, extending beyond the distribution of pre-existing pain.	Abrupt with short-acting opioids or antagonist administration; gradual with long-acting opioids.	Pain improves.
Opioid Addictive Disease	Increased sensitivity to pain; diffuse, may extend beyond the distribution of pre-existing pain.	Gradual onset.	Pain may improve but functionality may worsen.
Pseudoaddiction	Localized to site of pre-existing pain.	Variable, depending on source of pain.	Pain improves.

For free access to **The OIH Paradox: Can Opioids Make Pain Worse?** see:

 http://pain-topics.org/clinical_concepts/comments.php#ComptonOIH

Patients with Pain Should Not Be Punished for Opioid Medication Abuse/Addiction

“Any practitioner prescribing opioids for chronic use should be accountable for having a strategy in place if medication abuse or addiction occurs,” says Peggy Compton, RN, PhD. “Providing daily opioid pain relievers without suitable addiction expertise or support in place puts both the pain-management practitioner and patient at risk for poor outcomes.”

Unfortunately, the common practice of discharging patients from opioid therapy when there are concerns about substance abuse or addiction can do significant harm; not just to patients, but also affecting their families, the healthcare system, and society at large. Such practice should be avoided, Compton urges.

In her commentary for *Pain Treatment Topics*, Compton stresses that instead of denying patients their pain-relieving opioids, working partnerships between addiction and pain specialists should ideally be developed, with the pain practitioner continuing treatment for



(Continued on page 16)

(Current Comments... continued from page 15)

pain while also playing a role in addiction treatment. This does not require the pain-management practitioner to become an addiction specialist; however, pain practitioners should be involved in, rather than draw away from, addiction treatment for their patients with chronic pain who have need for such services. Important suggestions in the report include:

- It is very difficult to identify true addiction in patients with chronic pain.
- Patients taking opioids every day should be monitored for signs of drug abuse or addiction.
- If opioid-use problems arise, and are accurately assessed as such, substance-abuse treatment strategies should become an essential part of the pain treatment plan.
- Pain practitioners should attempt to stay involved, since there is a lack of special services for treating patients with both pain and addiction.
- Pain practitioners can support a patient's addiction recovery by encouraging attendance at 12-step programs, limiting the patient's access to opioid medicines, and monitoring the patient's mental health status.

Such participation by pain practitioners not only enhances therapy for chronic pain but provides them a unique opportunity to help stem the significant public health problem of opioid abuse and addiction. In this report, Compton outlines specific steps for any healthcare provider to follow.

Peggy Compton, RN, PhD, FAAN, is Associate Professor of Nursing at the University of California Los Angeles School of Nursing, Los Angeles, CA. She received her PhD in nursing science at New York University and completed postdoctoral training at the UCLA Drug Abuse Research Center. Dr. Compton serves as principal investigator for NIH-supported grants focusing on pain and opioid addiction from clinical perspectives and with a specific interest in how the presence of one affects the expression of the other.



For free access to **Should Opioid Abusers Be Discharged From Opioid-Analgesic Therapy?** see:  http://pain-topics.org/clinical_concepts/comments.php#Compton

Telltale Signs Identify Patients with Uncontrolled Pain – Guide Opioid Rx

Some believe that pain is a personal experience that cannot be accurately diagnosed. While healthcare providers ask patients to grade their pain on a 1-to-10 scale, this does little to help them separate genuine pain-relief-seeking patients from drug-seekers when prescribing potent opioid analgesics. Consequently, opioid analgesics are sometimes denied to patients in pain who would benefit from them.

In an evidence-based commentary article for *Pain Treatment Topics* – “Using Objective Signs of Severe Pain to Guide Opioid Prescribing” – Forest Tennant, MD, DrPH, outlines an objective approach for diagnosis that applies telltale physical signs of severe pain. “The fact is,” he says, “severe uncontrolled pain usually produces more objective physical evidence of its presence than does the average case of diabetes or heart disease.” Tennant has specialized in treating severe pain for more than 30 years and is the author of more than 200 scientific articles.

For one thing, he notes, severe pain – whether acute or chronic – causes stress on the whole body that can become life threatening. This can be easily measured by increased pulse rate, ele-



(Continued on page 17)

(Current Comments... continued from page 16)

vated blood pressure, and dilated pupil size. The patient may perspire heavily, and hands and/or feet can be cold to the touch.

Other signs are less obvious, but still observable. When severe pain has been present for a long time afflicted persons may avoid physical positions that worsen the pain. For example, they may always lean to one side or walk with a limp. Or, these individuals may try to limit physical sensations that cause pain, such as by always wearing loose-fitting clothing or not combing their hair. Some sufferers will attempt to distract their attention from the area that hurts to another area, even to the extent of cutting or burning themselves.

If they know what to look for, astute healthcare providers can, in many cases, use the diverse signs of pain to objectively determine if the pain is legitimate and is as severe as the patient claims. Once this is established, decisions about appropriate opioid prescribing and its proper dosing can be made. In his article, Tennant provides helpful tables that summarize key information for readers.

Forest Tennant, MD, DrPH attended the University of Kansas Medical School and served in the US Public Health Service. In 1975 he started the Veract Intractable Pain Clinic in West Covina, CA. Dr. Tennant has published more than 200 scientific articles and pioneered research on the complications and treatment of intractable pain. He is Editor in Chief Emeritus of the journal Practical Pain Management.



Recommended Objective Measures to Help Determine Uncontrolled Pain & Opioid Overmedication

UNCONTROLLED PAIN	GOOD PAIN CONTROL	EXCESS OPIOIDS
Pulse rate > 88 beats per minute	Pulse between 64 to 88 beats per minute	Pulse rate < 64 beats per minute
Blood pressure > 130/90 mm Hg	Blood pressure between 110/70 and 130/90 mm Hg	Blood pressure < 110/70 mm Hg
Pupil diameter > 5.0 mm	Pupil diameter between 3.0 and 5.0 mm	Pupil diameter < 3.0 mm
Cold hands or feet	Normal temperature	Very warm hands or feet

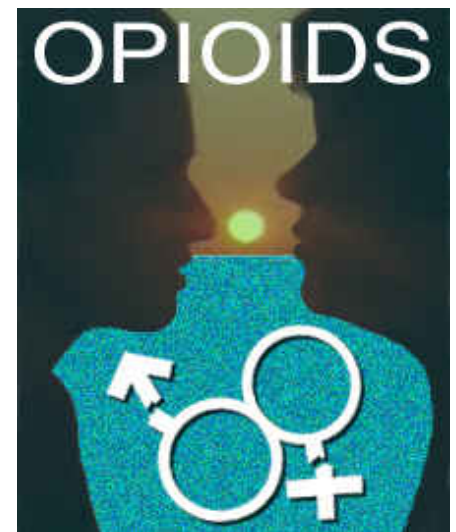
For free access to **Using Objective Signs of Severe Pain to Guide Opioid Prescribing** see: http://pain-topics.org/clinical_concepts/comments.php#Tennant2

Sexual Dysfunction – A Common Problem With Opioid Pain Relievers; Treatment Helps

Unfortunately, chronic pain can also cause sexual problems. Yet, many patients suffer in silence, healthcare providers rarely ask about patients' sexual concerns, and guidance literature on the subject is relatively scarce. Ironically, the long-acting opioid medications prescribed to relieve patients' pains often are the source of their sexual dysfunction.

In an evidence-based commentary article for *Pain Treatment Topics* – “Opioid-Induced Sexual Dysfunction: Causes, Diagnosis, & Treatment” – Stephen Colameco, MD, MEd, discusses the problem and how healthcare providers can help their patients.

Considerable evidence suggests that long-acting opioids used on a daily basis for more than a month can reduce hormonal function in both men and women. Besides



(Continued on page 18)

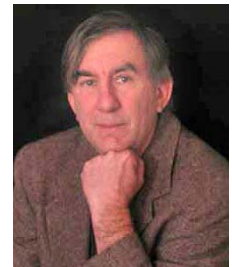
sexual dysfunction, symptoms can include weight gain, fatigue, depression, osteoporosis, and irregular menstrual cycles.

Causes and symptoms associated with hormonal deficiencies are summarized in the **Table**. These problems can be treated, if they are properly diagnosed, but different approaches are needed in males and females. Colameco provides a number of recommendations:

- Prior to the initiation of opioid therapy, prescribers should inform patients that hormonal disturbances are common with higher dose, long-term opioid treatment.
- After opioid treatment is started, patients should be routinely evaluated for signs and symptoms of hormone deficiency, including sexual dysfunction.
- When hormonal deficiency is suspected, appropriate laboratory testing should be ordered. There are no validated questionnaires for screening women for opioid-induced endocrine deficiencies, but structured interview instruments have been proposed to screen men for hypogonadism.
- An important treatment in men often is testosterone supplementation. Topical, buccal, or transdermal formulations are preferred over intramuscular injections. However, testosterone therapy must be used cautiously to avoid risks of prostatic hypertrophy or increased prostate cancer growth in afflicted patients.
- In women, testosterone treatment is controversial and supplementation with DHEA/DHEAS may be preferred due to its ability to raise hormone levels without significant side effects. Alternatively, rotation from one opioid medication to another may be effective.

In sum, opioid treatment is intended to reduce patients' pain, and to improve physical and social functioning. Opioid-induced hormonal deficiencies and associated sexual dysfunctions are common and often overlooked consequences of opioid therapy. If left untreated, they may negate the potential benefits of this analgesic. It is hoped that through a better understanding of these problems opioid therapy can be more effectively used in the treatment of chronic pain.

Opioid-Induced Deficiencies	
Hypogonadism Decreased GNRH Decreases LH Decreased Testosterone	Symptoms Anemia Decreased Libido Decreased Muscle Mass Depression Erectile Dysfunction
Adrenal Androgen Deficiency Decreased DHEA Decreased DHEAS Decreased androstenedione	Fatigue Hot Flashes Menstrual Irregularities Osteoporosis Sweating Weight Gain



Stephen Colameco, MD, MEd, is a graduate of Temple University School of Medicine and completed family medicine training at Hahnemann University School of Medicine. He has been practicing addiction medicine since 1982, and was among the first physicians in his locale to become certified as a Fellow in the American Society of Addiction Medicine (FASAM). He is a widely published author in the addiction treatment and pain management fields, and his book, "12 Steps for Those Afflicted with Chronic Pain" (2005), has benefitted many patients. In 2004 he left an academic teaching position to devote full time to his clinical practice – Addiction Pain Associates, Sewell, NJ – specializing in the treatment of patients with addiction, including those with chronic pain.

For free access to **Opioid-Induced Sexual Dysfunction: Causes, Diagnosis, & Treatment** see: http://pain-topics.org/clinical_concepts/comments.php#Colameco

PAIN TREATMENT TOPICS

202 Shermer Road
Glenview, IL 60025
<http://Pain-Topics.org>

Publisher/Editor-in-Chief:

Stewart B. Leavitt, MA, PhD

Research Editor:

Winnie Dawson, MA, RN, BSN

Medical Advisors/Reviewers:

Edward Hesterlee, PharmD, FACA

Associate Professor of Pharmacy Practice at the University of Arkansas Medical Sciences (UAMS) College of Pharmacy in Little Rock and a consultant to national pharmacy associations.

Seth I. Kaufman, MD

Pain management and palliative care practitioner at the West Clinic, and Baptist and Methodist Hospitals in the Memphis, Tennessee region.

Lee A. Kral, PharmD, BCPS

Faculty Member, Center for Pain Medicine and Regional Anesthesia at The University of Iowa Hospitals and Clinics in Iowa City, Iowa.

James D. Toombs, MD

Staff Physician in the Division of Primary Care/ Pain Medicine at the Harry S. Truman Memorial Veterans' Hospital in Columbia, Missouri.

This edition was supported by an unrestricted educational grant from COVIDIEN/Mallinckrodt, St. Louis, MO, USA.

© Copyright 2008, *Pain Treatment Topics*, all rights reserved.

Brand names of products mentioned in this *e-Briefing* are registered trademarks of their respective manufacturers.

DISCLAIMER: Pain Treatment Topics and its associates – advisors, sponsors, or affiliates – do not endorse any medications, products, services, or treatments described, mentioned, or discussed in this *e-Briefing*. Nor are any representations made concerning efficacy, appropriateness, or suitability of any such medications, products, services, or treatments. In view of the possibility of human error or advances in medical knowledge, Pain Treatment Topics and its associates do not warrant the information contained in this document is in every respect accurate or complete, and they are not liable for any errors or omissions or for results obtained from the use of this information.

To comment on this publication
e-mail to: Info@Pain-Topics.org

Release Date: December 2008

Recent Changes at Pain-Topics.org



Dual Certifications Received

Within 2 months of starting operation on January 1, 2006, Pain-Topics.org was certified by the Health On the Net (HON) Foundation and has been continuously inspected and recertified each year since then. This nonprofit organization, based in Geneva Switzerland and sponsored by government authorities, seeks to guide the growing community of healthcare providers and consumers on the World Wide Web to sound, reliable medical information and education. Qualifying medical and health websites must rigidly comply with extensive requirements of the HON Code of Conduct to be awarded HONCode certification.

In summer 2008, Pain-Topics.org qualified for Web Médica Acreditada (WMA) certification. Sponsored internationally by the Medical Association of Barcelona (COMB), and cosponsored by the European Union under the Directorate General for Health, WMA certification is awarded to medical websites meeting the highest-quality standards for the communication of education and information to the general public, patients, and healthcare professionals. Traditionally, this certification has applied to websites serving Spanish-speaking countries and Pain-Topics.org was one of the first in the United States to be certified, partly in recognition that we have a significant number of visitors from Spain, Latin America, and South America.

Awards Recognize Contributions to Healthcare Field

In addition to the prior "Hope Award" and "Gold Web Award" received by Pain-Topics.org more than a year ago, two recent awards specifically recognize our contributions to the healthcare field.

We received a Merit award in 2008 from the "World Wide Web Health Awards" program. This competition is organized by the Health Information Resource Center, a national clearinghouse for health-related programs and resources. The award recognizes the best web-based health-related educational content for consumers and healthcare professionals.

Also in 2008, Pain-Topics.org received "WebAwards" in 2 categories: *Medical Standard of Excellence* and *Health Care Standard of Excellence*. This award program, sponsored annually for the past 12 years by the Web Marketing Association, recognizes organizations and people responsible for developing some of the most effective websites on the Internet. Entries are judged on design, innovation, content, interactivity, technology, copy writing, and ease of use by the intended audience.

