



SPS NEWS

The Official Publication of The Southern Pain Society

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The Science of Epidemiology Illuminates the Pain Problem

Ike Eriator, MD, MPH

Pain is a leading public health problem and a significant source of personal and family suffering across different cultures and geographical boundaries (Gureje et al., 1998). Assisted suicide, substance abuse, narcotic regulation, alternative therapies, disability and compensation issues are all strongly related to pain and pain relief. The largest numbers of people turning to complementary and alternative medicine today are patients with pain (Astin, 1998). Improved pain management has been listed as one of the top 20 chronic medical problems that the US government and private healthcare organizations should focus on in order to have the broadest impact on patients, families and communities (Adams and Corrigan, 2003).

The National Institute of Health estimates that there are 49 million people with chronic pain in the United States. 32 million routinely take analgesics, and 14 million are limited in their routine activities due to pain. Americans spend about \$100 billion annually on pain care. 13% of employees take time off work due to pain, resulting in a loss of 4 billion workdays annually and a \$61 billion loss in productivity (Montrey, 2000, Stewart et al., 2003). Chronic pain is related to poor state of health (Mantyselka et al., 2003). It also results in increased use of health care services in direct relationship to the level of pain related disability (Blyth et al., 2004). Considering the effects of pain on society, community, family and individuals, the World Health Organization in 1997 made the "alleviation of pain, the reduction of suffering, and the provision of palliative care for those who cannot be cured" its sixth global priority (Montrey, 1999). The United States Congress has mandated the ten year period January 1, 2001 to December 31, 2010 as the decade of "Pain Control and Research", making pain management second only to the brain as a medical area to be so recognized.

Epidemiology studies the distribution, determinants and natural history of diseases in the population. Put another way, it is the study of the patterns of health or disease and the factors that influence these patterns. Epidemiology documents the extent of a problem, and it is therefore very useful in planning of health services and prevention of diseases. Understanding the pattern, for instance of pain, in populations can provide clues about etiologic and influencing factors as well as treatment outcomes. When we apply population-based information to decision-making about individual patients, we are doing clinical epidemiology. Epidemiology is the bedrock underlying evidence based practice.

Epidemiology has its own terms, and understanding these terms and how they are used can be very helpful in interpreting results and conclusions of published studies. Examples of terms commonly used include risk, incidence rate and prevalence rate. Risk refers to the likelihood or probability that persons who do not have a specific condition (but have particular attributes that predispose them to the condition) will develop the condition. Incidence rate refers to the rate of onset of the condition over a defined period of time (usually one year). The numerator for incidence rate is the number of *new cases* appearing over the defined time period, while the denominator is the number of people at risk of developing the condition. The Prevalence rate of a condition is more important for health care planning, and refers to the proportion of persons with the condition at a particular time. The numerator for prevalence rate is the number of persons with the condition, while the denominator is the total population at risk of having the condition. The prevalence rate of a painful condition depends on the rate of onset of the condition, for instance back pain, and how long it lasts after the onset.

Several studies to determine the prevalence of pain have been carried out in the general population (Crook et al., 1984, Sternbach, 1986; Von Korff et al., 1988; Brattberg et al., 1989; Anderson et al., 1993; EPIC/MRA, 1997; Gureje et al., 1998; Bassols et al., 1999). A nationwide telephone survey involving 1, 254 participants representing a cross section of the adult population of the continental United States showed that most respondents experienced 3 or 4 different kinds of pain, though the commonest sites were headaches, backache and muscle pain (Sternbach, 1986). Joint pains and backaches

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Mission Statement

The Southern Pain Society is a regional section of the American Pain Society and endorses and supports the mission and goals of the American Pain Society. The Southern Pain Society's missions are to serve people with pain by advancing research and treatment and to increase the knowledge and skill of the regional professional community.

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Editor's Desk

Kenneth L. Kirsh, PhD

I would like to take this opportunity to say hello and introduce myself to the community of the Southern Pain Society. I am taking over the SPS News editorial position from Jonathan Cole, Ph.D., and hope that I can make a contribution worthy of his previous efforts. Like Jonathan, I am trained as a clinical psychologist and have a strong interest in pain management (obviously!) as well as its interface with the full spectrum of aberrant behaviors, including addiction.

Born and raised in Ohio, I completed my training in Indianapolis and eventually moved down to Lexington, Kentucky, where I currently reside and practice. Thus, while not born and raised in the southern states, I am slowly working my way south. I hope to meet as many of you as possible over the next months and years and want to invite one and all to contact me with questions, concerns, and ideas that you feel might help to make the SPS News a better part of your experience in the Southern Pain Society. I can be reached most easily through my e-mail: klkirsh@email.uky.edu

With the introductions out of the way, I would like to point you towards some of the features in this edition. In addition to the traditional president's message, we have a new book chapter feature, and wonderful pieces on epidemiology in pain, pulsed RF treatments, and a couple of pieces on duloxetine. I hope you will find them enlightening and useful in your practices.

As we look to exciting developments and new discoveries for pain management, we also have to look at the state of our profession and the headline-worthy attention we have been receiving for quite some time. Most recently, I am disturbed by the disappearance of the Pain Management FAQ from the DEA website and the recent conviction and potential life-in-prison sentence of Dr. William Hurwitz, a northern Virginia pain expert. I can elaborate on the details in a later column, but suffice it to say that it is being touted as a landmark case with potentially damaging effects on physicians who practice pain management. Indeed, experts such as Russell Portenoy at Beth Israel Medical Center, are worried. Dr. Portenoy (a friend and frequent co-author) stated "such an extreme sentence sends the message to the medical community that the government will continue to go after doctors."

So, what do we do? I call to you not to give up hope, but to continue your good work and to keep up the fight. While none of us is truly protected these days, I wanted to highlight a few things that we need to keep in mind:

The healthcare provider who does pain management needs to first recognize that the problem of prescription drug misuse is not simply media hype nor is it confined to remote areas like eastern Kentucky (Hays et al, 2003).

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President's Column

It is my pleasure to serve as President to the present and future membership of The Southern Pain Society, whose mission is to:

- serve people with pain by advancing research and treatment
- increase the knowledge and skill of the regional professional community



The current erosion of healthcare reimbursements to providers, in an effort to control healthcare expenditures, have greatly diminished our profit margins, forcing us to work harder and more efficiently in order to meet our financial obligations to our practices and employees. Therefore we must ask the questions:

- Why join or participate in yet another medical association, and pay yet another membership fee?
- What am I getting for my investment of time and money in the Southern Pain Society?

Without a doubt, the greatest value of participating in the Southern Pain Society resides in the beneficial effects of belonging to an organization that is responsive to the regional and local needs of the providers of pain treatment services. The local chapters of the Southern Pain Society can assist their multidisciplinary membership in dealing with the issues in our states that influence our practices. Although there are several organizations that service narrow segments of the pain treatment market, such as interventional pain specialists, or headache specialists, there are few regional organizations that address the multidisciplinary needs and education of pain treatment specialists.

The Southern Pain Society has traditionally contained some of the most dynamic thought leaders in the nation; and this fact is evidenced by the composition of our present Board of Directors. Not only is the Board multidisciplinary by design; but it is also composed of thought leaders within each of the represented specialties. As spokesperson for the board of directors, I can state that there are few problems within the field of pain medicine that we cannot effectively address. Your SPS board members have extensive networking connections within the pain medicine field, and can provide guidance and direction to the needs and concerns of our members in a fashion that few national organizations can match.

The annual meetings of the Southern Pain Society continue to be an excellent value with excellent presenters and reasonable fees. Our next meeting in Lexington, Kentucky promises to be a superb educational experience with nationally recognized speakers, and a venue conducive to extensive multidisciplinary networking. One of the most desirable outcomes resulting

from our multidisciplinary pain educational activities is that your colleagues, including physical and occupational therapists, psychologists, physicians, and chiropractors will be better prepared to service patients experiencing painful conditions who are referred to them. Our patients benefit from more knowledgeable healthcare providers; and we as providers benefit from our colleagues' enhanced quality of services delivered. In addition, our society at large benefits from more efficient and effective evaluation and treatment of chronic pain patients, since chronic pain is one of the most expensive conditions to treat, due to its complex biopsychosocial nature.

Therefore, I urge you to become more active in the committees and educational venues of the Southern Pain Society, for the benefit of your patients, your practice, and yourself. We want more of our members to take leadership roles in this society, in order to influence healthcare agencies, insurance companies and legislators for the benefit of our patients. We welcome your involvement, and will do our best to continuously improve the value of your membership dollars to you and your practice.

Call for Nominations

This year we will have 2 At-Large Board positions up for reelection. Nominations are now being accepted for these two year terms. If you would like to nominate yourself, or another SPS member, please send your nomination in writing to

Chair, Nominations Committee
Southern Pain Society
Box 5033
Cary, North Carolina 27512

Please indicate why you are making the nomination, and ensure that that nominee has agreed to run if nominated.

Newsletter Submissions

All submissions to SPS News should be typewritten and double spaced with title and name of author(s). The article should be copy-ready. Please include biographical information.

Submission Deadlines

Winter edition-November 1; Spring edition-February 1; Summer edition-May 1; Fall edition-August 1.

Book Review

Benjamin Johnson, MD

Chronic Pain: A Primary Care Guide to Practice Management

by Dawn Marcus, MD

Humana Press, Totowa, NJ 2005. 333 Pages.

The purpose of this book, as presented by the author and series editor is to provide primary care physicians with a clear, succinct, evidence-based practical approach to the diagnosis and treatment of the various causes of chronic pain seen in the office of a primary care provider.

Since a large percentage of patients seen at a primary care provider's office present with a chief complaint of pain, the primary care provider is often the first person to evaluate the chronic pain patient. Since education in chronic pain management has remained lacking in most medical schools, many physicians, including primary care specialists, have had little preparation for dealing with the clinical and administrative complexities that often accompany patients experiencing chronic pain. Dr. Marcus attempts to address these issues in order to better prepare the primary care provider for the evaluation and management of the chronic pain patient.

The series editor and Dr. Marcus first provide a helpful introduction to the issues that are presented in the text, including the epidemiology, and legitimacy of chronic pain. The author then presents a basic, clear and concise version of pain pathophysiology in order to guide the reader towards a mechanism-based evaluation and treatment strategy.

The presentation of seven common painful conditions, including back pain, arthritis, headache, and myofascial pain provides the reader with a fundamental approach to evaluation and treatment principles concerning these clinical problems. Each chapter begins with an illustrative case history, and is replete with helpful graphs, tables, illustrations, forms and references. A special section addresses the unique problems encountered with pediatric, pregnant, and geriatric patients; and also addresses gender and ethnic concerns regarding chronic pain evaluation and management.

The author has additional chapters addressing the comorbid conditions, such as psychological and obesity issues, that commonly accompany chronic pain conditions. A special chapter on opioid usage presents a sensible and practical rationale for the appropriate use of opioids, accompanied by recommendations for documentation, goal-based opioid therapy, outcome measures, and an example of an opioid agreement form.

A useful appendix featuring information about the utility of exercise, the relevance of pain management skills, a pain medication dosing guide, and a chronic headache guide is included.

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From the Editor continued from page 2

The particular sociology of areas like Appalachia may have made them the most vulnerable early on, but it is now everyone's problem. A tactical and humane approach is required these days in the treatment of pain.

The healthcare provider needs to perform an appropriate evaluation of the patient before writing the first prescription for a controlled substance. This evaluation is a medical evaluation of the pain complaint but also includes a vulnerability assessment for misuse or aberrant drug-related behavior. Thus, an understanding of the patient's potential risk factors in the areas of chemical dependency history, psychiatric co-morbidities, social and familial situation, genetic loadings and spirituality must be reached. The results of this assessment are not to be used to categorically exclude patients from opioid therapy, but may dictate the level of agreed-upon boundaries that need to be put in place or the outside help that might be required to effectively manage a patient.

Hubris about the ability to treat anyone under any circumstances needs to be replaced by a sober assessment of who a particular practitioner can treat in his or her practice setting given the practitioner's time, expertise in complex psychiatric issues, and resources. Learning whom one can treat alone, whom they can treat with help and whom they should refer out is crucial for pain management to be done safely. Therefore, healthcare providers should obtain consultations as needed. And when drug therapy is begun, it should be done in the context of a treatment plan based on informed consent of the risks and benefits of all medicines prescribed.

Healthcare providers owe it to their patients to discuss realistic expectations about pain reduction, and help formulate functional goals to be achieved by prescribing rational pharmacology. Helping the patient understand how success or failure is to be measured, in terms of pain control (hopefully a meaningful reduction in pain intensity) but also in terms of function (stabilized or improved), toxicities (manageable or none), and aberrant behaviors (few or none) is crucial for gaining compliance and understanding of the goals of therapy. The healthcare provider must, of course, prescribe all medications consistent with state and federal regulations.

I look forward to being a productive member of the Southern Pain Society and hope you all keep the faith and practice good pain management. While tough times may lie ahead, I hope we can all pull through this together.

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Pulsed RF: Many Mis- understandings

William Rittman, MS

As a co-inventor of pulsed RF, it is concerning that many users are being mis-educated as to how to provide an optimum treatment. There is also confusion over how the different RF systems manage the pulsed RF output, and the result is many patients being less than optimally treated. I would like to clarify these misunderstandings-

The specifications for the parameters of pulsed RF are for the pulse to be on for 20 milliseconds and then off for 480 milliseconds. (one millisecond is the name for one thousandth of a second) This results in two "on" pulses per second. All RF lesion generators offer these parameters as suggested by Dr. Sluijter.

It is important that the temperature never goes above 42° C as higher temperatures risk permanent tissue damage.

The goal of a pulsed RF treatment is not to reach 42° C! This is not a thermal lesion! The perfect treatment delivers 45 volt pulses for the full duration of the treatment. If 42° C is reached, the pulsed RF must be modified to prevent further temperature increases. This reduces the efficacy of the treatment.
(Radiofrequency Part 1, Prof. dr. Menno E. Sluijter , Flivopress S.A. 2001, pgs. 59-65)

There are two ways to deal with the situation when the temperature unfortunately reaches 42°C. Either the pulse "on" amplitude must be reduced, or the pulse "on" time must be reduced. Since it is widely believed that the efficacy of pulsed RF is due to electric field intensity acting on cells, it is far more desirable to reduce the pulse width (meaning the pulse "on" time) as opposed to reducing the voltage amplitude.

Though some machines incorporate an automatic adjustment, and some have to be adjusted manually to ensure the temperature does not rise above the 42°C safety limit, they all do it by reducing the amplitude of the pulse. This means that the pulse voltage must be adjusted down in order to reduce the pulse energy and thus reduce the heating effect.

The recommended voltage (per Sluijter) for the required field effect is 45 Volts amplitude of the pulse. However, recent evidence* has indicated that current may be a more important parameter, as good patient outcomes correlate with higher currents. The new paradigm may be 100-200 ma as opposed to 45 Volts. * Menno Sluijter unpublished paper. Copies available on request.

continued from page 1 were the commonest sites for chronic pain. The author concluded that the social and economic consequences of pain were enormous and justified expenditure of research funds for better understanding, prevention and treatment of pain.

A telephone survey in Catalonia, Spain, used a randomized sample of 1,964 adults stratified by age, sex and effects of pain on activities of daily living in the last six months (Bassols et al., 1999). The participation rate in the population was 91.7%. Pain was reported by 78.6% of the participants; 84% had pain for longer than six months and rated the average pain level as 6/10. Daily and social activities were affected in 24.6%. Severe disability was reported in 10%, while 10.2% of participants took time off work due to pain-related problems. There were no differences related to age or living area. However, the prevalence of pain was significantly higher in women than in men, and significantly higher with less education. Common pain complaint sites included the back (50.9%), head (40.2%) and legs (36.8%). Back pain affected all age groups, while headache affected mostly young women. Leg pain affected mostly elderly people.

The Michigan Pain Study used a stratified random sample of 1,500 adults and found that 20% of adults had current or recurrent chronic pain. 77% of those with pain had experienced it for more than one year. 36% of people with pain missed work on account of pain related reasons. More than 2.5% of the adult population missed more than 20 days of work due to pain; 21% of those with pain were seen in the emergency room an average of four times, and 10% contemplated suicide (EPIC/MRA, 1997).

Hospitalized patients have high prevalence of pain. Thurston et al (1996) reported the prevalence in a tertiary care teaching hospital in Canada. 258 patients were surveyed using validated pain scales. The participants had been in the hospital from 1 to 240 days. The average age was 58 years. 51% of the respondents were females. 72% of these respondents experienced pain in the last 24 hours. 50% reported worst pain level of 7/10 or greater in the last 24 hours. Prevalence and intensity varied little with duration of hospitalization. However, patient's satisfaction with pain management was high. This study suggested that satisfaction with pain management may be more related to the concern shown by the care provider, and less strongly to the variability in pain intensity.

These previous surveys have consistently shown a high prevalence of pain in different countries, with the most frequently reported sites being the back, head and legs. However, prevalence rates have varied according to the definitions used, the multidimensional nature of pain, the design of the study and the subjective nature of pain, which is always based on self-report. Differences related to cultural and socioeconomic characteristics have been receiving more attention recently (Todd et al., 1993, Cleland et al., 1997, Todd et al., 2000, Blake et al., 2002, Carmen et al., 2003, Portenoy et al., 2004).

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continued from page 5 Some of the problems inherent in pain epidemiology stem from the lack of consensus on basic definitions and inconsistencies in measures. We all know about the inherent subjectivity of pain. We still do not have an objective measure, like a thermometer, for measuring pain. In addition, some people do not regard pain, ache and hurts as being the same. Recall bias is also an important problem. Pain is often forgotten once it is over. The threshold of recall of previous pain varies with the severity of the symptom, the associated events, how recent the episode is, and the persistence of the questioning. So epidemiologic surveys trying to determine the prevalence of a painful disorder like low back pain, depending on how the questions are worded, may end up with different results. Moreover, many other operational definitions are yet to be standardized for the patients and providers. We frequently talk about low back pain. What are the landmarks of the low back? Do we really know that our conception of the lower back is the same as that of our patients?

Epidemiologic data not only illuminate the patterns of pain and its impact, they also help to determine treatment effectiveness and the best ways to reduce pain-related health care costs. For instance, a multinational cohort study showed that our rate of back surgery here in the United States is five times that in Sweden, and there is no evidence of positive effects on back function, pain level or work (Hansson et al., 2000). Since epidemiology helps us to see the changing pattern of pain over time, it helps us to provide answers to questions like: How quickly will the patient recover? Will this occur again? Will future attack become more severe? Is there anything that can be done to prevent future attack? These are important questions for the patients with low back pain, trigeminal neuralgia or even patients with non fluctuating painful conditions. While the discipline of epidemiology initially focused on infectious disease control, modern epidemiology - or the second epidemiological revolution- is focused on the etiologic role of behavioral and environmental risk factors and the methods for preventing chronic diseases and disability. We need to harness this to help that most desolate of mankind – the patient with pain.

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Science

Article by Charles A. MacNeill, MD

Review and commentary by Dan Doleys, PhD

Charles A. MacNeill, M.D.

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“There’s Something Happening Here,
What It Is Ain’t Exactly Clear”

So sang Stephen Stills, et al, of Buffalo Springfield in his an-themic paean to the late 1960's. Today, I have the same curios-ity about therapeutic effects I am seeing with the newly re-laxed drug Cymbalta (duloxetine) by Eli Lilly.

Introduced in late 2004, Cymbalta is touted as a new novel combination drug, dually FDA approved for depression and diabetic peripheral neuropathy. Even before its release, Cym-balta was mentioned in the neurology literature, and in reports from the Summer 2004 meeting of The American Neurological Association, as an effective treatment for diabetic neuropathic pain. With both serotonergic and noradrenergic properties available at low dose, reports were favorable for Cymbalta's efficacy in treating depression and, most interesting to me, helping those suffering with diabetic neuropathy. In the usual spirit of most pain medicine practitioners, I took the "suggestion" of the FDA, and applied the medication to clinical practice, hoping that Cymbalta would be beneficial in the treat-ment of neuropathic pain of any stripe, whether diabetic, radicular, post-traumatic, viral, postsurgical, or idiopathic in origin.

After more than 25 years in the clinical practice of pain medi-cine, I have amassed quite an array of patients with neuropathic pain complaints. They have come from original referring phy-sicians and from other area pain practices, in hopes of finding a suitable method for controlling their pain. Most simply "get by" with currently available medications such as long-acting opioids, anti-seizure, and topical medications, plus adjunctive modalities including biofeedback, exercise therapy and occa-sional interventional therapy. Some have improved with spinal cord stimulation and/or subarachnoid infusion. Many are de-pressed, but this is usually treated effectively with current anti-depressants such as Lexapro, Effexor and Wellbutrin. Depend-ing on the longevity of their pain, these patients have tried the "neuropathic pain remedy" of the day including IV lidocaine in the 1960's and 1970's, tricyclic antidepressants with or without a major tranquilizer in the late 1970's and 1980's, Dilantin or Tegretol, also in the 1970's and 1980's, Neurontin in the early 1990's, and Neurontin's spawn to include Gabitril, Zonegran, Keppra and Topamax more recently. As an anesthesia-trained pain practitioner, I have not been shy in the use of interven-tional procedures. Most of the patient's have been through a course of sympathetic, plexus or regional blocks, subcutaneous infiltration, continuous epidurals, or more advanced pain thera-pies, depending on location and duration of pain.

In the Fall, 2004, once Cymbalta samples were available and the drug was in local pharmacies, I began to trial this medica-tion using a set dosing protocol with a 19-day titration to reach optimal dose of 60 mg b.i.d. as advocated in the neuro-l-ogy literature. I soon found that nausea, sometimes quite se-vere, was more common than predicted, and a prescription for Phenergan accompanied each of the samples. A few pa-tients opted out because of nausea, while three others stopped because of prolonged attacks of "the sweats," but 22 of the first 30 patients completed the titration or experienced dra-matic pain relief at a lesser dose. Each of the patients chosen for Cymbalta consistently scored 7/10 or higher on their monthly visual analog scale (VAS) prior to starting the drug.

I have been astounded by the results noted in this trial. Cer-tainly, there are patients who have seen little change in pain intensity or pattern, but 18 of the 22 patients completing the titration continue on with Cymbalta as their primary source of pain relief. As you will see from the patient profiles pre-sented below, Cymbalta seems to work in a very diverse ar-ray of pain complaints.

1. P.O. is a 42-year-old female executive who flies 100,000+ miles per year for her job. At age 15, she unde-went extensive left ankle surgery for excision of vascular tumors. She has experienced intractable burning and ex-treme hypersensitivity for 27 years in the surgical area. Her VAS score was always in the 7-8/10 range. After the fifth day on Cymbalta (30 mg b.i.d.), her pain reduced to a 0-1/10 VAS. She now takes no other pain medications.
2. G.K. is a 58-year-old, disabled patient suffering a traumatic amputation of the left arm over 37 years ago. He has experienced painful phantom limb pain ever since, unre-sponsive to all modes of treatment, relief best achieved with high-dose methadone (80 mg per day). After three weeks on Cymbalta (60 mg b.i.d.), his VAS score is 3/10 and metha-done dose has been reduced by half with continued weaning.
3. V.T. is a 33-year-old computer programmer wh crushed her left ring finger in a door at work 3 years ago. After recovering, she experienced digital hypersensitivity, stiffness and weakness, disallowing competent work on the keyboard, this despite topical, local and regional neural treatment plus extensive P.T. and O.T. After 19 days on Cymbalta (60 mg b.i.d.), she is back at work with out complaint and takes no other pain medication.
4. P.D. is a 79-year-old English woman who flew to Atlanta from London to live with her daughter. P.D. was given a sleeping pill to use on the plane. Accordingly, P.D. did not move from her seat for the entire 9-hour flight, and upon arrival in Atlanta, was noted to have swol-len lower legs and feet more than twice their usual size. Once diuretic treatment was completed, she was left with intractable burning pain felt as pins-and-needles throughout the lower legs and feet. She responded short-term only to sympathetic blocks, and could not tolerate Neurontin or similar drugs. After one week on Cymbalta (30 mg b.i.d.), she is now pain-free (VAS is 0/10), as long as she takes the medication.

5. S.C. is a 48-year-old legal secretary who underwent L5-S1 micro discectomy 3 years ago. She experienced complete relief of radicular symptoms for 6 months, then began to develop a sciatic distribution pain, burning, sharp/electrical in nature. MRI scan indicated no abnormal findings. She eventually underwent spinal cord stimulator placement with excellent early relief, but with return of pain despite accurate simulation within months post-implant. She underwent repeat surgery with L5-S1 fusion, but no change in radicular symptoms. Her only relief came with Duragesic 100 mcg per hour, plus Actiq 800 mcg t.i.d. She was eventually asked not to come to work with a swab hanging out of her mouth, and she became suicidally despondent. She was started on Cymbalta in October 2004. After 19 day titration (60 mg b.i.d.), the VAS score at 10/10 was down to 4/10. She has stopped all Actiq and other breakthrough medications, and Duragesic is now down to 25 mcg per hour. She is back at work full-time.

Other examples are similarly impressive. This is not simply an antidepressant effect. Some patients are seeing results at first dose, others only after full titration. As Buffalo Springfield continued:

“Hey, what’s that sound?”
(But, I really don't know)
"what's going down."

Disclaimer: I am in the full-time clinical practice of pain medicine in Atlanta and Marietta, Georgia. I am in no way affiliated with Eli Lilly or any associated company. I am not engaged in any research with Lilly nor have I ever received any grant money from them. I am not on the Eli Lilly's speaker's bureau, nor any other speaker's bureau for that matter. I do own a small amount of Lilly stock in a retirement account, but this is not actively traded. My father-in-law did once work for Eli Lilly, but more than 20 years ago. Also, I have only recently met the Eli Lilly representative for my office, and he is not real pretty.

A brief review of Cymbalta®: and commentary on the cases of Dr. MacNeill by Daniel M. Doleys, Ph.D

Duloxetine hydrochloride (Cymbalta®) was released by Eli Lilly in 2004 and is indicated for the treatment of Major Depressive Disorder (MDD) and Diabetic Peripheral Neuropathic Pain (DPNP). It inhibits the reuptake of both serotonin (5-HT) and norepinephrine (NE) and, to a lesser extent, dopamine (Kirwin & Goren, 2005). Duloxetine is a 4.8 fold more potent inhibitor of 5-HT reuptake than fluoxetine. Venlafaxine (Effexor®), another commonly used dual action antidepressant, is 7-17 times more selective for the 5-HT transporter, 66% less potent inhibitor of 5-HT and 77% less potent for NE (Kirwin & Goren, 2005). Therefore, duloxetine is thought to be a more balanced inhibitor of 5-HT and NE than venlafaxine. Duloxetine's mean half life approximates 12.5 hours, time to maximum concentration 6 hours, with steady state achieved in 3 days. Presumably, it can be taken any time of the day, with or without food. Apparently, no adjust-

ments need to be made for older women. Duloxetine is not recommended for patients with end stage renal disease. The most common side effects include nausea (20%), dry mouth (15%), constipation (11%), decreased appetite (8%), fatigue (8%), and somnolence (7%). Clinical studies indicate that up to 17% of patients discontinue therapy because of one or more adverse events. Abrupt discontinuation of duloxetine therapy, whether after short or long term use, may be accompanied by the usual 5-HT withdrawal syndrome including abnormal dreams, anxiety, nausea, irritability, insomnia, dizziness and headache. (The above and other more detailed information can be found in the package insert and the recent review by Kirwin & Goren, 2005).

A brief MEDLINE search carried out 2-22-05 using the key words “Cymbalta, Duloxetine, Pain”, and dating to 2002, yielded 24 references, four of which were animal studies (see attached list). Both nociceptive and neuropathic pain models were examined in animals. Acetic-acid, carrageenan, capsaicin, formalin, nerve constriction and nerve ligation models of pain were used to create persistent or acute pain. Mechanical and thermal allodynia and hyperalgesia were examined. Duloxetine was compared with morphine, ibuprofen, amitriptyline, mirtazapine, gabapentin, fluoxetine, and paroxetine. Duloxetine was associated with a dose-dependent reversal of carrageenan induced thermal hyperalgesia and mechanical allodynia, capsaicin induced mechanical allodynia, as well as mechanical allodynia in the spinal nerve ligation model of neuropathic pain. The effect tended to be observed in the persistent vs acute pain model. When compared to amitriptyline, mirtazapine and citalopram, only duloxetine and amitriptyline reversed thermal hyperalgesia. Unlike some of the other substances, duloxetine did not produce significant neurological deficits on the rotarod test.

A number of studies, pooled data analysis, and reviews were found relating to the effects on duloxetine on patients with MDD with and without associated physical symptoms such as headache, back pain, abdominal pain, general musculoskeletal pain. In general duloxetine was found to be effective at dosages ranging from 40-120 mg/day with 60mg/day appearing the most optimal. Most clinical trials extended from 9-12 weeks. Duloxetine separated from placebo as early as the one week for mood and physical symptoms. The effect on melancholic and non-melancholic patients was equal. Pooled analysis of eight studies on MDD patients showed an equal response in male and females. However, in a multi-center study using fibromyalgia patients with and without MDD, males failed to show a significant improvement on any of the dependent measures compared to females. The impact of duloxetine on physical symptoms, including pain, appears to be separate from its effect on mood. In some instances the persistence of somatic symptoms appeared to be associated with a higher rate relapse even when there was a reported decrease in core emotional symptoms. One study reported 25-50% reduction in measures of pain vs 19-39% in a placebo group.

Most of the above studies used depressed patients with and without accompanying complaints of pain. It is unclear if this

population responds in the same fashion as patients whose depression emerges as a result of injury or disease associated pain and dysfunction. Commonly used measures of depression such as the Hamilton-D Scale, which was found in most of the above studies, may not be sensitive or specific enough in the pain population. The Beck Depression Inventory appears to have greater utility in the pain population. One would expect the persistence of some physical symptoms in the pain patients. In such cases, "depression" may represent a maladaptive response to the "pain" or as a partial measure of the degree of pain "unpleasantness". Thus, it may be more important to reduce the 'unpleasant' or affective component of pain rather than the sensory component. The later may, in fact, be represented as physical symptoms.

The cases present by Dr. MacNeill are important in many ways. First, because these patients are well known to him, he is familiar with their response, or lack there of, to other treatments, potentially eliminating novelty or treatment, natural history of the pain, and the "placebo effect" of a new treatment setting and practitioner as variables associated with the outcome. Second, the cases cover a variety of etiologies and ages. And third, the reporting of individual patient data in and N=1 fashion. Oftentimes the emphasis on 'statistically significance' diverts our attention from the individual patient and may obscure otherwise important observations. Many of the 'discoveries' in science are foretold by the acute observation of a small number of instances. In this spirit, SPS Newsletter would like to invite and encourage the submission of case studies, particularly from the clinical sector, highlighting baseline history of the patient and multiple outcomes measures examining the different dimensions of pain i.e. sensory, affective, cognitive, measures of pain outcome (see Doleys, SPS Newsletter 2004), and quality of life measures including function and mood.

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Book Review continued from page 4

This text also includes an opportunity to earn 5 hours of Category I continuing medical education; and also includes a CD-ROM for downloading the book contents into either a computer or PDA.

In summary, this text represents an admirable effort to present a brief, clear and concise approach to chronic pain evaluation and management to the busy primary care provider. It also includes guidelines for timely referral to a pain specialist. The text includes a wealth of helpful table, graphs, chart, and algorithms to aid rapid understanding of the material presented. A text of this nature should be in every primary care provider's library. The author and series editors are to be congratulated for their efforts to equip primary care providers with the necessary information to approach patients experiencing chronic pain conditions.

Save the Date!

**Southern Pain Society
Annual Scientific Meeting
In conjunction with
The Kentucky Pain Society**

**October 14-16, 2005
Lexington, Kentucky**



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