ABSTRACT

There is growing appreciation for the prevalence and importance of comorbid conditions associated with epilepsy, including migraine as well as other disorders. In managing a patient with epilepsy and migraine, the first consideration should be to assure that both disorders are not symptomatic of a common treatable cause, such as a structural brain lesion. Following a negative evaluation, attention must turn to treatment, particularly seizure control. Although an occasional, nondisabling headache is tolerable for most people, even a single seizure has severe medical, psychological, and social ramifications. Also, controlling seizures may also improve migraine symptoms. Even if migraines persist, standard migraine abortive and preventive therapies work well for most patients with epilepsy. Therefore, treating epilepsy initially, and seizures and migraine symptoms independently (either sequentially or in parallel), is reasonable and usually successful in patients with comorbid epilepsy and migraine. Medications are the first line of therapy for both seizures and migraine. The choice of medications depends on specific aspects of a patient’s personal profile (such as age, sex [particularly for women of childbearing potential], weight, cognitive function, potential adverse medication events, and drug-drug interactions) and coexisting or comorbid conditions such as migraine. Some antiepileptic drugs (AEDs) may also prevent migraine. Therefore, such AEDs warrant special consideration as initial therapy or when changes or additions are necessary to control seizures in patients with epilepsy and migraine. There are practical and theoretical advantages to treating these 2 comorbid conditions with a single medication, but there are no systematic studies of AEDs for managing patients with both epilepsy and migraine. With more than 15 different drugs currently available for treating epilepsy, physicians have many choices and should carefully tailor AED therapy for each individual, considering such comorbidities as migraine to optimize outcomes.

Numerous advances in epilepsy diagnosis and management shed insight not only on the disease process, but also on medical treatment options that can be tailored for the benefit of an individual patient. For instance, the development of technologies such as video electroencephalography, magnetic resonance imaging (MRI), positron emission tomography, and single-photon emission computed tomography increase the accuracy of epilepsy diagnosis, reveal the types and causes of seizures, and help to guide optimal therapy. Medication remains the mainstay of initial epilepsy treatment, and we are fortunate to have more than 15 effective antiepileptic drugs (AEDs) currently available for treating patients with seizure disorders (Table 1). Surgery is a useful option for some of the approximately one third of our patients who are refractory to drug treatment. In addition, clinical and basic science research is continually increasing our knowl-
edge of seizures as well as the basic mechanisms and genetics of epilepsy. All of this holds great promise for improving epilepsy treatment and patient care. Such clinical investigations have also given us a greater appreciation for the prevalence and importance of comorbid conditions, including migraine, depression, cerebral palsy, and mental retardation, when formulating optimal treatment strategies for people with epilepsy and seizures.

**APPROACH TO THE PATIENT WITH MIGRAINE AND EPILEPSY**

When managing a patient with comorbid epilepsy and migraine, the first consideration should be to assure that both disorders are not symptomatic of a common treatable cause, such as a structural lesion. Both migraine and epilepsy are now recognized as episodic and paroxysmal neuronal disorders that share some clinical features and potentially some pathophysiological mechanisms.¹

Conditions such as head trauma, cerebrovascular malformations, presence of tumors, or vasculitis can cause or are associated with both epilepsy and migraine.¹ Thus, these conditions should also be considered as potential causes for symptoms when clinically appropriate in patients who present with epilepsy and migraine. Depending on the clinical situation, brain imaging studies, such as MRI or other studies, may be warranted in such patients to exclude a treatable cause for the symptoms of seizures and migraine in a given patient. In most instances, these studies are unlikely to reveal structural brain disease. Indeed, epilepsy and migraine are comorbid conditions that often occur together without a clear explanation (for more detail, see the article by Dr Lipton in this monograph).

Although both seizure and migraine are relatively common disorders and are known to occur together frequently, they can still sometimes be the consequence of or be associated with some more rare syndromes or conditions. These disorders include such conditions as mitochondrial encephalopathy lactic acidosis and seizures (MELAS) syndrome, occipital lobe epilepsy (or Panayiotopoulos syndrome, a syndrome of benign childhood partial seizures with ictal vomiting and electroencephalogram occipital spikes; for more detail, see article by Dr Lipton in this monograph); familial hemiplegic migraine (for more detail, see article by Dr Haut in this monograph); and antiphospholipid syndrome.¹ Most of these are rare disorders, but, when appropriate, they may warrant special consideration in individuals presenting with epilepsy and migraine, based on the specific clinical circumstances in some patients.

**TREATMENT OF THE PATIENT WITH COMORBID EPILEPSY AND MIGRAINE**

In regard to treatment of patients with comorbid epilepsy and migraine, control of seizures warrants initial emphasis because, for most such patients, seizures are the more limiting disorder. Unlike in migraine, in which a sporadic occasional headache is usually tolera-

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**Table 1. Principal Mechanisms of Antiepileptic Drugs**

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<thead>
<tr>
<th>Ion Channel (Na, Ca) Modulation</th>
<th>GABA Potentiation</th>
<th>Multiple, Other, or Unknown</th>
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<tbody>
<tr>
<td>Phenobarbital</td>
<td>Valproate</td>
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<tr>
<td>Carbamazepine</td>
<td>Felbamate</td>
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<tr>
<td>Lamotrigine†</td>
<td>Topiramate</td>
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<td>Ethosuximide</td>
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<td>Zonisamide†</td>
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<td>Oxcarbazepine</td>
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*US Food and Drug Administration approved for migraine prevention.
†Some evidence indicates possible effectiveness for migraine prevention, but these agents are not US Food and Drug Administration approved for migraine.
GABA = gamma-aminobutyric acid.
ble, even an occasional seizure has severe ramifications. For example, after even a single seizure, many states revoke driving privileges for up to 1 year, and employers may prohibit certain types of work. A rare seizure may therefore result in loss of independence, loss of driving privileges, loss of or decreased income, disability, stigma, low self-esteem, and even increased risk of death. Sudden unexpected death in epilepsy occurs in roughly 1 of every 500 to 1000 epilepsy patients each year, rising to 1 per 200 persons among those with more severe and uncontrolled seizure disorder.9 Therefore, my emphasis at the initiation of therapy for the patient with epilepsy and migraine is to control the seizures.

My optimal treatment goal for the patient with epilepsy is well expressed in a phrase that I often relate to my patients. I start out by telling them that our goal of seizure control begin with proper diagnosis and determination of the seizure type. After that initial evaluation, medication treatment is the first line of therapy (see Sidebar). Drug choices are narrowed to those that have shown benefit for the particular type of seizure or epilepsy that the patient manifests. The majority of seizures are partial in onset, and most of the currently available AEDs are reported to be similarly efficacious in controlling seizures in clinical trials. Some specific epilepsy syndromes such as absence epilepsy or juvenile myoclonic epilepsy (JME) and its variants respond best to specific AEDs and this will more strictly guide therapy choices (eg, ethosuximide and valproate in absence epilepsy and valproate for JME and its variants). The next consideration in selecting an AED is side-effect profile. In that regard, the various AEDs are far from equivalent, and this is where we really need to focus our attention in selecting the best agent for an individual patient with seizures to try to maximize outcomes and quality of life. For example, as in migraine treatment, choice of medication should be guided by many aspects of the patient's profile, such as age, sex (particularly women of childbearing potential), weight, cognitive function, comorbidities, medication adverse events, and potential for drug-drug interactions. As with migraine, it is reasonable to start low and go slow in dosing AEDs for patients with epilepsy. One particular concern is for women. Recent information from pregnancy registries in the United States and worldwide indicate that valproate is considerably more teratogenic than other AEDs, particularly at higher doses.10-12 In view of those types of findings, many individuals are already recommending and several groups are considering recommendations for clinicians to specifically consider alternatives to valproate in women of childbearing potential.10-12

In general, monotherapy is preferred for treating seizures, but sometimes patients with epilepsy benefit from the addition of a second or even a third AED (see Sidebar). Some thought has been given to using AEDs with different mechanisms of action in combination to optimally control seizures, so-called “rational polytherapy” (Table 1), but this approach is not of established value in the treatment of epilepsy or migraine.

AED therapy changes are sometimes necessary to achieve the best outcomes. For instance, Kwan and Brodie prospectively studied 525 patients with newly diagnosed epilepsy to identify AEDs and factors associated with the best seizure control.13 Previous studies had shown that approximately one third of patients with epilepsy never achieve remission or complete seizure freedom.14,15 In the Kwan and Brodie study, the authors confirmed that finding and found that 63% of study participants achieved seizure freedom with AED therapy. Persistent seizures were more common in patients with symptomatic epilepsy or seizures due to a known cause or likely cause, compared with so-called idiopathic epilepsy (40% vs 26%, P = .004). Seizure-free rates were essentially the same between those taking older AEDs versus newer AEDs (67% vs 69%). If the treatment response was incomplete or the adverse events were intolerable, patients could switch or add AEDs. Only 47% of study participants became seizure-free with the first AED tried. An additional 14% were seizure-free when changes were made and a different AED was tried. Only an additional 3% were seizure-free when 2 or more AEDs were used in combination.13 This study nicely illustrates what patients and physicians can expect from AED therapy, and that AED changes may be necessary and appropriate to achieve optimal seizure control. Indeed, each time AEDs are changed or added may be an opportunity for physicians to reconsider comorbidities, such as migraine, in their choice of medication in an effort to obtain the best patient outcomes (see Sidebar).

Another reason to focus on seizure control first in patients with epilepsy and migraine is that control of seizures may sometimes reduce or even eliminate headaches. For example, some headaches and migraines in patients with seizures are a consequence...
of or closely associated with their seizures. Headaches such as postictal, ictal, or preictal headaches are associated with seizures, and these may have features of migraine. Clearly, if seizures are a trigger for migraine, seizure control can be helpful and important in managing the headache symptoms.

When migraine persists as a symptom in patients with epilepsy, even after optimal therapy of seizures, I turn to the proven standard migraine therapies, just as I would in any other type of patient, and these are usually effective (Table 2). Abortive therapy for migraine is the starting point, with trials of over-the-counter medications such as aspirin or nonsteroidal anti-inflammatory drugs. For persisting migraine, one can move to triptans or ergotamine as necessary. Frequent or disabling migraines merit preventive therapy. Prevention includes both lifestyle changes (ie, avoiding triggers) as well as drug therapy such as AEDs, tricyclic antidepressants (TCAs), beta blockers, or calcium channel blockers (as discussed in detail by Dr Silberstein elsewhere in this monograph). TCAs may lower seizure threshold for some patients, but TCA-induced seizures are not common in my experience (and I prescribe these drugs frequently). TCAs also have the potential advantage of treating another prevalent comorbidity in epilepsy, depression. Controlling a comorbid condition such as migraine or depression to me outweighs the potential small risk of lowering seizure threshold to the point of triggering seizures with TCAs.

Appreciation of the coexistence or comorbidity of migraine and epilepsy also offers some potential therapeutic advantages because both disorders may sometimes be treated with the same medication. With a single drug, there are several practical and theoretical advantages. In particular, there are likely to be fewer drug-drug interactions, less risk of adverse events, increased compliance because of the convenience of single-drug dosing, and cost reduction.

It seems reasonable to expect that some AEDs might be useful in treating migraine, and some are (Table 1). Both migraine and epilepsy are episodic, paroxysmal, neuronal disorders and AEDs are, in the broadest sense, neuronal stabilizers or neuronal modulators. Specifically, 2 AEDs (valproate and topiramate) are US Food and Drug Administration (FDA) approved for migraine prevention and others have been reported in case reports or small series to benefit some patients with migraine but are not FDA approved (Table 1).

Still, there are no studies of any AED in treating comorbid epilepsy and migraine in a patient population. Therefore, some caution is appropriate in trying to use AEDs to treat both migraine and seizures in the same patient. For example, the dosage of AEDs to which migraine responds is considerably lower than the doses reported to control seizures, so factors such as these must be taken into consideration when using or adding AEDs in attempts to control or prevent migraines in patients with epilepsy.

### CONCLUSION

Treatment approaches for the patient with comorbid epilepsy and migraine are similar to approaches to patients with only epilepsy or only migraine. Standard proven medications that are usually effective in treating each of these disorders independently are likely to be successful in patients with this comorbidity. In general, epilepsy is the more critical of the disorders to control fully because of the more serious consequences of a seizure as compared with a migraine. In choosing medications, the clinician must be mindful of the patient’s profile (eg, age, weight, concomitant medications) and choose a medication that suits that profile most appropriately. When necessary, standard acute abortive therapies for migraine are also usually effective and adequate to manage migraine symptoms in patients with epilepsy. Should migraine symptoms be severe and frequent enough to require preventive therapy, some consideration to using AEDs that may also prevent migraine seems warranted. Some AEDs are useful in preventing migraine. In particular, valproate

<table>
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<th>Table 2. Principal Mechanisms of Antiepileptic Drugs</th>
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<tr>
<td><strong>Abortive Therapy</strong></td>
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<tr>
<td>Pain medications (ASA, NSAID, etc)</td>
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<tr>
<td>Triptans</td>
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<tr>
<td>Ergotamines</td>
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ASA = aspirin; NSAID = nonsteroidal anti-inflammatory drug; AED = antiepileptic drug.
and topiramate are proven and FDA approved as effective in migraine prevention, while others may also be helpful but are not so well established or FDA approved. So, it seems reasonable and prudent to consider AED therapy, either as monotherapy or in combination, for some patients with comorbid migraine and epilepsy, particularly if the migraines are not sufficiently controlled by acute therapy. There are practical and theoretical advantages to treating these 2 comorbid conditions with a single medication, but there are no systematic studies of AEDs for managing patients with both epilepsy and migraine. AED treatment of seizures can and should be tailored for each individual considering such comorbidities as migraine and striving to achieve optimal outcomes and quality of life for our patients.

**DISCUSSION**

**Dr Kossoff:** Dr Krumholz, you mentioned that some of the anticonvulsants with multiple mechanisms seem to be the effective ones. Has anyone looked at vagus nerve stimulation? We do not know how it works; it probably has multiple mechanisms. I know they are looking at it for depression.

**Dr Silberstein:** They are also looking at it for migraine. Alex Mauskop presented some data a couple of years ago showing it to be beneficial in migraine.

**Dr Krumholz:** I was not aware of those trials, but I know that the people at the vagus nerve stimulator company, Cyberonics, are very interested in therapy of comorbidities associated with epilepsy. Some investigators noted early on that patients with epilepsy who were treated with vagus nerve stimulation had better mood, so now they are working very hard for an indication for using vagus nerve stimulation in depression, which we recognize as an important comorbidity with epilepsy.

I cannot say much about my personal experience with vagus nerve stimulation for migraine or depression. Fortunately, when patients with epilepsy control their seizures, they feel better, and it is hard to know why they feel better, apart from the fact that their seizures are controlled. For example, if they have fewer seizures, their mood may be better, and their headaches may be better. From an epileptologist’s point of view, I think that if we can get seizures under control, the patient’s quality of life is much better, so it is hard to tease out whether that is why their migraines and depression are better—or if it is because the treatment or medicine is working on both in some unique way.

**Dr Lewis:** The comorbidity of obesity in migraine, or obesity in any disorder in childhood and adolescence is a big concern. It was mentioned that with topiramate there is about a 4% weight loss across the board. Comparing the epilepsy trials and the migraine trials with topiramate, was that weight loss principally in the patients with higher BMIs [body mass index], or was that clearly across all weight spectrums?

**Dr Krumholz:** I cannot answer that specifically. My recollection is that weight loss will certainly affect some patients more than others, and some patients actually have to discontinue drug because of the severity of the weight loss. But I think it is across the board. I do not think it is selective to the patients who are very overweight.

**Dr Silberstein:** I have not been able to get the data analyzed yet for the migraine trials, but that percentage was across the board. What I understand from the epilepsy trials, the more you weighed, the more you lost, and what we are trying to do is get the exact same breakdown for the headache trials.

**Dr Gidal:** Bill Rosenfeld in St. Louis has presented his analysis. He found that across the board there is weight loss and it was sustained, but the magnitude of the weight loss was greater in patients with a higher BMI.

**Dr Lipton:** Is there any evidence that obesity is an exacerbating factor, or prognostic factor, in epilepsy, as it is for migraine?

**Dr Krumholz:** I am not aware of it.

**Dr Gidal:** Unless they get sleep apnea because of it.

**Dr Haut:** It seems that when people present with new-onset seizures in an age group where you do not expect it (eg, in their 30s or 40s), without a structural lesion, you should explore the sleep history and see if there is undiagnosed sleep apnea as the trigger.

**Dr Krumholz:** There certainly is an interest in weight loss in epilepsy. Dr Kossoff is looking at the issue of whether the Atkins Diet, or similar diets such as the ketogenic diet, benefits people with epilepsy. There are data going back to ancient times that starving could improve seizure control.

**Dr Kossoff:** For years we have talked about it being ketosis, but there has been more recent animal data that maybe caloric restriction is just as important. It is hard to know. Some people have talked about that with topiramate, that along with its other mechanisms (carbonic anhydrase inhibition, AMPA/kainate antago-
nism) there may be a caloric mechanism, too. Patients lose their appetite a bit on topiramate.

**Dr Krumholz**: Dr Silberstein presented very nice data showing that the side-effect profile of topiramate, in terms of cognitive side effects, was not particularly terrible. Yet, in the epilepsy literature, the side-effect profile of topiramate in terms of cognitive side effects or problems with speech, is much higher. I think it is important to keep in mind that topiramate, in its initial clinical drug trials, was used at some very high doses (up to 1000 mg daily) and we no longer feel that that high of a dose is necessary or appropriate. So, I think you have to be very careful in looking at the clinical drug trials on topiramate and extrapolating that to what its side-effect profile is. In clinical practice today it is probably not nearly as bad, particularly if it is used as monotherapy. Those drug trials were wonderful in showing the effectiveness of topiramate for seizures, but it stamped topiramate with the label of a terrible side-effect profile on cognitive ability. There are certainly concerns in that regard, but they are probably not as severe as the initial clinical trials suggested.

**Dr Gidal**: We now know that you can use lower doses for both migraine and epilepsy, especially new onset. There are still some subtle effects, especially if you talk to the spouse or the significant other, but I think it is extraordinarily well tolerated in most people.

**Dr Gidal**: We know from the recent pregnancy registries about the teratogenicity of valproate. There are other reproductive abnormalities with epilepsy that we have become concerned with, such as menstrual cycle anomalies, and polycystic ovary syndrome. It is always confusing because we do not know whether there is some limbic involvement. Do you see this in migraine?

**Dr Silberstein**: There is no evidence I know of that it occurs in other populations of patients. A study in patients with bipolar disorder did not show it. To the best of my knowledge, that is unique to the epilepsy population treated with the drug.

**Dr Gidal**: In the migraine population of your study, were women specifically asked about menstrual cycle irregularity?

**Dr Silberstein**: Not in that trial. I have been trying for years to get them to study that population, but I do know they studied the population with bipolar disorder and did not find anything.

**Dr Krumholz**: Dr Gidal, do you think this issue of valproate and its effects on menstrual cycle and polycystic ovary syndrome in women with epilepsy is a credible concern?

**Dr Gidal**: I think it is a real concern. I was somewhat skeptical initially (Isojarvi’s work from a homogeneous population), but then Martha Morrell in New York has generated some data that seem to be compatible with Isojarvi’s work. I think there are some good mechanistic reasons to explain it, but I have always had the same concern—whether there is an interaction with the disease state when you have limbic involvement, hypothalamic involvement.

**Dr Silberstein**: There is no evidence that it occurs in other populations.

**Dr Gidal**: As I understand, though, it is not clearly dose dependent, is it?

**Dr Gidal**: Yes. There does not appear to be a relationship to concentration, but I do not know if those studies have ever been done to exactly tease it out. I can tell you from our work with weight gain it does not appear to be concentration dependent.

**Dr Silberstein**: Does it occur in patients who are on polytherapy with an enzyme-inducing AED, or only in those on monotherapy?

**Dr Gidal**: The best evidence for that comes from Isojarvi’s work. It occurred with monotherapy as well as combination. There is an over-representation of endocrine abnormalities compared with women who are just on carbamazepine or something else, or controls.

**Dr Kossoff**: I think Dr Morrell found that there are certain women who are susceptible to the problems and certain ones who are not, and there may be something potentially identifiable in the future, but it was not dose related.

**Dr Silberstein**: Do people still believe Andy Herzog’s explanation, that the other AEDs correct the abnormal metabolism?

**Dr Gidal**: It sounds reasonable, that you are actually treating it with an enzyme inducer because you are decreasing testosterone concentrations. I don’t know. I cannot comment on whether people believe that or not.

**Dr Haut**: We are very aware now of the risk of bone loss with chronic AED use. Are you conscious of that in migraine? We are ordering bone densitometries on many patients now.
**Dr Silberstein:** Not yet. Part of the reason is that we do not have the same long-term concerns because we try to get people off the drugs after a period of time, but it should be [a concern] in patients on long-term use.

**Dr Silberstein:** Since we are talking about comorbidity in treating depression in people with epilepsy, the recommendation now is no longer to use tricyclic antidepressants [TCAs], but use either SSRIs [selective serotonin reuptake inhibitors] or SNRIs [serotonin-norepinephrine reuptake inhibitors], because of compliance. I think the professional societies made that recommendation. We have always recommended for comorbid depression and migraine that we pick a tricyclic first because it will hit 2 birds with 1 stone. Should we change those recommendations? Maybe we should give a drug that, instead of getting a 2-for-1, is better tolerated so the depression is treated, and then give an additional drug to treat either the migraine or the epilepsy. Our recommendations are really based on TCAs and not modern treatment of depression.

**Dr Lipton:** When we treat migraine with antidepressants, we typically do not give antidepressant doses. We say we are getting a therapeutic two-fer, but in reality we are undertreating depression. In patients who have migraine and depression together, antidepressant doses of antidepressants have an antidepressant efficacy, but sometimes the migraine is effectively treated but the depression is undertreated, and I then need to add an SSRI to the tricyclic to manage the depression. The parallel issue comes up with migraine and epilepsy, because the effective dose of topiramate for migraine is 75 mg or 100 mg, and the average dose for epilepsy is about twice that. So, in going for the therapeutic two-fer, the risk is undertreating the disorder that requires the higher dose of medication.

**Dr Krumholz:** So when there are 3 coexisting disorders, what type of comorbidity is that? One of the very common comorbidities in epilepsy is depression. It is very serious because in various studies looking at quality of life, depression clearly is a major predictor of quality of life in people with epilepsy, perhaps as much or even more so than seizures.

**Dr Lipton:** Comorbidities are usually discussed in pair-like fashion, but in reality, if you look at migraine, depression, and epilepsy as a triad, we know that each of the disorders is associated with the other. If, for example, your real interest is migraine and epilepsy, the association of depression with each disorder could allow you to falsely conclude or to overestimate the association between migraine and epilepsy. So if you look at the disorders 2 at a time, and if you are in a situation where 3 disorders are comorbid, the third disorder is the confounder whose influence needs to be taken into account.

**Dr Gidal:** In North America, the majority of patients with epilepsy are still treated with phenytoin and carbamazepine—enzyme inducers. Most of the antidepressants—SSRIs, SNRIs, and TCAs—are metabolized through the P-450 system. Case reports and some smaller, purely kinetic studies suggest dramatic reductions in the area under the curve of these drugs. Typical doses used for headache or depression may be wholly inadequate for treating epilepsy, and no one has really explored that yet. There may be real differences in the dose requirements, especially if you are going from carbamazepine to topiramate. There are a lot of outcomes that need to be teased out. I do not think we know what the right dose is yet.

**Dr Krumholz:** Everything we are talking about is based on looking at people with epilepsy or people with migraine. I do not know of any studies looking at true comorbidity of epilepsy and migraine together, in terms of treatment. So we are hypothesizing what would work, but the studies in which they take people with epilepsy and migraine and treat them in some specific way, as far as I know, they do not exist. I am sure that there are anecdotal or small case series, but clinical trials are not available that I am aware of.

**Dr Lipton:** The randomized trials do not exist. The underlying assumption when we talk about going for the therapeutic two-fer, given a patient with migraine and epilepsy, is that somehow headache control, seizure control, quality of life, or adverse-event profile would be better if you gave 1 agent rather than 2.

**Dr Krumholz:** I do not think we know that even in our more common comorbidities, such as depression and epilepsy. We have ideas about it, but we do not know.

**Dr Silberstein:** We are discussing the advantages of going from polytherapy to monotherapy. There are some disadvantages. There is no synergism, and the dose may be higher. We may misdose one disorder, and the adverse events may be higher if you use 1 drug alone. So, for example, if you had a tricyclic, you may need a higher dose than you would with another drug.
and the patient is less likely to be compliant. That is just something we had not thought about before.

**Dr Lipton:** The epilepsy world is a step ahead of us in recognizing that sometimes 2 drugs are better than one.

**Dr Gidal:** I think we are moving away from ideas on rational polytherapy, because it presumes we know the mechanisms of the drugs, and we realize we really do not. The evidence is really somewhat lacking there.

**Dr Lewis:** We were talking earlier about using low doses of tricyclic antidepressants. We notice in the adolescent and young adult population that when they are having 2 headaches a month, very often they are having significant comorbid depression, and if we get their headaches down to 1 a month, their depression gets better. Their school activity improves; their at-home activity improves. I am not sure that the depression is being directly treated as much as removing the burden of their headache.

**Dr Gidal:** In my VA [Veterans Affairs] population, we have a significant number of patients who are very well controlled with respect to their seizures, but they have clinic visits because of their headaches. We probably do not pay as much attention to it as we should. That tends to be their most disabling complaint. But many times the headaches just do not sound migraine-like. They have chronic daily headaches or these other types of disorders.

**Dr Silberstein:** Most of them probably have medication-overuse headache.

**Dr Lewis:** Diet intervention has fallen out of favor in adolescent migraine.

**Dr Silberstein:** I say the single best treatment in the world for migraine is a chocolate bar. Here is the problem: somebody has the desire to eat chocolate and gets a migraine headache, and you blame it on the chocolate. But if somebody goes out and eats pickles and ice cream and they find out they’re pregnant a week later, I do not know anybody who would blame it on the pickles and ice cream. Fundamentally, I think many of the food triggers are really premonitory desires. I think we have good scientific evidence for caffeine withdrawal, alcohol, maybe MSG [monosodium glutamate]. Nothing else has any good evidence. Instead of recommending to my migraine patients dietary avoidance, I recommend just the opposite. I tell them to eat all they want.

**REFERENCES**