



# Behavioral Approaches to Headache and Migraine Management

Moderated by **Dawn C. Buse, PhD<sup>1</sup>**

Discussants: **Frank Andrasik, PhD<sup>2</sup>; Alvin E. Lake III, PhD<sup>3</sup>; Donald B. Penzien, PhD<sup>4</sup>**

**DR. BUSE:** I am Dawn Buse, PhD, an Associate Professor of Neurology at Albert Einstein College of Medicine and Director of Behavioral Medicine at the Montefiore Headache Center in New York City. Today we are going to talk about nonpharmacologic treatments for migraine and other forms of headache, specifically the empiri-

cally supported behavioral interventions, and to do so we are privileged to have three expert clinician-scientists with us.

Dr. Frank Andrasik is a Distinguished Professor and Chair of the Department of Psychology at the University of Memphis. He also serves as Director of the Center for Behavioral Medicine at UM. Dr. Alvin Lake is a founding member of the Michigan Head-Pain and Neurological Institute and is both Director of the Behavioral Medicine Division and Associate Program Director of the inpatient Head Pain Treatment Unit at Chelsea Community Hospital. Dr. Donald Penzien is a Professor of Psychiatry and Human Behavior at the University of Mississippi Medical Center and founder and Director of the Head Pain Center. All three of our panelists have extensive clinical experience working with patients with headache and pain disorders. They have also

conducted research in these areas and collectively published hundreds of peer-reviewed scientific articles. Welcome, gentlemen.

Although the range of acute and preventive pharmacologic treatments for migraine continues to grow, non-pharmacologic treatments play an important role in the comprehensive effective management of primary headache disorders including migraine. Nonpharmacologic treatments include behavioral approaches such as cognitive behavioral therapy (CBT), biofeedback, relaxation training, stress management, lifestyle modification and patient education. They also include physical and occupational therapies, acupuncture, and other non-drug modalities. Today we will focus on the behavioral and cognitive interventions with empirical evidence for their use. For ease of parsimony, we will refer to this group of treatments collectively as “behavioral treatments.”

## ABSTRACT

The discussion focused primarily on: 1) Review of empirically supported behavioral treatments for headache and migraine management including cognitive behavioral therapy (CBT), biofeedback, relaxation training, stress management, education, and lifestyle modification; 2) review of the empirical evidence for the use of behavioral therapies; 3) evidence for the combination of pharmacologic and behavioral treatments; 4) guidelines for headache management; 5) cost as a factor for treatment; 6) psychiatric comorbidity and medication overuse; 7) improving adherence and enhancing patient motivation and self-efficacy; 8) review of data on medical communication in migraine management; and 9) suggestions for healthcare providers (HCPs) to incorporate in practice. *Med Roundtable Gen Med Ed.* 2012;1(2):131-144.

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In today's conversation we will review the data on efficacy of empirically supported behavioral therapies for migraine, discuss how to identify appropriate patients by matching patient characteristics and needs with available treatments, and review important areas for clinical assessment. We will also review suggestions for healthcare providers (HCPs) for enhancing adherence and improving medical communication among other topics.

There is a large body of published evidence examining the use of behavioral and cognitive therapies for migraine (and other forms of primary headache) including meta-analytic studies and evidence-based reviews. The US Headache Consortium developed evidence-based guidelines for the treatment and management of migraine headache based

on an extensive review of the medical literature and compilation of expert consensus.<sup>1</sup> In the published guidelines, they suggest that nonpharmacologic treatments<sup>2</sup> might be particularly well suited for patients who have a preference for nonpharmacologic interventions; display a poor tolerance for specific pharmacologic treatments; exhibit medical contraindications for specific pharmacologic treatments; have insufficient or no response to pharmacologic treatment; are pregnant, are planning to become pregnant, or are nursing; have a history of long-term, frequent, or excessive use of analgesic or acute medications that can aggravate headache problems (or lead to decreased responsiveness to other pharmacotherapies); or exhibit significant stress or deficient stress-coping skills.

Dr. Andrasik, what are the behavioral approaches with empirical evidence supporting their use for headache and migraine and what does the evidence show?

**DR. ANDRASIK:** There are several behavioral treatments that have been examined starting with biofeedback beginning in the late 1970s. There are a number of different biofeedback approaches. Researchers have also looked at relaxation training and cognitive behavior therapy.

When I think of the evidence base I like to examine it from two stand-

listed some situations in which behavioral treatments were particularly indicated, such as those mentioned in the opening comments.

Then if we look at the meta-analytic side, we also have a large number of analyses that have been conducted.<sup>4,5</sup> When I talk about this to audiences I jokingly refer to the fact that we have so many meta-analyses that the next one I expect to see is a meta-analysis of the meta-analyses. I wanted to mention one in particular, just briefly, that shows not only the support for various biofeedback procedures in improving pain parameters, but also demonstrates that biofeedback can impact variables not directly targeted but are nonetheless important to consider.<sup>6</sup> In this most recent meta-analysis, we were able to examine some

of the co-occurring symptoms associated with migraine headache. We found that upon receiving biofeedback treatments, anxiety scores improved, depression improved, and self-efficacy also improved. This meta-analysis was probably one of the first to look at correlated or concomitant changes in addition to headache parameters.

**DR. PENZIEN:** I agree, there are many different ways to look at these data. But many do not recognize that there is a wealth of published evidence examining data on behavioral interventions for primary headache disorders. Empirically validated behavioral treatments include biofeedback training, relaxation training, combinations of the two, stress management training, and cognitive behavioral therapy.

*"Strategies including the use of open-ended questions, the "Ask-Tell-Ask" technique, active listening, and being fully present with the patient can significantly improve the quality of the medical relationship, with more satisfying outcomes for both patient and healthcare provider."*

**Dawn C. Buse**

points. One includes reviews by special panels of experts convened to conduct evidence-based reviews according to specific criteria. Also, another way is to look at large-scale statistical analyses or meta-analyses of what the data show. So this way we have both qualitative and quantitative reviews.

The expert review of most interest to our audience perhaps would be the evidence-based guidelines developed by the US Headache Consortium<sup>2</sup> based on evidence reports produced under the auspices of the Agency for Healthcare Research and Quality.<sup>3</sup> The Consortium consisted of seven member organizations where they strongly endorsed various cognitive and behavioral procedures for treatment of migraine. They also

Those behavioral interventions have yielded improvements on the order of 35% to 55% reductions in headache from pretreatment to post-treatment indicating that they're viable interventions. Those observed outcomes are approximately equivalent to the best prophylactic medications for primary headache. By comparison, wait list control treatments show almost no evidence of improvement. In fact, Dr. Andrasik was involved in a couple of trials years ago where he and his colleagues looked at the wait list control groups for periods ranging from a few months up to 3 years post treatment and found no improvements.<sup>7,8</sup>

Then medication placebo for migraine prophylactics yields, on average, approximately 12% to 14% improvement.<sup>9-11</sup> So all of the active behavioral interventions show much higher outcomes with respect to medication placebo. In fact, those outcomes tend to be sustained over time, at least over the short run of 2 years. And there is some evidence that the improvements with behavior therapy are well maintained without necessity of additional therapy over time.

**DR. ANDRASIK:** Dr. Penzien made a good point that in these meta-analyses, he and others have been able to directly compare literatures on the behavioral treatments with the most common prophylactic treatments, and almost to a decimal point they come out at the same efficacy level.

**DR. LAKE:** One question that treatment providers may raise relates to the efficacy of combining pharmacologic and behavioral treatments. Some of the research with which we are all familiar shows synergistically better outcomes from the combination of the two approaches, as in a now classic study by Holroyd and colleagues published in JAMA over a decade ago.<sup>12</sup> Combining tricyclic an-

tididepressant therapy with behavioral stress management led to a 50% or greater reduction in headache index scores for 64% of chronic tension headache patients randomly assigned to that condition, compared to 38% of those who only received tricyclic medication, 35% of those who only received stress management therapy, and 29% of those who were given placebo medication. The gain from the combination of behavioral therapy with a tricyclic antidepressant was both statistically significant and clinically meaningful.

I think we all agree that empirically sound evidence-based behavioral treatments should be included as a standard part of the basic headache-care toolkit, and need to be made available to more patients before the provider moves on to more esoteric, less proven, and sometimes far more expensive medical therapies. However, the value of behavioral therapy is not limited to the basics of headache management, but may need to be a critical part of the intensive treatment of intractable or refractory headache on both outpatient and inpatient levels as well.<sup>13</sup>

**DR. PENZIEN:** You raise a good point, Dr. Lake, regarding the value of combining behavioral and pharmacological treatments for headache. The US Headache Consortium made the following recommendation<sup>2</sup>: "Behavioral therapy (i.e., relaxation, biofeedback) may be combined with preventive drug therapy (i.e., propranolol, amitriptyline) for patients to achieve additional clinical improvement for migraine relief (Grade B)." The only reason the Consortium's recommendation regarding the use of combined drug and non-drug therapies was not stronger is because so few studies have directly evaluated the combined therapies. But all of the published evidence seems quite consistent in showing that benefits accrue when

## STUDIES DISCUSSED:

AMPP  
AMCS I and AMCS II

## COMPOUNDS DISCUSSED:

triptans  
topiramate  
valproic acid

drug and non-drug therapies are combined for primary headache disorders.

So, as you're pointing out, these are viable interventions that have stood the test of time and are supported by ample empirical evidence but frankly remain underutilized.

**DR. BUSE:** Do you have any hypotheses about why these treatments are underutilized given their strong evidence base?

**DR. ANDRASIK:** Well, I think one simple explanation is that the word is just not getting out. Perhaps we've not done a good job in this respect. The direction that some of my and the research of others has gone recently is to address the issue of costs of these treatments. A lot of patients are looking for a very quick and less time demanding and less expensive cure.

Our treatments work but they take a motivated patient. They take time. They take effort. They take multiple trips to the clinic. So one of the things that I and others have been doing is looking at ways that we can trim back the amount of treatment time, without reducing effectiveness.

I now use the acronym "PLOT" to describe this approach; prudent, limited, office treatment (a term originated by a close friend and biofeedback pioneer, Dr. Mark S. Schwartz, formerly of the Mayo Clinic). We and others have found that we can teach these behavioral procedures with

fewer sessions if we prepare training materials that patients can study at home or work. The impetus for this approach came after examining the self-help literature, which showed that a number of conditions could be successfully treated in this manner, but that attrition was quite high. We reasoned that a few office visits, judiciously scheduled, had potential to engage and hold patients in treatment, ensure understanding, and allow the therapist to troubleshoot with them as needed.<sup>14</sup> Two reviews showed that PLOT was essentially equivalent to more intensive in-office treatments and resulted in considerable cost savings.<sup>15,16</sup> This conserves monetary costs for the patient and can also conserve time on the therapist's part. But it doesn't conserve time on the

patient's part. They still have to work hard at learning the techniques.

But, as we explore those kinds of treatments—and people are also looking at Internet-based treatment now—and investigate those new and different ways to deliver treatment, I think we may actually extend the reach of our treatments.<sup>14</sup> The few published internet-based studies have shown good outcomes, but nearly all have revealed high rates of attrition (similar to pure self-help approaches). Hedborg and Muhr is the notable exception. They, too, added some appropriately timed face-to-face contacts and reduced their dropout rate to under 10%, which is much lower than any prior investigators obtained.<sup>17</sup>

**DR. LAKE:** Dr. Andrasik mentioned cost, which includes expenses in

terms of effort and time. But we also have to think about the cost of medical treatment, which goes way beyond the charge for physician consultations, and includes the enduring costs of the various pharmacologic options that we use, some of which can be quite expensive and may not be covered well by some insurance providers. From both pharmacoeconomic and behavioral-economic perspectives, it makes sense to make these behavioral treatments available to as many headache sufferers as possible.

*"Our treatments work but they take a motivated patient. They take time, considerable effort, and typically require multiple trips to the clinic. So one of the lines of research that I and others have been pursuing is examining ways that we can trim back the amount of in-office treatment time, without detracting from its effectiveness."*

**Frank Andrasik**

**DR. PENZIEN:** We've recently published a study focused upon empirically modeling relative costs of behavioral treatments compared with drug therapies over time.<sup>18</sup> We found that even the more expensive of the clinic-based behavioral therapies within a couple of years post treatment are no more expensive and often are less expensive to administer than continuing drug prophylaxis. In fact, the minimal-contact behavioral therapies for migraine are cost-competitive relative to pharmacological therapies by one year post treatment, and they become more cost efficient as the years of treatment accrue. Again, this is statistical modeling, not evidence from real-world experience, but there nevertheless is ample evidence that behavioral interventions can prove considerably more cost-effective than medication therapies.

**DR. ANDRASIK:** Many years ago we conducted a retrospective study addressing this very issue. It wasn't a well-controlled study, but it was one of the first that actually tried to collect some kind of data.<sup>19</sup> Two years after we treated patients with in-office therapy we had them retrospectively estimate what they had spent in the 2 years prior to treatment and the 2 years following treatment. We asked them to check tax forms, check book statements, receipts and the like as possible. Our results showed, again, with less well-controlled data, that the treatment actually did pay for itself after a couple of years, which fits with the statistical model that you just described.

**DR. BUSE:** Thank you for those excellent points. Another way to contain costs and maxi-

mize the power of these approaches is to match patients with approaches that are going to be most effective for them. Are these approaches appropriate for all patients or are there ways that HCPs can identify patients who will benefit most from the behavioral interventions?

**DR. LAKE:** The behavioral approaches do require, as already mentioned, motivation and interest on the part of the patient. We need to ask patients what their goals are for treatment and ensure patients' awareness of options and costs. Most patients who come to a headache clinic are looking for diagnostic information and understanding of their headache, as well as a means of gaining better headache control, but do not necessarily come with a preference for medication-oriented treatment.<sup>20</sup> Medication-

related adverse effects can outweigh the benefits of treatment for some patients, and the cost of some medications can be prohibitive.

**DR. BUSE:** Migraine can be divided into episodic and chronic forms based on headache day frequency. According to the second edition of the International Classification of Headache Disorders (ICHD-2), chronic migraine (CM) is defined by headache on 15 or more days per month for at least 3 months with at least 8 days per month either meeting criteria for migraine without aura or responding to migraine-specific medication. Episodic migraine is defined by migraine with less than 15 headache days per month.<sup>21,22</sup>

It has been established that chronic migraine (CM) can be an especially disabling and burdensome condition. Both clinic and population-based studies have demonstrated that CM is associated with greater migraine related disability, impairment in headache related quality of life (HRQoL), worse socioeconomic status and sociodemographic factors, and higher rates of medical and psychiatric comorbidities.<sup>23-28</sup> Dr. Lake, should headache frequency be taken into account when creating a treatment plan for a patient?

**DR. LAKE:** Absolutely. The distinction between chronic and episodic migraine is important. Patients need to understand that very frequent headaches require a preventive approach. This holds true for both behavioral therapy and prophylactic pharmacotherapy. Behavioral medicine needs to be “dosed” on a prophylactic basis – skills need to be practiced daily if at all possible, and applied proactively in advance of

stressors and headache flares, rather than as a reactive response to events that have already happened.

Many patients with chronic migraine do experience some pain-free days. In contrast, true daily headache or continuous pain is a distinct phenomenon. Most of the patients we see in our inpatient program, for example, experience headache every day, continuous pain in many cases, and may have experienced daily pain for anywhere from several months to many years.<sup>29</sup> The traditional gold standard in outcome research has been a reduction in the frequency of headache. The problem is that for pa-

the brain’s pain matrix and less desirable treatment outcomes.<sup>31</sup> A significant component of behavioral therapy often involves the patient learning methods of both self-calming and distraction, as well as pain tolerance, and coming to some level of acceptance in terms of “this is where I am at this moment in time – I may not like it, but I can choose how to deal with it.”<sup>32</sup>

**DR. ANDRASIK:** I’ve been impressed by some functional magnetic resonance imaging (fMRI) studies that were conducted a while ago where they actually put patients into a chamber and subjected them to various painful stimuli. When they had them engage in distraction and things opposite to what Dr. Lake was talking about, the pain pathways actually didn’t light up as much as they did when they had them focus on the pain.<sup>33,34</sup> This research convincingly shows that how patients view their situations really has an impact deep within the brain in the pathways responsible for regulation of pain.

**DR. BUSE:** Dr. Lake, how should patients with medication overuse be managed from a behavioral perspective?

**DR. LAKE:** Effective treatment involves making a correct diagnosis, educating the patient about problems and issues related to medication overuse, enhancing non-drug coping skills, and involving the patient in follow-up over time to prevent relapse. Medication overuse headache (MOH) is defined as the use of certain prescription analgesics or abortive medications—for example, opiates, triptans, or combination drugs

*“From both pharmacoeconomic and behavioral-economic perspectives, it makes sense to make these treatments available to as many patients as possible.”*

**Alvin E. Lake III**

tients with daily or continuous pain, it may be very difficult to achieve a reduction in frequency of headache, and yet significant change can occur in the overall severity of pain and improved quality of life.<sup>30</sup>

Patients benefit from a frank discussion of the goals of treatment. Rather than pursuit of an elusive “cure” for chronic headache, the clinician can highlight goals of improved quality of life, less stress-aggravated headache, less pain-related affective disturbance or anxiety, and increased functioning. It’s not just about focusing on reduced frequency of pain. In fact, neuroscience and outcome research information has begun to reveal that hypervigilance, excessive attention to pain, and catastrophizing about headache’s impact, actually facilitate more pain-related activity in

with barbiturates—10 or more days a month for at least 3 months by a patient whose headaches occur at least 15 days/month. MOH can also arise from the use of over-the-counter analgesics such as acetaminophen or caffeine-containing drugs for 15 or more days a month over a 3 month period or longer.<sup>21</sup> MOH is considered a secondary headache—a primary headache such as migraine can transform into a near-daily or daily headache if the patient relies too heavily on these medications. The mechanisms underlying MOH continue to be elucidated, but appear to range from a hyperalgesic and hyperinflammatory state stemming from opioid overuse,<sup>35</sup> to an increase in neuronal hyperexcitability in the cerebral cortex related to enhanced expression of serotonin [5HT(2A)] receptors in the cerebral cortex and trigeminal ganglia related to overuse of acetaminophen (paracetamol).<sup>36</sup>

When a patient meets criteria for MOH, clinical experience and research have generally underscored the necessity of withdrawal from the overused medication as necessary before the patient will benefit from prophylactic therapy. In recent controlled studies with both topiramate and onabotulinum toxin A, about half of the patients with chronic migraine and medication overuse responded to those treatments with both a reduction in migraine days and acute drug use, without first undergoing withdrawal.<sup>37</sup> However, patients with severe forms of MOH—and patients with continuous or daily headache—were excluded from these studies.

From a behavioral perspective, our group has suggested that it's important to break patients who are overusing some of these medications into two different categories. One might be called simple medication overuse (Type I—e.g., frequent over-the-counter analgesics or frequent use of triptans) and the other complex overuse (Type II). The complex (Type II) category includes patients who may have a long history of using daily opioids or barbiturates, who may have histories of medication misuse, significant psychiatric comorbidity, and in some cases, a history of relapse after periods of limited analgesic consumption.

many patients with complex MOH<sup>39,40</sup> are refractory to prophylactic therapy without withdrawal from the overused medication, require multidisciplinary treatment and are vulnerable to relapse if they do not learn headache management skills other than reaching for a pill. Some of these skills, incidentally, involve learning to tolerate headache rather than focusing on pain reduction alone, or seeking chemical sedation.<sup>41</sup> For a given acute headache, the effects of behavioral skills in terms of pain reduction may not be as immediate or dramatic as an opiate analgesic, but may still reduce pain-related distress enough to help the patient avoid the slippery slope of increasing reliance on those analgesics that may lead to relapse and cyclical perpetuation of MOH.<sup>41</sup>

*"Behavioral interventions have yielded improvements on the order of 35% to 55% reductions in headache from pretreatment to post-treatment indicating that they're viable interventions. Those observed outcomes are approximately equivalent to the best prophylactic medications for primary headache."*

**Donald B. Penzien**

**DR. ANDRASIK:**

I'd like to mention one particular study that I was fortunate enough to be

This distinction was initially highlighted by my colleague and director of our center, Dr. Joel Saper.<sup>38</sup> We think these are two different populations of patients, with different treatment requirements. Other researchers have subsequently agreed on the existence and relevance of distinguishing between two types of MOH, although the distinction has yet to become a standard in diagnosis and in pharmaceutical outcome research with chronic migraine. Some patients with simple MOH may respond well to educational information and encouragement to reduce consumption along with appropriate prophylactic therapy and behavior therapy, as Dr. Hans Diener has suggested.<sup>37</sup> However,

able to conduct with some Italian collaborators at the Headache Centre at the National Neurological Institute C. Besta, Milan.<sup>42</sup> In this particular study we looked at patients who met the criteria that Dr. Lake was talking about: patients who had very frequent forms of migraine that were complicated by medication overuse (Type II patients).

It wasn't a fully randomized design because we conducted this in a clinical setting, and so we had to break randomization a few times. All patients were first withdrawn from all offending medications and then begun on an appropriate prophylaxis during a brief hospitalization. Some

received behavioral treatment in addition to medication. When we followed the patients up at 3 years, clearly the patients who received the combination of treatments were doing much better overall in terms of headache days and medication consumption. Equally, an interesting finding was that far fewer patients assigned to the combined condition actually had relapsed and returned to overusing medication, because relapse is a serious problem to be concerned about with this particular group of patients.

**DR. LAKE:** In my opinion, the study that Dr. Andrasik summarized is a classic in the field. The fact is that there are a number of studies that have shown high rates of relapse in the treatment of MOH for treatments that only involved withdrawal from the overused drug with additional prophylactic pharmacotherapy without an additional behavioral coping skills component – as high as 71% relapse for analgesic overuse when patients were assessed four years after drug withdrawal.<sup>43</sup> In your study, Dr. Andrasik, I believe that the relapse rate for the combination of behavioral treatment with drug withdrawal and prophylactic pharmacotherapy was 12.5% when patients were assessed 3 years after withdrawal, compared to 42% for withdrawal and pharmacotherapy without the behavioral component.<sup>42</sup>

**DR. ANDRASIK:** Yes, the differences were quite pronounced and exactly as you mentioned, in favor of the combination of medication plus behavioral training.

**DR. BUSE:** We know that the behavioral treatments that we have discussed lead to change in behavior. Do they also lead to changes in brain function or biochemistry? Dr. Andrasik, could you review some of your findings involving fMRI data?

**DR. ANDRASIK:** One topic my Italian colleagues and I have begun to examine is how does overuse of medication affect brain pathways involved in pain transmission and, if differences occur when consuming excessive amounts of pain medications, are these differences reversible. In a recently published paper utilizing fMRI,<sup>44</sup> we noticed significant differences between patients experiencing chronic forms of medication when overusing pain medication and headache-free controls. The migraine patients showed hypoactivity in several structures within the lateral pain system. However, when the patients were successfully withdrawn from their excessive medication and rescanned 6 months later, their scans were indistinguishable from the healthy controls.

**DR. BUSE:** It has been well established that migraine is comorbid, or occurs at a rate higher than chance, with a number of medical and psychiatric conditions. There is strong evidence showing increased comorbidity between migraine and several psychiatric conditions including depression, anxiety disorders, post-traumatic stress disorder (PTSD), personality disorders, as well as stressful life events such as a history of childhood maltreatment, abuse, and neglect.<sup>47-52</sup> Psychiatric comorbidities are burdensome to the patient and are related to worse outcomes such as progression from episodic to chronic migraine.

Psychiatric comorbidity among migraineurs was examined in the American Migraine Prevalence and Prevention (AMPP)<sup>54</sup> study, a longitudinal study of 24,000 individuals with “severe headache” from the US population. In a population sample of 655 respondents with CM and 11,249 respondents with EM, 30.2% of those with CM and 18.8% of those with EM reported that they had re-

ceived a diagnosis of anxiety from a healthcare professional while 41.2% of those with CM and 25.6% of those with EM reported receiving a diagnosis of depression. When current depressive symptoms were measured using a clinically validated tool (the PHQ-9), 30.2% of those with CM and 17.2% of those with EM met criteria for depression. Rates of depression and anxiety are even higher among clinic populations. Similar results have been noted in Taiwan<sup>28</sup> and European samples.<sup>55</sup>

Dr. Lake, are there tools that HCPs can use in their clinical practice for identifying and monitoring comorbidities? Also, can you provide any pearls that you suggest for management of these comorbidities in clinical practice?

**DR. LAKE:** First, there is real value in discussing with patients both the definition and clinical significance of comorbidity. In group sessions on our inpatient unit with patients, I find that most have never encountered the word or concept, unless they work in a health care setting. And yet, comorbidities tend to be most prevalent and severe in this group of patients! On this issue, there appears to be a large chasm between the language and understandings of health care providers and the headache patients we treat. I first explain the concept of comorbidity in epidemiological terms, as the statistically significant co-occurrence of migraine with psychiatric disorders in the general population, and what this implies about the underlying mechanisms and reciprocal influence of these disorders. I then discuss the importance of identifying and addressing comorbidities in the individual patient, and the importance of treating the whole person, not just the headache. Explaining comorbidity as the mutual interaction of headache and psychiatric disorders is a very useful educational tool, and underscores the importance

of attending to comorbid conditions while never losing sight of headache management goals. Incidentally, this is a huge transformation in our theoretical perspective from decades ago, when chronic headache was viewed by some as a psychosomatic disorder secondary to depression, anxiety, or stress; or at the other extreme, seeing depression as the inevitable result of chronic headache rather than as an associated disorder with bidirectional influence between the two conditions.

For those of us who specialize in headache, we assume that patients come to us primarily to address their headache condition, but we do not want to lose track of other concerns. This holds true for both behavioral and pharmacologic therapies. For example, some of the anticonvulsant drugs, such as topiramate, have proven efficacy in migraine management and yet can trigger serious depression in a minority of patients.<sup>58</sup> If we do not monitor potential comorbidities over the course of treatment, we may do our patients a serious disservice. It is as if we were to say “the treatment was successful, you should be happy” while turning a blind eye to any escalation in depression. We have also seen circumstances where patients’ headaches improve and their anxiety or depression worsens for nonmedication reasons. These situations can range from the patient spending an inordinate amount of time ruminating about how much they have lost to their previously uncontrolled migraine, despite feeling better at this point in time, to excessive worry about how long their improvement may last before they relapse, to feeling lost at sea as he or she faces an uncertain future with less of the headache activity that had demanded so much attention. For most patients, mood improves when the headache burden lifts. However, paradoxical responses can and do occur. Rather than wait for patients

to volunteer these concerns, we need to monitor the status of potentially comorbid conditions over the course of treatment.<sup>32</sup>

Comorbidity may be important in prognosis. A study in Italy reported by Guidetti and colleagues found that the presence of 2 or more comorbid psychiatric disorders in adolescents and young adults was predictive of a poor headache prognosis when the subjects were reassessed 8 years later—headaches were the same or worse in 57% of this group, with 29% improved and 14% headache free. In contrast, for those with only 1 comorbid disorder or less at initial assessment, between 7–15% were the same or worse compared to 46–53% improved, and 39–40% headache free.<sup>59</sup>

Histories of physical and/or emotional abuse as well as emotional neglect have been identified as possible risk factors for development of chronic headache in one recent survey of 1,348 migraineurs.<sup>50</sup> These findings imply that identifying and then intervening to address these comorbidities may help prevent headache chronification, although that has not yet been demonstrated. We also think it’s important to pay some attention to dysfunctional personality styles and personality disorders such as borderline personality that can affect response to treatment and pose significant challenges in patient management.<sup>32,49,60</sup> The primary concern, again, is to relate to the headache patient as a whole person.

**DR. PENZIEN:** One issue we’ve often encountered when speaking with practicing physician groups is that some HCPs seem hesitant to delve into managing psychiatric comorbidities and arguing, “This is not what I do. This is not my area of purview. Why would I ask about depression or anxiety when I do not treat depression or anxiety per se?”

From my perspective, psychiatric comorbidities are fundamentally important for any practitioner treating headache to address. Even if the practitioner opts not to personally address comorbidities, these are issues that merit attention in their own right. So when comorbidities are suspected or identified, it generally is prudent to make a referral for additional evaluation and treatment or at a minimum have a conversation with the patient about these concerns. As you’ve been hearing, these issues certainly can complicate headache treatment outcomes, so they’re well worth addressing.

**DR. BUSE:** Rather than presenting to mental healthcare professionals, a large percentage of depression and anxiety is actually managed by primary care providers. How can busy HCPs identify and manage patients with psychiatric comorbidities?

**DR. LAKE:** I know we talked a bit about simple ways of trying to address these issues in a limited amount of time in the HCP’s office. This may include the use of clinically validated assessment tools.

One instrument that we have been using is the Quick Inventory of Depressive Symptomatology 16 Item Self-Report (QIDS-SR16).<sup>61</sup> This is freely available in the public domain, is two-pages in length, and takes about 60–90 seconds to complete. It covers all the criteria for DSM-IV major depressive disorder. It goes into detail on sleep issues, which is a major headache-related psychiatric comorbidity in itself that can respond to behavioral intervention. It asks about the primary major depression symptoms of sadness and lack of interest in activities. One limitation is that it does not inquire about anger or irritability, which may be the predominant depressive mood disturbance in some patients. It is validated. It

has been used in drug studies. It can be used as a repeated measure. In fact, we just saw a patient recently with a very jovial, outgoing, and almost flippant but delightful sense of humor, whose level of severe underlying mood disturbance might have remained hidden if she had not completed this questionnaire. The assessment of clinical depression should be based on clinical criteria, and not on a quick “gut” impression.<sup>62,63</sup>

**DR. BUSE:** Another well validated and brief instrument for screening depression and anxiety is the Patient Health Questionnaire (PHQ-4), a 4-item screener for depression and anxiety.<sup>64</sup> It is comprised of the two primary criteria for major depressive disorder and generalized anxiety disorder from the Diagnostic and Statistical Manual of Mental Disorders- 4th Ed (DSM-IV).<sup>65</sup> The instrument can be completed in a matter of minutes and summed scores can be rated as none/minimal, mild, moderate, or severe symptomology. If the response to the screener is positive, HCPs can use the Patient Health Questionnaire (PHQ),<sup>66</sup> which includes DSM-IV criteria for several Axis I disorders, including depression, anxiety, somatoform disorders, alcohol abuse and eating disorders. The PHQ also includes a standalone depression screener: the Patient Health Questionnaire- depression module (PHQ-9),<sup>67</sup> a validated measure of major depressive disorder based on DSM-IV criteria. The PHQ-9 assesses symptoms and functional impairment over the preceding two weeks with nine items, each with four frequency response-options. A summed score places participants into one of five depression categories: none/minimal, mild, moderate, moderately severe or severe. The Generalized Anxiety Disorder-7 (GAD-7)<sup>68</sup> is a self-administered questionnaire assessing clinically significant anxiety. Its questions evaluate the frequency of symptoms over the preceding two-

week period. Sum scores can be quickly calculated to determine none, mild, moderate and severe levels of anxiety. These instruments can be used both for initial assessment and at follow-up visits to monitor change over time. All of these instruments are well validated and available for use free of charge. They can be accessed at: <http://www.depression-primarycare.org/clinicians/toolkits/materials/forms/phq9>.

**DR. BUSE:** Successful management of migraine is a collaboration between the HCP and patient. Dr. Penzien, are there strategies that HCPs can use to improve adherence with treatment and enhance patient motivation?

**DR. PENZIEN:** This is a particularly pertinent question in the sense that medications are the principal tools that most HCPs use to manage headaches. There is ample evidence in the general medical literature that patients are often nonadherent with their medication regimens—the same holds true for head pain management. And with respect to head pain management, medication overuse or misuse that can produce serious negative consequences.

Head pain management also is often complicated by inappropriate self-medication with over-the-counter drugs, which are readily available at a low cost, and so patients often perceive their use as relatively inconsequential or harmless. Moreover, issues often arise regarding adherence with appointment keeping and with adherence to recommendations for lifestyle modifications—such as improving sleep hygiene, dietary recommendations, and application of stress management techniques. Most HCPs seem to recognize that patients, in general, are nonadherent, but they often neglect to consider that the individual patient sitting

in their office may be among those who are nonadherent. It's worthwhile to recognize that over a third of prescriptions are never even filled, let alone used, about half or more of the prescriptions are not taken sufficiently to get the therapeutic benefit, and that patients with chronic illness are even less likely to be adherent than patients with more acute illnesses. And adherence with lifestyle change recommendations, of course, can prove even more problematic.

What are some things that HCPs can do to facilitate adherence? A primary strategy is to understand the factors that can have a bearing on adherence. For example, HCPs should recognize that choice of dosing regimen makes a difference. The more doses a patient is instructed to take per day, the more likely it is the patient will be nonadherent. It is much more likely for a patient to be adherent to a one-a-day dose than multiple doses. Prescribing using complex regimens where the patient is advised to take certain doses under certain conditions or combining multiple medications also reduces the likelihood of adherence. Likewise, prescribing medications having a poor side effect profile can greatly contribute to nonadherence—particularly if the patient is not well advised about the likelihood and seriousness of these side effects. Furthermore, carefully advising patients—preferably in writing—about when and how to optimally use their medications as well as what and when benefits may accrue with their use also can greatly facilitate adherence. This latter point taps into the issue of quality of patient-provider communications, which is a key determinant of treatment adherence. Additional strategies are suggested in Table 1.

**DR. ANDRASIK:** We know that patients are not always ready for change and methods have been determined

for gauging a patient’s readiness for change with respect to a number of medical and psychological problems. However, few attempts have been made in headache research. Within the area of addictions, motivational interviewing has been found to be helpful in engaging patients.

**DR. BUSE:** Thank you for providing those strategies for enhancing motivation and improving adherence. Dr. Penzien also mentioned the importance of good communication. I could not agree more. Effective medical care is dependent on effective medical communication. The American Migraine Communication Studies (AMCS) I and II evaluated current HCP-patient communication in headache care and tested a simple educational intervention. The AMCS I was an observational study of in vivo discussions and diagnoses of migraine in clinical practice. 78 patients likely to discuss migraine were recruited immediately before their

normally scheduled appointment. Appointments were video recorded and separate interviews with patients and HCPs were conducted following the visits. Sixty interactions were evaluated. The average migraine discussion lasted 12 minutes and HCPs asked an average of 13 questions, of which 91% were closed-ended or short-answer questions focused on frequency (primarily number of attacks per month), severity, headache symptoms, triggers, and other similar features. Questions regarding headache-related impairment and quality of life were infrequent. Low levels of agreement between HCPs and patients were seen immediately following the visit when asked about migraine attack frequency and headache-related disability. HCPs and patients did not agree on headache frequency following 55% of visits and did not agree on the level of impairment following 51% of visits. It is likely that the disagreement on headache frequency was due to asking about

“migraine attacks” instead of “migraine days” or days with migraine. This led HCPs to underestimate the number of headache days per month. In addition to asking about days with headache, it can also be helpful to ask about days without headache. Patients with chronic migraine may have some type of headache every day, but severe headache or migraine only on specific days. When asked about the number of headache days, they may report the number of migraine or severe headache days but disregard the number of days with other types of less severe headache. Following up a question about headache days, with the question, “On how many days were you headache-pain-free in the past month?” will help gather complete data and facilitate an accurate diagnosis. For those patients who respond that they did not have any days without headache pain, the follow up question, “Were you completely headache-pain-free for any moment in the past month?” will help identify continuous headache for those patients who reply in the negative. The lack of open-ended questions probably limited patients’ ability to express their level of disability and impairment and did not allow them to share the effect that migraine had on their lives.

Researchers followed this study by testing an intervention designed to address the areas of concern observed in the first study. In AMCS II,<sup>71</sup> 15 HCP participants from the first study participated in a 90-minute training session that reviewed the results of AMCS I<sup>72</sup> and provided two communication strategies: “Ask-Tell-Ask” strategy to assess headache frequency and the use of open-ended questions to assess migraine-related impairment.

The “Ask-Tell-Ask” strategy is based on the theory that effective education requires assessing what the patient already knows and believes

### Facilitating Headache Treatment Adherence\*

**Nonadherence is prevalent among headache patients and undermines treatment efficacy.**

**Recalling Appointments (appointment reminders) is fundamentally the most cost-effective adherence-enhancing strategy.**

**Simplified and individually tailored medication regimens improve adherence.**

**Screening and management of psychiatric comorbidities is encouraged as psychiatric comorbidities (e.g., anxiety, depression) are often associated with poor adherence.**

**Self-efficacy (in this instance, the degree to which a headache sufferer believes that his/her actions can impact headache symptoms) is a modifiable psychological process that often can predict and improve adherence.**

Adapted from Rains JC, Penzien DB, and Lipchik GL. Behavioral facilitation of medical treatment of headache: Implications of noncompliance and strategies for improving adherence. *Headache*. 2006;46(Suppl 3): S142–143.

**TABLE 1**

then building on (or correcting when necessary) that understanding. This strategy can be used for any medical communication, but in this study it was used primarily to ensure optimal communication about migraine frequency in headache days. This strategy is based on three simple steps: Step 1 is to “ask” the patient to explain or restate the issue, problem, or treatment in his or her own words. This step, which allows the HCP to assess the patient’s personal beliefs, emotional responses, and understanding of the situation, helps guide the HCP in furthering effective communication. Step 2 is to “tell” the patient the relevant facts, diagnosis, or treatment plan, using language at a level that he or she understands. This provides opportunities to correct any misunderstanding or incorrect information communicated by the patient in response to the first question and to reinforce and validate the correct information that the patient shared. Step 3 is to again “ask” the patient to rephrase the information given in step 2 in his or her own words. This allows the HCP to reassess the patient’s level of understanding and gives the patient an opportunity to ask questions and express concerns. Results showed that use of the “Ask-Tell-Ask” strategy led to a more accurate assessment of migraine frequency and impairment during and between attacks, more frequent discussion and prescription of preventive therapy, greater satisfaction with office visits on the part of the HCPs and their patients, and more frequent discussion and prescription of appropriate migraine therapies.

One concern expressed by 79% of HCP participants was that using the “Ask-Tell-Ask” strategy and asking open-ended questions would significantly increase the length of the interview. Conversely, visit length was actually 90 seconds shorter on

average compared with visits in the observational stage of the study without the intervention (AMCS I).

Such strategies as the use of open-ended questions, the “Ask-Tell-Ask” technique, active listening, and “being fully present” with the patient can significantly improve the quality of the medical relationship, with positive and more satisfying outcomes for both patient and healthcare provider.

**DR. BUSE:** Thank you Drs. Andrasik, Penzien and Lake for this interesting and informative discussion. To summarize, behavioral treatments with demonstrated empirical

efficacy for headache management have become standard components of specialty headache centers and multidisciplinary pain management programs. They can be essential components of a comprehensive headache management plan for appropriate patients. They can be used independently or in conjunction with pharmacologic treatments and, in fact, data show that patients fare better with a combination of these therapies compared with either type alone.

These therapies are endorsed by the American Medical Association, the World Health Organization, and the National Institutes of Health, and

## Clinical Implications

- ▶ Behavioral treatments play an important role in the effective management of headaches and migraine. Behavioral treatments refer to behavioral and cognitive interventions including cognitive behavioral therapy (CBT), biofeedback, relaxation training, stress management, lifestyle modification and patient education.
- ▶ Behavioral treatments are well suited for patients that prefer such interventions; display a poor tolerance for specific pharmacologic treatments; exhibit medical contraindications for specific pharmacologic treatments; have insufficient or no response to pharmacologic treatment; are pregnant, are planning to become pregnant, or are nursing; have a history of long-term, frequent, or excessive use of analgesic or acute medications that can aggravate headache problems (or lead to decreased responsiveness to other pharmacotherapies); or exhibit significant stress or deficient stress-coping skills.
- ▶ Empirical evidence supports the use of behavioral interventions for headache and migraine management. They can be used independently or in conjunction with pharmacologic therapies.
- ▶ Behavioral interventions are also helpful in managing psychiatric comorbidities of migraine and medication overuse.
- ▶ Several strategies exist for improving medical communication, enhancing patient motivation and improving adherence.

many other professional Organizations. Some behavioral techniques can be incorporated by HCPs during an appointment (e.g., communication strategies, adherence enhancement, education); some can be practiced by the patient independently (e.g., diaphragmatic breathing and visual imagery); and some require a referral to an appropriately trained professional (e.g., biofeedback training, cognitive behavioral therapy). Once learned, these behavioral interventions and strategies give patients a set of tools that they can use and benefit from throughout their lives.

Psychiatric comorbidities are common with migraine, especially in chronic migraine and other chronic forms of headache. These conditions are difficult for patients, may compli-

cate treatment, and lead to worse outcomes. There are several instruments that can be used in clinical practice to assess and monitor psychiatric comorbidities. Referral to a mental healthcare professional may be warranted, in which case open communication and coordinated care may help in providing optimal care and managing clinical challenges.

Effective communication is essential for effective medical care. Communication between HCPs and patients is the basis of the therapeutic relationship and can help or hinder medication and treatment adherence, outcomes, and both patient and provider satisfaction. The use of open-ended questions and the ask-tell-ask strategy can improve the quality of communication and enhance

the interactions and relationships. Several suggestions were offered that can be used to improve communication, adherence and motivation.

Drs. Lake, Andrasik, and Penzien, thank you very much for your participation. This has been an engaging and enlightening discussion.

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