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On Psychiatric Treatment

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Using Psychiatric Meds for Pain

Where does it hurt?

These are the "four little words" that Eli Lilly (in ubiquitous ads) is encouraging us to ask our depressed patients. The idea, evidently, is that if we psychiatrists get into the habit of evaluating somatic pain symptoms, we will discover them in many of our patients, and we will adjust our treatment plans accordingly. Lilly, of course, is hoping that our plan will include a prescription for duloxetine, but any drug company would be foolish not to jump on such a bandwagon: there are a lot of people out there who hurt.

The proper use of antidepressants (ADs) for pain in psychiatric patients is both complex and controversial, and Dr. Scott Fishman weighs in with his own views in this month's interview. In this article, we'll cover some of the relevant research and end with some common sense recommendations. We'll also touch, somewhat lightly, on the use of anticonvulsants for pain, focusing on those meds psychiatrists are most likely to use.

To begin with, how good is the evidence that ADs work for "straight" pain-

Continued on Page 2

IN THIS ISSUE:

Focus of the Month:
Chronic Pain and Psychiatry

Pain Treatment Update: The Opiates and NSAIDs

Here's a fairly typical scenario: An elderly woman comes to you as a referral from her PCP for the treatment of depression and anxiety. She hands you a well-worn 3-by-5 card with her meds listed in shaky handwriting. The list is long, and pain meds make up a good portion: "Vioxx, 12.5 mg QD; baby aspirin 81 mg QD; Prilosec, 20 mg QD; Percocet, 1-2 twice a day; Imitrex, 1 pill a day as needed for migraines."

This purpose of this article is not to teach you how to prescribe conventional pain medications (most psychiatrists are happy to leave that job to PCPs), but rather, to help you decipher and understand what your patient is taking, and why.

How Pain Works

Nociceptors are neurons found throughout the body that are activated by tissue damage. When tissue damage occurs, a now-famous enzyme called **cyclooxygenase-2** (Cox-2) converts arachidonic acid to **prostaglandins**, which, in turn, do the dirty work of telling the nerve endings that it's time to start hurting. Right on cue, an inrush of calcium occurs, leading to the sodium influx and progressive depolarization that axons are so famous for. This signal gallops to the back of the spinal cord (the dorsal horns), where the neurotransmitter **Substance P** takes the baton and facilitates neurotransmission right to the very center of things, the **thalamus**, which is in charge of receiving pain signals and deciding what to do with them. Luckily, our brains do not accept pain passively. From both the **frontal cortex** and the **hypothalamus**, signals cause the release of several pain-busting chemicals, including the endogenous opiates **beta-endorphin and enkephalin**, which do battle with Substance P in the dorsal horn. Of course, exogenously administered opiates can do us this same favor. Of even more relevance to psychiatrists is the fact that

Continued on Page 6

Learning objectives for this issue: 1. Recall the neurobiology of pain. 2. Describe the evidence for and against the use of psychiatric medications for pain syndromes. 3. Cite the most effective treatments for fibromyalgia.

This CME activity is intended for psychiatrists, psychiatric nurses, and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

Using Psychiatric Meds for Pain

Continued from Page 1

that is, pain in the absence of depression? Well, the evidence is surprisingly strong. Hundreds of studies have been published, along with several meta-analyses. Fishbain, for example, did a meta-analysis of 93 placebo-controlled trials of various ADs for various pain syndromes. **A majority of studies found tricyclics more effective than placebo** for headache, fibromyalgia, chronic low back pain, arthritis pain, and miscellaneous acute pain syndromes. **SSRIs largely flunked in this analysis**, however (*Ann Med* 2000; 32:305-316).

Other reviews have also concluded that SSRIs are only marginally effective pain meds, but what about SNRIs, such as Effexor (venlafaxine) and the soon-to-be-released Cymbalta (duloxetine)? **Of these two, Effexor is the only one with published efficacy data for pain without depression**; it was shown to be as effective as imipramine for painful polyneuropathy (*Neurology* 2003; 60:1284-1289), and showed promise in uncontrolled trials for migraine and tension headaches (*Headache* 2000; 40:572-80), and for fibromyalgia (*Ann Pharmacother* 2003; 37:1561-5).

When it comes to comorbid depression and pain, however, Cymbalta has plenty of controlled data to recommend it (see *TCR* Jan 2004 for a review). As mentioned in that review, the methodology used in the Cymbalta studies included an outcome measure--the Visual Analog Scale for pain (VAS)--that has rarely been used in trials of other ADs. Thus, whether Cymbalta is actually more effective for "achy depression" than other ADs is still an open question.

Indeed, Effexor has recently entered the VAS fray with an uncontrolled study in which patients with depression and chronic pain showed improvement in both Ham D and VAS scores over the course of a year (*Am J Ther* 2003; 10:318-23). And we would guess that most *TCR* readers would have little trouble recalling depressed, somatizing patients in their practices in whom standard SSRIs have apparently quelled both physical and emotional anguish.

What about the anticonvulsants for psychiatric patients in pain? Of course, the only approved psychiatric indication for anticonvulsants is the treatment of bipolar disorder, an approval shared by Depakote (valproic acid) and Lamictal (lamotrigine). In addition, Tegretol (carbamazepine) is widely considered effective for bipolar disorder. All three of these medications are decent analgesics, and are approved for some painful conditions.

Depakote ER is FDA-approved for migraine prophylaxis, and is started at 500 mg QD for the first week, then increased to 1000 mg QD. As you can see, these doses are somewhat lower than what we are accustomed to prescribing for our bipolar patients. It's irksome and odd that Depakote ER is approved for migraine but not bipolar disorder, whereas standard Depakote is approved for bipolar but not migraine, but experienced clinicians won't let these relics of corporate marketing strategies get in the way of good patient care.

Tegretol is approved for one pain condition (trigeminal neuralgia), and considered effective for most types of neuropathic pain. **Lamictal** is not quite as well studied as Tegretol, but is also considered effective for neuropathic pain (*Drugs* 2000; 60:1029-52). Of these two, most psychiatrists would prefer to prescribe Lamictal, given the lack of drug interactions or need for blood monitoring. True, it may rarely cause Stevens-Johnson syndrome, but so can Tegretol (see *TCR* 1:9).

One of the most effective anticonvulsants for pain is **Neurontin** (gabapentin), which unfortunately is almost useless psychiatrically other than as a very expensive hypnotic (see *TCR* 1:3 for a review of these studies). But if you feel moved to treat your patients's neuropathic pain, Neurontin is a good bet because it's so safe and widely effective (*Clin Ther* 2003; 25:81-104). Just be forewarned that it has to be dosed fairly high for analgesic efficacy, in the range of 1800-3600 mg QD.

Of course, the list of novel anticonvulsants hardly ends here. The newer darlings, all of which have been used in psychiatry, are Topamax (topiramate), Trileptal (oxcarbazepine), Gabitril (tiagabine), Zonegram (zonisamide), Keppra (levetiracetam), and the soon-to-be-approved pregabilin. See *TCR* 1:9 for coverage of Topamax and Trileptal, and stay tuned--we'll get to all of them eventually! ❖

TCR VERDICT:

Pain: There's plenty we can do with the meds we know.

Anecdotes from the Field: When Meds Do Harm

Manuel Pacheco, M.D. is Chief Resident of Psychiatry at Boston Medical Center and offers this anecdote as a cautionary tale to those eager to heap medications on patients with comorbid pain and psychiatric issues.

Dr. Pacheco has disclosed that he has no significant relationships with or financial interests in any commercial companies pertaining to this educational activity.

"A clinician who was leaving the area referred a 53-year old Latina female to me who was on 12 different psychiatric medications. She had PTSD, borderline personality disorder, migraine headaches, and diabetic neuropathy. Her meds included Paxil, Effexor, Trazodone, Ambien, two different tricyclics, Klonopin, and Neurontin as prescribed by her neurologist. Despite all these meds (or perhaps because of them!), she was doing poorly, with depression, anxiety, and cognitive fogginess. I began gradually weaning her off some of her meds. Eventually, I got her down to Paxil 40 mg QD, amitriptyline 50 mg QHS, and Klonopin 0.5 BID--and she continued the Neurontin from her neurologist. She improved vastly, with less depression, less pain, and improved memory."

Fibromyalgia: What Should We Make Of It?

When a patient tells you that she has fibromyalgia, what should you, a psychiatrist, do? Should the diagnosis alter your treatment in any way?

While fibromyalgia (FM) has the reputation of being a vague entity, in fact the diagnosis is remarkably precise, according to criteria devised by the American College of Rheumatologists in 1990. The "ACR Criteria" require two things: 1. The presence of widespread pain that persists for at least 3 months (to qualify for the term "widespread," the pain must be present above and below the waist and on both the sides of the body); 2. The identification of at least 11 from a list of 18 possible tender points. Now these are the kind of criteria that DSM-IV-trained psychiatrists can understand!

However, things are not as clear as you might think. For disease criteria to be meaningful, they should be constructed in relationship to a gold standard, or reference standard. But there is no objective test to diagnose FM, and the reference standard used by the ACR was simply a group of 293 patients who had been given the label "fibromyalgia" by rheumatologists based on their "usual method of diagnosis." If you think academic psychiatrists squabble, check out the fibromyalgia wars in rheumatology journals. Recently, one of the main architects of the ACR criteria advocated abandoning the notion of "tender points" altogether because of concerns that they are unreliable (*J Rheum* 2003; 30:1671-1672).

Nonetheless, you will continue to see FM patients in your practice, and you should know what you can do to make their lives better. The disorder affects 2% of adults, strikes females much more often than males, and the risk is highest in the 55-79 year age group. As psychiatrists, we have plenty of work to do, because more than two thirds of FM patients have a current or past mood disorder. Comorbid anxiety disorders are nearly as common (*Psychosomatics* 1999; 40:57-63).

Given these figures, it is not surprising that the treatments shown most effective for this chronic pain condition are treatments often delivered by psychiatrists and psychologists: antidepressants (ADs), cognitive behavior therapy, and the prescription of an exercise program.

The most well-studied antidepressants are, you guessed it, tricyclics, which do tend to diminish pain symptoms and improve sleep (see *Ann Behav Med* 1999; 21:180-191, for a thorough review). Amitriptyline is the tricyclic with the most data: start at 25 mg to 50 mg QHS, but try to inch up on the dose if there are clear depressive symptoms. One study tried the combination of Prozac and amitriptyline and achieved unusually good results.

While ADs help with pain and insomnia in FM, only physical exercise has consistently been shown to help all aspects of day-to-day functioning (*Cochrane Database Syst Rev* 2002; 3:CD003786). Patients who can comply with aerobic exercise at least twice a week, for at least 6 weeks in a row, report improved well-being and less tender point pain.

Finally, cognitive behavior therapy helps FM patients. A typical regimen used in studies is a weekly 2 hour session focusing on coping with chronic pain, increasing self efficacy, and combating the tendency to catastrophize each pain event (*Arthritis Care and Research* 2004; 51: 184-192). It works well in diminishing pain, but the effects tend to wear off after a year.

Patients might ask you about recent studies reporting neuroimaging findings in FM. Here's the scoop. Functional MRI studies have shown that certain brain regions show greater activity in response to pain in FM patients than in control subjects (*Arthritis & Rheumatism* 2002; 46:1333-1343, *J Rhematol* 2004; 31:364-378). These are interpreted as evidence that FM is a biological disease caused by "cortical or subcortical augmentation of pain processing." However, a more recent study throws doubt on this conclusion. In this study, researchers found that the degree of brain activity in response to pain was proportional to the degree that FM patients cognitively "catastrophized" their pain (*Brain* 2004; 127:835-843). This is consistent with the data on the efficacy of cognitive behavior therapy in FM, and once again makes FM seem closer to a psychiatric than a rheumatologic disorder.

But no matter how FM is sliced and diced diagnostically, the pain and suffering are real, and psychiatrists can do plenty to help. ❖

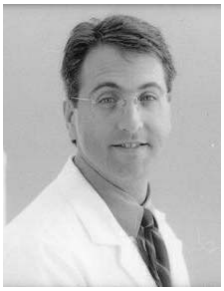
TCR VERDICT: *Fibromyalgia: Real enough to hurt.*

Q&A With the Expert

This Month's Expert:

Scott M. Fishman, M.D., M.Sc.
On Psychiatric Approaches to Pain

Professor, Department of Anesthesiology and Pain Medicine
Chief, Division of Pain Medicine
University of California, Davis



Financial Disclosure: Dr. Fishman has disclosed that he has received research grants from, is a consultant to, and is a member of the speakers bureaus of the following companies: Janssen, Elan, Endo, Merck, Pfizer, and Purdue.

TCR: Dr. Fishman, you are boarded in both internal medicine and psychiatry, and have gone on to specialize in pain medicine. Can you outline your basic approach to pain symptoms in a psychiatric patient?

Dr. Fishman: Sure. The problem that physicians of all disciplines have is that when you see patients with chronic pain who have comorbid affective disorders, it is very easy to assume that the affective disorder is causing the pain and that the patient doesn't "really" have physical pain, or on the other hand to assume that the depression is secondary and ignore it, but the fact is that the two drive each other. Treating both the depression and the pain is critically important to patients's affective well being and also their pain state. The interesting part for those of us who specialize in pain management is that we often see doctors who try to treat both the pain and depression with one drug with the idea that antidepressants can be analgesics. It is often a mistake because not all antidepressants are independently analgesic.

TCR: Are some antidepressants more analgesic than others? There certainly has been a lot of publicity about duloxetine lately, for example, touting its analgesic efficacy.

Dr. Fishman: There's a great quote about drugs never being as efficacious after release as they were pre-release. The jury is out on duloxetine but the data is very strong and the hype is even stronger--we've seen this kind of thing before. The bottom line is that the antidepressants that have been shown to be independently analgesic are probably effective not because of their dual reuptake properties, but because they are local anesthetics. This is primarily true of the tricyclics which are well known to be sodium channel blockers. This sodium channel blockade is what causes the local anesthetic effect and also why these drugs, unlike other classes of antidepressants, affect the ECG intervals and why overdose requires ICU level cardiac monitoring.

> **"The bottom line is that the antidepressants that have been shown to be independently analgesic are probably effective not because of their dual reuptake properties, but because they are local anesthetics."**
>
> **—Scott Fishman, M.D.**

TCR: So the analgesic effect of tricyclics is due mainly to their local anesthetic effect.

Dr. Fishman: Right. To date, there are no antidepressants that are not also sodium channel blockers that have shown independent analgesia in well-controlled studies.

TCR: What about Effexor (venlafaxine) and the SSRIs? Occasionally you run across an article showing some analgesic effect with these.

Dr. Fishman: Yes, there are many small studies that suggest analgesia with SSRIs or Effexor; however, any lessening of depression in a patient with pain will be analgesic since depression magnifies pain. But in general, the studies that have carefully excluded patients with depression have not shown independent analgesic efficacy in neuropathic pain for non-tricyclic antidepressants. The interesting thing about Effexor is that it has properties that are different from any other antidepressant in that it may have direct opioid effects. There have been a couple of very small studies in normal volunteers that have shown that venlafaxine has raised the pain threshold; whether that is clinically meaningful or not, we don't know.

TCR: What about the SSRIs and SNRIs for comorbid pain and depression?

Dr. Fishman: Depression is such a magnifier of somatic sensations that treating the depression may be just as analgesic as treating the pain with a direct analgesic. So that secondary effect shouldn't be unappreciated. The point is that if you give an SSRI to someone who is not depressed, you are probably not going to see a lot of analgesia.

TCR: But if you have somebody who has depression and is also complaining of headaches, shoulder pain, back pain, etc., chances are that if you adequately treat the depression with an SSRI, some of those pains will go away as well.

Dr. Fishman: Correct. That's why you want to use a good antidepressant to treat the depression maximally, and then you

Continued on Page 5

Q & A With the Expert

Continued from Page 4

can use a separate agent for independent pain relief. Whether you use a tricyclic for this has more to do with safety, tolerability and ease of use of the drug rather than its efficacy since all analgesics for neuropathic pain appear to be equally effective.

TCR: We see a lot of primary care doctors and psychiatrists using very low doses of Elavil - 10-25 mg QHS -- sometimes as an adjunct to an SSRI for pain relief. Is that reasonable?

Dr. Fishman: It is reasonable to add a tricyclic, but the myth about the tricyclics and pain is that they work in low doses, and that has been shown to be wrong. They may give you some efficacy at low dose, but they maximize their effect over dose increases. I recommend pushing the dose up to the point of tolerability of side effects. However, side effects with tricyclics are common and not only limit how much we can give, but have relegated tricyclics below other choices for neuropathic pain such as some of the newer (safer) anticonvulsants.

TCR: Another medication, Neurontin, is a medication that psychiatrists are comfortable prescribing for a variety of off-label psychiatric uses, and it is effective for pain.

Dr. Fishman: Yes, and I think the choice to use Neurontin is notable not because it is better than any of the other neuropathic analgesics or anticonvulsants, but because it is the safest. It has no P450 hepatic metabolism and it is not protein-bound, so the risk of drug-drug interactions is nil. But it is not the easiest to dose and it is often less tolerable than generally assumed.

TCR: Is it effective for pain?

Dr. Fishman: Yes, but like antidepressants, the response is idiosyncratic. Incidentally, the "son" of Neurontin--Pregabilin-will be approved soon.

TCR: For what indications?

Dr. Fishman: For post-herpetic neuralgia, fibromyalgia, and probably generalized anxiety. It will be similar to if not stronger than Neurontin, but will be approved for BID dosing instead of the QID dosing of Neurontin.

TCR: What about opioid analgesics? Patients on opioids tend to get stigmatized as being "addicted" and there is confusion in the medical community about whether the patient is really "an addict" or is using the medication appropriately. Any ideas about how to help sort that out in a given patient?

Dr. Fishman: The definition of "drug addiction" is the compulsive use of a drug that causes dysfunction, and the continued use of the drug despite that dysfunction. And the definition of "pain relief" is an improvement in functioning due to analgesic treatment. Pain is essentially an alarm that gets your attention and, with enough pain, makes it impossible to do anything beyond attending to the pain. If you have been in pain day in and day out, you lose function in your life. When you treat the pain, their functioning improves. And that is the complete opposite of what we see with addiction. If a patient is taking an opioid and has improved function, you really can't make the argument that he or she is addicted unless there is increased dysfunction elsewhere in their life. There may be physical dependence or tolerance, but these are pharmacological properties of the drugs, and must not be confused with addiction.

TCR: How do you recommend we evaluate patients on chronic opioids?

Dr. Fishman: It requires that you look at functional outcomes. When I put someone on a chronic opioid, the question I ask them is, what are you going to do with this medication that you can't do now? And then we target those things. And if they can't come up with things that are meaningful, then I say, well I have good news for you, you don't really need this medicine. Basically, if you are successfully treating pain, people's lives should get better and there should be objective evidence of that and that objective evidence is diametrically the opposite of the evidence you would get with addiction.

TCR: And so as psychiatrists, when we are not directly treating the pain, but we are treating an emotional problem, we can basically go ahead and treat these patients as we would any other patients and assume that they are going to respond in the same ways.

Dr. Fishman: Yes, I would agree to that and I would add that the psychiatrist can play a critical role in looking at functional outcomes. Because if I am prescribing an opioid and think that the patient is functioning better, and you as the psychiatrist see functional or psychological decline, I need to know that. It doesn't necessarily mean the patient is addicted, but it means that treatment is not going in the right direction.

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Pain Treatment Update: The Opiates and NSAIDs

Continued from Page 1

both **norepinephrine** and **serotonin** are released from the brain and descend the spinal cord in order to dampen the pain response. This may explain the analgesic effects of tricyclics and dual reuptake antidepressants (although this is controversial--see this month's Q & A for a dissenting view).

NSAIDS (Nonsteroidal Anti-inflammatories)

So named because they decrease inflammation without being in the prednisone family, NSAIDs include an ever-expanding list of moderately effective pain meds. They are divided into two categories: **conventional NSAIDs** and **Cox-2 inhibitors,** or **"coxibs."**

Conventional NSAIDs work by inhibiting both isoforms of the Cox enzyme--Cox-1 and Cox-2. Disabling Cox-2 is a good thing, since it reduces pain-producing prostaglandin (PG) levels, but inhibiting Cox-1 is bad, because this slows the production of the good type of PG that protects the stomach lining. This leads to the GI distress that NSAIDs are famous for. Conventional NSAIDs include **aspirin**, **ibuprofen** (available as a generic as well as marketed as Motrin, Advil, and other brands), and a slew of me-too NSAIDs that are listed here mainly to help you recognize what type of medications many of your patients are taking: **naproxen** (available in generic form, as well as Anaprox, Naprosyn, Aleve, and other brands), **Indocin** (indomethacin), **Voltaren** (diclofenac), **Clinoril** (sulindac), **Lodine XL** (etodolac), and **Relafen** (namubetone).

The Cox-2 inhibitors first became available in 1998 and were quickly adopted because, by not inhibiting Cox-1, they don't produce the GI side effects of the NSAIDs. Cox-2 inhibitors include **Celebrex** (celecoxib), **Vioxx** (rofecoxib), and **Bextra** (valdecoxib). All three are approved for osteoarthritis, rheumatoid arthritis, and pain of menstrual cramps. In the battle for market share, Celebrex recently got a boost from a new study showing that patients on Vioxx have a higher risk of congestive heart failure than patients on Celebrex (*Lancet* 2004; 363:1751-56). On the other hand, Bextra, the newest entry in the Cox-2 field, is on the outs because it has caused several cases of Stevens-Johnson Syndrome since its approval.

You'll notice that many of your patients who are on conventional NSAIDs are also on one of the **proton pump inhibitors**, such as Prilosec (omeprazole), Prevacid (lansoprazole), or Nexium (esomeprazole)--because guidelines recommend adding a PPI to such agents for patients at risk for ulcers. By contrast, Cox-2 inhibitors probably don't increase the rate of ulcers at all.

Opiates

Opiates work primarily at the level of the dorsal horn of the spinal cord, by binding to opiate receptors and inhibiting the effects of Substance P. In a much earlier era, opiates were one of the major tools of psychiatry for dealing with agitation and depression, and still might be if they weren't so addictive. These days, few psychiatrists prescribe opiates, but given the array of formulations your patients are on, the following may be helpful.

It all begins with the **opium poppy**, from which the main alkaloid, **morphine**, was isolated in 1806. **Heroin** was synthetically derived from morphine in 1874; it is four times more potent than straight morphine. **Methadone** is a synthetic morphine with a similar potency to heroin, but can be taken orally and has a longer half-life than heroin.

In an outpatient practice, you won't see too many patients on morphine, because the oral versions, **MS Contin** (morphine sulfate) and **Dilaudid** (hydromorphone), have poor and unpredictable oral absorption. You'll also rarely see patients on **Demerol** (meperidine); it is usually used by injection only for acute pain because it can cause death when combined with MAOIs.

You will see plenty of **oxycodone**, a synthetic opiate that is the active ingredient in **Percocet** (oxycodone plus acetaminophen) and **Percodan** (oxy plus aspirin). More recently, oxycodone has gotten packaged as a long-acting version called **OxyContin**, dosable twice a day and often diverted onto our city streets where it is known as "poor man's heroin." **Hydrocodone** (not to be confused with hydromorphone above) is usually packaged with acetaminophen to produce **Vicodin**; this has roughly the same potency as Percocet. **Codeine** (generic) is a weaker synthetic opioid, also usually combined with acetaminophen in **Tylenol #4** (codeine, 60 mg and acetaminophen, 325 mg). **Ultram** (tramadol) is a narcotic that for a while was thought to be less addictive than other opiates, but this was largely wishful thinking. It both binds opiate receptors and mildly inhibits serotonin and NE reuptake, this last mechanism leading to concerns that it could cause serotonin syndrome if combined with SSRIs. It's dosed at 25-50 mg QID. A new formulation combined with acetaminophen is known as **Ultracet**.❖

TCR VERDICT: *Cox-2s are hot; OxyContin, maybe too hot*

Tales from the History of Psychiatry: Heroin for All

Although heroin-then known as diacetylmorphine-was first derived from morphine in England in 1874, it was the Bayer company in Germany that saw its commercial value as a cough remedy and pain reliever. Employees who were asked to test it said it made them feel "heroisch" (heroic)-hence the brand name Heroin. Bayer began marketing the drug in 1898, advertising it widely and distributing free samples to physicians. Sales were initially brisk, but slowed as evidence of tolerance and addiction accumulated. Bayer stopped making the drug in 1913, but by then it had established a new blockbuster analgesic that it had given the brand name of Aspirin. Perhaps not surprisingly, this chapter of Bayer's history is absent from the corporate story that appears on its website.

Source: http://opioids.com/heroin/heroinhistory.html

CME Post-Test

To earn CME credit, you must read the article(s) and complete the quiz below, answering at least four of the questions correctly. Mail a photocopy or fax the completed page to Wolters Kluwer Health, Office of Continuing Education, 530 Walnut Street, 8th Floor East, Philadelphia, PA 19106; fax: (215) 521-8637. Only the first entry will be considered for credit and must be received by WKH by June 30, 2005. Acknowledgment will be sent to you within 6 to 8 weeks of participation.

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Please identify your answer by placing a check or "X" mark in the box accompanying the appropriate letter.

1. An accurate characterization of tricyclics is:
- [ ] a. They are probably no more effective than SSRIs for neuropathic pain.
- [ ] b. They have been impressive analgesics in case reports, but not in controlled trials.
- [ ] c. If they are analgesic, it is only through their antidepressant effect.
- [ ] d. They are considered effective analgesics for a variety of pain syndromes.

2. Depakote is best thought of as:
- [ ] a. An effective mood stabilizer that also helps to prevent migraine headaches.
- [ ] b. A good medication for post-herpetic neuralgia.
- [ ] c. An analgesic with the same potency as OxyContin but with no addictive potential.
- [ ] d. One of the better choices for comorbid depression and pain.

3. Conventional NSAIDs inhibit both Cox-1 and Cox-2.
- [ ] a. True [ ] b. False

4. Effective treatments for fibromyalgia include:
- [ ] a. Cymbalta, Effexor, and pregabilin.
- [ ] b. Exercise, cognitive behavior therapy, and tricyclics.
- [ ] c. Oxycontin because of its BID dosing.
- [ ] d. Ultram in combination with SSRIs.

5. According to Dr. Fishman, dual reuptake inhibition is the crucial analgesic mechanism of tricyclic antidepressants:
- [ ] a. True [ ] b. False

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This Month's Focus:
Chronic Pain and Psychiatry

Next Month in *The Carlat Report*: All about obsessive-compulsive disorder (OCD), including meds for tough cases and a review of CBT techniques.