Adherence to antiepilepsy drug therapy

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A R T I C L E   I N F O

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A B S T R A C T

Adherence to antiepilepsy drug (AED) therapy is critical for effective disease management, yet adherence and persistence rates are low due to several barriers. The definitions of adherence (80% rate of total pills taken, medication possession ratio, and days covered by prescriptions filled) and methods of measurement (patient self-reports, serum drug levels, pill counts, electronic bottle tops, and reviews of pharmacy records) are not without limitations, and their applicability to epilepsy is not clear. The use of simple adherence scales during office visits can provide an overall impression of a patient’s adherence and can serve as a basis for practitioner–patient dialog. Efforts to improve adherence should focus on provider and healthcare system determinants versus those focused only on the patient. These interventions include non-judgmental communication, patient education, simplification of the dosage regimen with once-daily therapies, and the use of patient reminders.

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1. Introduction

Daily antiepilepsy drug (AED) medication is the foundation of epilepsy treatment. Because epilepsy is so common (0.5–1.0% of the population are affected), there are enormous public health consequences for any systematic treatment failure. If one accepts the premise that AEDs are effective, then the daily medication regimen is critical. A quote attributed to C. Everett Koop, MD, former Surgeon General of the United States [1,2], states the obvious: “Drugs don’t work in patients who don’t take them.” Indeed, the frequency of nonadherence and misadherence that occurs during chronic medical therapy is surprising. Adherence, in the context of medicine, means the degree to which a patient follows a prescribed treatment program. The term implies an agreement between practitioner and patient and is generally preferred to the older term “compliance,” which suggests to some a more authoritarian, practitioner-commanded relationship. Adherence has many components and may include interventions such as lifestyle changes as well as specific therapies and may be considered a category of patient self-management [3].

Because epilepsy is characterized by sporadic symptoms (i.e., seizures) rather than a continually perceptible phenomenon like pain, the patient is required to take medications which do not have immediately obvious benefit. The consequences of nonadherence may not appear immediately; thus, patients who miss doses without adverse results may conclude, erroneously, that rigorous medication adherence is not important. Furthermore, patients with epilepsy must take daily medication for years or for a lifetime. The ability to continue taking medications for long periods of time is sometimes called persistence, as contrasted with short-term adherence. Persistence may be affected by the variability of seizure frequency within a single patient’s course; long periods of remission may induce complacency, and periods of exacerbation may induce fatalism.

These epilepsy-specific factors complicate the assessment of adherence, its effects, and the task of improving adherence. In this review, I will describe methods of measuring adherence, examine the general problem of adherence in chronic diseases, and, with a focus on epilepsy, elaborate on the phenomenon of adherence, examine its medical and economic consequences, and discuss reasons for and strategies to reduce nonadherence.

2. Measuring and defining adherence

The first issue to be considered is how to measure adherence. In the medical literature, attempts to assess adherence have included the use of patient self-reports, including calendars, measurement of serum drug levels, and counting the number of remaining pills at clinic visits. More sophisticated methods include the use of electronic bottle tops that register the time the bottle is opened and the reviews of pharmacy records to determine when the patient filled prescriptions. However, all of these methods have limitations. Patient self-reports may reflect fallible memory or efforts to appear responsible. Serum levels of many drugs are extremely variable between individuals taking the same dosage and may also vary diurnally in a given individual. Electronic monitoring is expensive, and neither this method nor prescription-filling frequency information directly proves ingestion. Measuring persistence commonly proves to be problematic in epilepsy and other chronic diseases because it requires a lengthy observation period in order to account for the variability observed in disease severity and other factors affecting patient behavior.

The simplest method of measuring adherence is to ask the patient about their adherence during an office visit. In addition, practitioners
can ask patients to complete the Morisky Medication Adherence Scale (MMAS) [4,5]. The original version of the scale consisted of 4 questions (Table 1), with a score of 4 representing high adherence, a score of 1 or 2 indicating low adherence, and a score of 3 representing a variable level of adherence subject to the interpretation of the practitioner/investigator. The MMAS was used in a study of 50 patients from the Ohio State University Medical Center’s Comprehensive Epilepsy Clinic to assess medication self-management behaviors. Only 42% of patients achieved a score of 4 [3]. However, this was a cross-sectional study, and patients at a tertiary referral center may differ in systematic ways from the general population with epilepsy.

The MMAS has been studied extensively and expanded in different ways (including the introduction of an 8-item version in 2008 [6]), is internally valid, and has been widely used. Nevertheless, it may strike some as blunt or naïve. It beggars belief that anyone would answer the first question truthfully if they were nonadherent. Question 2 seems like a restatement of question 1, though they each contribute independently to the predictive power. Question 3 may not be very relevant to AEDs since feeling better is not especially a goal of AED therapy or a guide to an effective dosage. Question 4 is very pertinent, although perhaps better wording would be, “Do you ever skip doses?” Moreover, the population in which it was originally validated was skewed toward blacks (91%), women (70%), and patients with relatively little education (mean 8 years) [4]. Nevertheless, the MMAS–4 is a quick and easy method for practitioners to assess adherence and initiate dialogue with patients.

If one defines adherence as taking the exact prescribed amount of medication at the precise times of day every day for an extended period of time, then probably few persons are truly adherent. Researchers must, therefore, agree on a reasonable and practical definition of adherence, preferably based on less subjective data than patient self-reports. Although not specific to any particular disease, an 80% rate of total pills taken, using various methods of assessment, is a common threshold for measuring adherence. In some clinical trials, residual pill counts > 20% may lead to a subject being ejected. The 80% threshold appears to have some validity for cardiovascular diseases [7], but whether it is relevant to epilepsy is uncertain. Obviously, this is a continuous variable and is more likely to produce a continuously varying outcome rather than an abrupt dichotomy between effective treatment and ineffective treatment.

For studies using pharmacy prescription databases, the two common measures of adherence are medication possession ratio (MPR; the percentage of time a patient has access to medications), with a maximum value of 1.0 (i.e., 100%), and days covered by prescriptions filled (the proportion of days in a measurement period covered by a prescription claim for a medication), which can exceed 1.0 to account for overfills. A patient who fills his or her prescription for a 30-day supply exactly every 30 days without fail has an MPR of 1.0 or 100%. One who fills a 30-day supply on average every 60 days has an MPR of 50%. Because patient behavior varies over time but seizures may ensue after a short period of medication omission, it is best to divide the results of long observation periods rather than averaging them. Assessment of adherence over time periods of quarter years (i.e., 90 days) or less is desirable for epilepsy.

### 3. Adherence in chronic medical conditions

During an observation period of 1 year, Briesacher and colleagues assessed adherence among patients with 7 chronic conditions, including epilepsy [8]. Adherent patients were defined as having prescriptions filled covering at least 80% of days. With this criterion, adherence rates ranged from 37% for gout to 72% for hypertension. The adherence rate for “seizure disorders” was intermediate, at 61%. It may be that conditions for which the benefits of medication are perceived to occur in the distant future are associated with poor adherence: a striking 60% of patients prescribed statins stopped taking them within a year, and 90% had stopped by 6 years [9]. This steady erosion of adherent behavior also suggests a need for continuous practitioner reinforcement of the goals of therapy. Adherence is poor even for drugs directly relevant to prevention of deadly outcomes, such as those caused by cardiovascular disease [10]. The problem of nonadherence is confined neither to particular diseases nor to particular cultures and has been shown to persist across national boundaries [11].

### 4. Adherence in epilepsy

Several studies have measured adherence among persons with epilepsy [8,12–16]. Assessment of adherence has gradually become more sophisticated. In a 1982 study of 106 patients, patients were simply divided into 2 groups: “compliant” if they self-reported missing their medication less than once a month and “noncompliant” if otherwise; about half reported themselves compliant by this criterion, and amazingly, this correlated quite well with prescription records indicating fills within 1 week of due date over a 6-month period [17]. Later studies using self-reports have used semi-quantitative scales, especially the Morisky scale. In one such study, 21 (42%) patients fell into a “high adherence group and 29 (58%) into “medium” or “low” groups, but no difference in seizure control between groups was found in this small study [3]. We may guess from self-reporting that about half of patients believe themselves to be quite adherent, but more quantitative and objective measurements are preferable. The later studies using prescription tracking data or electronic caps provide a clearer picture. They indicate that 50%–80% of patients are adherent, applying the looser criterion of taking the dose or at least having the medication in hand at least 80% of the time (Table 2).

What conclusions can we derive from these studies? Firstly, we can conclude that short periods of observation (1 month or quarterly) are associated with higher levels of adherence. Secondly, we can infer that a very large number of patients fail to maintain adherence over a period even as short as a single year. Finally, we can conclude that the average patient is nonadherent by these arbitrary criteria for one quarter out of four or five. If these rates of nonadherence can be extrapolated to signify that patients are relatively unprotected from seizures, these figures are disturbing. What level of adherence is necessary to control seizures? Clearly this will vary widely between patients and within patients over time, making adherence more or less critical for each patient. One way of approaching this question is to examine the actual results of nonadherence.

### 5. The medical consequences of nonadherence

It probably makes little difference whether patients are adherent to a schedule of witch hazel treatment for seizures. However, the more effective the treatment, the more critical to success is adherence and the easier it is to measure the consequences of nonadherence. Unfortunately, the most important outcome measurement in epilepsy is seizure occurrence, which can be measured directly only in hospital monitoring units. Otherwise, we are dependent on patient reports. Clinical drug trials are surprisingly successful using these secondhand reports. However, they do not address the question of adherence versus outcomes because subjects bringing in more than 20% or so of residual

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**Table 1**

Morisky Medication Adherence Scale.

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you ever forget to take your medication?</td>
<td>No</td>
</tr>
<tr>
<td>2. Do you ever have problems remembering to take your medication?</td>
<td>No</td>
</tr>
<tr>
<td>3. When you feel better do you sometimes stop taking your medication?</td>
<td>No</td>
</tr>
<tr>
<td>4. Sometimes if you feel worse when you take the medicine, do you stop taking it?</td>
<td>No</td>
</tr>
</tbody>
</table>

Scoring: high-low; yes = 0, no = 1, Range 0–4

Mean (weighted): n=290, x=2.31

Cronbach’s alpha: 0.61

Reproduced with permission from Morisky and DiMatteo [5].

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prescribed drug to visits are ejected from the trial, and everyone exceeding this criterion is deemed to be fully adherent for purposes of outcome analysis. One searches in vain for clinical trial reports relating pill counts to seizure frequencies.

For population-based studies, especially those based on insurance claims, it is impossible to obtain direct data on seizure frequency. We must resort to surrogate measures thought to reflect the results of seizures. These may include practitioner visits, hospital visits or admissions, emergency responder data specifically coded for seizures or epilepsy, or more indirect events commonly associated with seizures such as head injuries, fractures, automobile accidents, or even death. The causal link between nonadherence and these adverse occurrences is, thus, indirect. However, this is also true for similar links in other diseases; for example, nonadherence to statin therapy after myocardial infarction is associated with a 25% increased risk of mortality over 1 year [18]. There are also compelling links between nonadherence and poor outcomes in epilepsy.

We have assumed that medications prevent at least some seizures, and it has been demonstrated that nonadherence, therefore, increases seizures by 21% in one study [14]. One must also accept that seizures themselves produce negative consequences. The literature on this is abundant, with clear correlations between seizure frequencies and injury rates [19,20] and death rates [21], suggestive correlations between seizure occurrences and intellectual functioning [22,23], and structural changes in the brain [24,25]. With these data and assumptions, can we relate medication nonadherence directly to negative consequences?

The risk of death (the worst consequence of nonadherence) was found to be 3-fold higher during quarters of nonadherence (defined as <80% MPR) among a 9-year, multistate sample of Medicaid recipients with epilepsy [13]. Although the causes of death in this study could not be identified from the information in the database, it was noted that the relative risk of several serious events was much higher during nonadherent versus adherent quarters (Table 3) [13].

Similar results were obtained from an adult managed care population of over 10,000 patients [12], among whom the odds of an emergency department visit were 1.5 times higher and of a motor vehicle accident 1.4 times higher among nonadherent patients. Interestingly, the relationship between practitioner visits and these negative outcomes was inverse; whether patients were also nonadherent with practitioner visits or whether frequent visits prevented nonadherence or negative outcomes is unknown.

6. Economic consequences of nonadherence

Even with the high costs of many drugs, not taking them is more expensive than taking them. Patients with epilepsy generate higher health-related costs than the average population as a group [26]. It is probable that costs not directly related to health care but attributable to epilepsy—absenteeism, poor work performance, disability payments, etc.—are even higher though harder to measure [27].

Having epilepsy is expensive personally and for society. Some of this can be attributed to increased emergency care usage for seizure occurrences [28]. Nonadherence to AED regimens makes epilepsy care much more expensive. In the Medicaid population, this was found to be driven mostly by higher costs for hospitalizations (incident rate ratio [IRR] 1.39 versus adherent), inpatient days (IRR 1.76), and emergency department visits (IRR 1.19) [29]. These factors alone translated to an additional cost per quarter of $4623 for each nonadherent patient compared with an adherent patient. Although costs for outpatient visits and medications were, not surprisingly, lower for the nonadherent group, these amounts were trivial by comparison. Finally, reestablishing control of seizures after it is once lost is more expensive than maintenance therapy, entailing more medical encounters, laboratory studies, and perhaps higher medication dosages [28].

7. Why don’t people take their medicine?

This is a puzzle, and it has been approached in 4 ways; each of which has led to attempts to modify these factors: 1) asking patients directly, 2) correlating patient characteristics with adherence (e.g., age, sex, socioeconomic background, religious beliefs, race and culture, education, type of illness, comorbidities, etc.), 3) correlating medication characteristics with adherence (e.g., costs, number of daily doses, number of

### Table 2

<table>
<thead>
<tr>
<th>Author</th>
<th>Population</th>
<th>Methodology</th>
<th>Measure</th>
<th>Observation</th>
<th>Adherence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Briesacher, 2008 [8]</td>
<td>Adults (N = 706,032)</td>
<td>Longitudinal study using the MarketScan Research Database</td>
<td>80% MPR</td>
<td>1 year</td>
<td>61%</td>
</tr>
<tr>
<td>Davis, 2008 [12]</td>
<td>Adults, managed care (N = 10,892)</td>
<td>Retrospective claims analysis from the PharMetrics Database</td>
<td>80% MPR</td>
<td>&gt; 1 year</td>
<td>61%</td>
</tr>
<tr>
<td>Manjunath, 2009 [14]</td>
<td>Adults 21–64 years of age (N = 18,073)</td>
<td>Retrospective claims analysis from the PharMetrics Patient Centric Database</td>
<td>80% MPR</td>
<td>1 year</td>
<td>50%</td>
</tr>
<tr>
<td>Faught, 2008 [13]</td>
<td>Adults on Medicaid (N = 33,658)</td>
<td>Retrospective, open-cohort design study</td>
<td>80% MPR</td>
<td>9.5 years, quarterly</td>
<td>74%</td>
</tr>
</tbody>
</table>

MPR = medication possession ratio.

### Table 3

<table>
<thead>
<tr>
<th>Event</th>
<th>Nonadherent quarters (32,365 patient-years)</th>
<th>Adherent quarters (91,678 patient-years)</th>
<th>Nonadherent/adherent IR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED visits</td>
<td># of events</td>
<td>Incidence rate</td>
<td># of events</td>
</tr>
<tr>
<td>47,859</td>
<td>1.48</td>
<td>90,562</td>
<td>0.99</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>43,167</td>
<td>1.34</td>
<td>65,913</td>
</tr>
<tr>
<td>MVA injuries</td>
<td>349</td>
<td>0.011</td>
<td>477</td>
</tr>
<tr>
<td>Fractures</td>
<td>17,419</td>
<td>0.54</td>
<td>41,039</td>
</tr>
<tr>
<td>Head injuries</td>
<td>11,942</td>
<td>0.37</td>
<td>46,213</td>
</tr>
</tbody>
</table>

CI = confidence interval; ED = emergency department; IR = incidence ratio; MVA = motor vehicle accident.

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concomitant medications, side effect rates, and perceived efficacy), and 4) correlating characteristics of the patient–practitioner and patient-care system interactions with adherence (e.g., educational effort, visit frequency, reminders, pharmacy system practices, etc.). The results of these approaches are not always intuitively obvious. For example, adherence rates among the Medicaid population, by definition in a low economic status, are not lower than those in managed care populations. In contrast to this finding, socioeconomic status was the only predictor that was significantly associated with nonadherence ($P<0.001$) in a group of 124 children with newly diagnosed epilepsy from Cincinnati Children’s Hospital Medical Center [16]. If one asks patients directly, the most common reason given is simply forgetting [30]. This is not too helpful unless we know who forgets and why.

What factors are correlated with nonadherence in general medical conditions and in epilepsy? In other chronic diseases, older patients with comorbidities, ethnic minorities, and evidence of disparities between patient and doctor beliefs have been implicated, with weaker correlations between age as a single factor, sex, social class, education, clinical symptoms, and particular drugs identified [31]. Among patients with cardiovascular diseases, for example, nonadherence has been correlated with higher drug co-payments [32], disease knowledge and health literacy [33], and depression [34].

These factors may or may not be applicable to epilepsy. Earlier studies focused on patient-reported factors and demographic factors in small groups [17,35,36]. Among a large group of patients with epilepsy ($N=465$), we did not find a correlation between depression scale scores and adherence (Duh, Manjunath, and Faught, unpublished observations). In a large Medicaid study, nonadherence was higher among patients aged $\geq 65$ years, among females (a surprising finding), and among blacks [13].

There is evidence for an inverse linear relationship between number of daily doses of drug and adherence [37]. This is intuitively reasonable since the act of remembering to take one’s drug several times per day is more likely to fail at least once compared with taking a drug once per day. In a recent meta-analysis of 20 studies of a variety of chronic diseases [38], there was a clear difference in adherence even between once-daily and twice-daily dosing; there were 2% to 44% more “adherent days” (all prescribed doses taken) with once-daily than twice-daily dosing, with “most studies clustering between 13% and 26%”, and this increase in adherence is likely to be clinically significant.

Persistence of medication taking is also a problem in epilepsy. The rate of missed doses was found to rise with duration of treatment by about 60% from <1 year of treatment to over 11 years of treatment [39]. On the other hand, exactly the opposite effect was reported in a group of 75 interviewed patients, among whom adherence was positively correlated not only with age but also with duration of treatment (but not with seizure control) [40].

Finally, besides measurable factors such as demographics and medication schedule, we must ask: what are the psychological reasons for nonadherence? Shea, in an excellent guidebook on how to improve medication adherence [41], lists three key issues that concern patients: efficacy, cost, and meaning. Efficacy refers to a patient being able to believe that a medication will help with a condition that ought to be treated. Cost does not imply simply a financial cost but costs of convenience, stress, and stigma associated with medication taking. Finally, the “meaning” of taking medications for many patients is negative; it suggests dependence, chronic illness, and even lost dreams. The practitioner must explore these issues thoroughly, gently, and with positive reinforcement.

8. Improving adherence

The critical importance of adherence is established. How can we improve it? One approach would be to target patient groups that are most notorious for nonadherence for special attention. I would like to make the radical suggestion that this is unlikely to be very productive. The reason is clear from the discussion in the previous section: there is no real consensus on who constitutes these patient groups, especially in epilepsy.

In a recent article on the importance of medication adherence in cardiovascular outcomes, Ho et al. stated, “To date, interventions targeting medication adherence have produced only modest success” [10]. This discouraging statement reflects, for instance, attempts to use informational mailings, pharmacist-led interventions, and packaged medications in cardiovascular diseases, which resulted in improvements typically between 4% and 11%.

Clearly, we need better approaches. A recent review of strategies for improving adherence to antiepilepsy drugs suggests that intensive reminders and “implementation intention” provide positive effects on adherence, whereas education and counseling have met with mixed success [42]. The World Health Organization (WHO) has suggested several methods for consideration, with the opinion that one method alone is unlikely to be effective [43]. Furthermore, the WHO states, “Despite evidence to the contrary, there continues to be a tendency to focus on patient-related factors as the causes of problems with adherence to the relative neglect of provider-related and health system-related determinants.”

What are provider-related determinants? Firstly, the patient must have confidence in the provider. This is about the art of medicine, and no recipe can be provided. There are some concrete steps that should be included in the patient–practitioner encounter, especially when a new prescription is offered:

1) Explain the goals of the therapy clearly; if not complete seizure freedom, is it modification of seizure severity or reduction of seizure frequency? If a medication switch is being undertaken, what are the reasons? If polytherapy is prescribed, why are both drugs needed? Patients must believe that they have a condition requiring treatment and that the treatment being prescribed is likely to help; if either condition is dubious, nonadherence is likely.

2) Provide, verbally and in writing, instructions for initial dose and titration.

3) Inform the patient about what to do if a dose is missed (in order to do this accurately, the practitioner must understand the pharmacokinetic concept of “forgiveness” as it applies to that medication [44]). Forgiveness can be expressed quantitatively as the duration of therapeutic action divided by the dosing interval. This is difficult to assess in epilepsy because of the varied, and often unknown, pharmacodynamic durations of action of drugs and great inter-individual variation in seizure threshold. In general, drugs with long elimination half-lives and sometimes those with indirect therapeutic compartments, e.g., reservoirs, provide more “forgiveness” for missed doses. Although the consequences of missing a dose may be higher for long dosing intervals, this is balanced by improved adherence and by the use of drugs with prolonged effects after each dose.

4) Educate the patient on expected minor side effects, which should not be cause for stopping the medication, and on whether they are likely to persist.

5) Educate the patient on unexpected, rare, but serious side effects which warrant a call to the practitioner and/or drug discontinuation.

6) For epilepsy, it is important for the patient to understand the trial-and-error flavor of both drug selection and dosing, to avoid discouragement.

7) Find out whether the drug is covered by the patient’s prescription plan and, if possible, the amount of co-pay (some electronic medical record systems can now do this automatically). Tell the patient and get their consent.

8) Simplify dose regimens as much as possible. Give the fewest number of daily doses consistent with the drug’s kinetics and the “forgiveness” factor (the likely consequence of missing a dose). This usually means prescribing extended-release preparations,
preferably administered once a day, when available and affordable. Several epilepsy studies have indicated that patients prefer once-daily dosing compared with more frequent dose-administrations [45–47].

9) Reduce trips to the pharmacy. This means not only prescribing 90-day supplies when allowed but also harmonizing all the patients’ prescriptions so that they don’t fall due on varying days of the month.

10) Fully explore the details of medication taking. When do you take your doses? Before or after your meals? Do you use any reminders? What about weekly pill boxes (a great idea)?

For return visits, especially the first return after a new medication has been instituted (which should occur within 2–6 weeks or when the titrated target dose is reached), there are some other considerations:

1) Probe for specific side effects for that drug. Ask family members.
2) If side effects are present, find out if the patient is willing to take the drug longer, or if they don’t improve, find out if the patient would like to stop it.
3) Encourage patients to report side effects that may be embarrassing (e.g., impotence) or that the patient may not associate with the drug (weight change and mood effects).
4) A most important question: What do you do when you forget a dose? Support, don’t blame: assume everyone misses a dose sometimes, and open the discussion in an encouraging way rather than asking “Have you been taking your medicine?”
5) Patients may not understand the variable relationship between missing doses and having seizures; this is especially true to new patients or to those with infrequent seizures. It is wise to explain the risk in simple terms.

What are health system-related determinants?

1) Personal reminders—phone, text, or email from a nurse after a couple of weeks to enquire about problems with access, side effects, and to reiterate the plan.
2) Electronic reminders—cell-phone alarms are underutilized in this regard, and pharmacies can generate reminders several days before refills are due; large pharmacy systems are increasingly equipped to do this.
3) Alerts to practitioner offices when gaps in prescription coverage occur—this is an appealing though technically difficult and time-insensitive idea.
4) Post-hoc reviews by the practitioner’s office: bringing back pill bottles, checking off a paper or electronic calendar (see epilepsy.com and others), or reviewing data from electronic bottle caps (expensive but may become cheaper).
5) For epilepsy, formularies that include extended-release preparations and insurance regulations allowing 90-day supplies with refills up to 1 year (the recent classification of new AEDs as Drug Enforcement Administration scheduled items is a step backward).
6) A step beyond once-daily drug preparations is a formulation that could deliver drug for many days or weeks. Weekly patches, monthly injections, subcutaneous reservoirs, and the like are no longer science fiction and may become available for epilepsy.

Refractory nonadherence is a special problem. This is often caused by one of the factors above, especially financial, but the problem is often simple misinformation. Patients may have heard that their drug can cause liver failure and may not understand that this is not a cumulative effect. Most drug labels provide warnings regarding taking drugs with alcohol; this is unrealistic for many patients, who may be better off taking the drug anyway if they drink moderately. Patients often cut down their dose without telling the practitioner because of side effects. There are other examples, but willful nonadherence simply because of pigtheadedness is not as common as practitioners believe. Furthermore, nonadherence is sometimes misdiagnosed when serum levels are low because of failure to recognize the tremendous interindividual variability in metabolism.

9. Summary

Nonadherence to AED therapy is a common and serious problem. The effect on therapeutic success is not directly measurable among large populations, but based on secondary effects of seizures such as injuries and economic costs, nonadherence markedly reduces treatment success. The cost of nonadherence among the population clearly exceeds the cost of the average adjunctive medication. Therefore, if we were to improve adherence by 30%, would it reduce epilepsy seizures in the population by 30%? Probably not, since the drugs are not 100% effective, and there is also a “forgiveness factor” based on individual patient characteristics and individual drug pharmacokinetics. Nevertheless, the results would not likely be trivial.

A narrow focus on patient-related factors, whether related to individual responsibility, demographics, or disease, is misplaced. These factors are important and deserve additional emphasis and study, but health care system-related improvements will have a more universal impact. These range from attention to certain details during office visits to electronic techniques usable by individuals or systems. Improvements in drug delivery systems, including the use of extended-release AEDs when appropriate, will also help. One thing that has held the study of adherence back is the disease-silo perspective: in fact, adherence issues are applicable to many chronic diseases. We who treat epilepsy can learn from the experience of other practitioners. A new website, www.iadherence.com, may facilitate the sharing of ideas. There are resources describing practical interviewing techniques for both promoting and assessing adherence as well [41].

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