Ethical Human Psychology and Psychiatry, Volume 10, Number 3, 2008

Homicidal Ideation Causally Related to Therapeutic Medications

Donald H. Marks, MD, PhD

Cooper Green Mercy Hospital, Birmingham, AL
Wallace Kettering Neuroscience Institute, Kettering, OH

Peter R. Breggin, MD

Ithaca, New York

Derek Braslow, Esq

Pogust, Braslow & Millrood, LLC
Conshohocken, PA

[AuQ1]

Five patients with hepatitis C (HCV), three of whom were treated with interferon alpha2 (IFN) and two who were not treated with IFN, developed homicidal ideation (HI) during a 4-year period. Following accepted rules for determining causation, there appeared to be a causal relatedness between IFN use and the development of homicidal ideation for those patients taking IFN. None of these patients attempted a homicidal act while on treatment with IFN, nor in the follow-up period after treatment. The incidence of HI while treated with IFN in our patient population is estimated to be less than 1%. The ability of prescription medication to cause homicidal ideation is reviewed, and legal implications are discussed.

Keywords: homicide; murder; suicide; violence; adverse effect; interferon; medication; SSRI; antipsychotic

[AuQ2]

The ability of medications to affect the central nervous system (CNS) is well known (Brunton, Lazo, & Lazo, 2005). In some cases, the effects are desired—for example, medications designed to treat seizures, depression, or Alzheimer's disease. In other cases, the effects are unwanted—for example, decreased coordination and problems when operating machinery when taking anxiolytics. Recently, there has been an increased awareness of the ability of antidepressant medications to cause a paradoxical increase in depression and, in some cases, suicidal ideation (SI) (Breggin, 2003, 2008; Food and Drug Administration, 2005a; Healey, Herxheimer, & Menkes, 2006; Khan, 2002). The clinical pharmacology and mechanism of the later effect may be related to the known ability of medications in the SSRI class to cause or exacerbate levels of anxiety, agitation, irritability, akathisia, aggression, hostility, emotional blunting, and disinhibition. Clinically all of these phenomena have been associated with violence. It is reasonable from a psychological perspective to understand how a medication that can induce or increase feelings of anxiety, agitation, akathisia, aggression, hostility, irritability, and/or disinhibition could lead toward self-directed or outwardly directed violence in a predisposed individual. In at

DOI: 10.1891/1559-4343.10.3.136

least one product liability case (*Tobin v. SmithKline Beecham*, 164 F. Supp.2d 1278 [D.Wy. 2001]), the courts have accepted a causal relatedness of an SSRI medication and homicidal acts.

The prescribing information for Pegasys and Peg-Intron, interferon alpha 2 antiviral medications used to treat hepatitis C, caution that:

> Life-threatening or fatal neuropsychiatric reactions may manifest in patients receiving therapy with [PEGASYS or Peg-Intron] and include suicide, suicidal ideation, homicidal ideation, depression, relapse of drug addiction, and drug overdose. These reactions may occur in patients with and without previous psychiatric illness. [PEGASYS or Peg-Intron] should be used with extreme caution in patients who report a history of depression. Neuropsychiatric adverse events observed with alpha interferon treatment include aggressive behavior, psychoses, hallucinations, bipolar disorders, and mania.

[AuQ3]

[AuQ4]

Because these adverse events can reasonably be thought to be precursors to or exacerbate preexisting SI or HI, a causal relatedness between IFN and HI is plausible. This article describes the occurrence of HI in five patients with HCV at a hepatitis clinic based in a large inner-city hospital.

METHODS

Medical records of over 460 patients seen at an inner-city hepatitis clinic, all of whom were patients of the first author, were reviewed for complaints of HI and other neuropsychiatric problems, predisposing conditions, and correlated with IFN use. Entered into a database were patient demographics; viral load at start of, during, and after treatment; decision to treat; risk factors for drug response; urine drug screens; adverse effects; and other data for all patients with viral hepatitis seen in the hepatitis clinic at Cooper Green Mercy Hospital for the 4-year period 2004 to 2007. A directed search of the data for HI and SI was prepared; no change in therapeutic decision was based on the collection of this data. The hospital institutional review board approved the use of anonymous demographic and incidence data collection for the purpose of preparing this publication.

ASSESSMENT OF CAUSATION

A determination of causal relatedness between the administration of IFN and the development of HI was made by means of universally accepted algorithms (Marks, 2005). Factors considered included temporality of the HI to IFN use; preexisting HI or other psychiatric problems; criminal history; absence of alternative explanations; and the challenge, dechallenge, rechallenge phenomenon. Causal relatedness was divided into five categories: definite, probable, possible, unlikely, or unrelated.

In addition to IFN, the prescribing information for all medications was searched using electronic databases (www.PDR.net and www.Medscape.com), and the occurrence of specific relevant keywords related to psychological adverse effects was prepared.

RESULTS

Since 2004, over 460 patients have been seen at the hepatitis clinic at Cooper Green Mercy Hospital, including 408 patients with HCV, of whom treatment was initiated in 134. Of those 134 patients, 5 reported having experienced homicidal ideations (see Table 1), 8 reported suicidal thought (Marks, 2008), and 4% of all cases experienced significant new or worsening depression (Marks, Adineh, Wang, & Gupta, 2007).

Patients 48, 97, and 123 stated that they did not experience HI immediately before IFN, that they did have HI that began after starting IFN, and that their HI resolved once IFN was stopped. None of these three patients carried out a homicidal act. The three persons who experienced HI while taking IFN were accessed as having had a probable causal relatedness, using standard accepted definitions of pharmaceutical specific causation (Marks, 2005).

Patients 130 and 189 also experienced HI during the study period, but were not taking IFN or any other medication (see Table 2) with a reported association to HI.

The possibility of experiencing HI during treatment with IFN is not unexpected and is warned of in the prescribing information. Similarly, increases in depression and anxiety due to IFN were expected and have been reviewed elsewhere (Marks et al., 2007).

For comparison, the prescribing information for most prescription medications was searched using electronic databases (www.PDR.net and www.Medscape.com), looking for

TABLE 1. Individuals With Hepatitis C Who Developed Homicidal Ideation

	Case ID	48	97	123	130	189
	Sex	M	M	M	F	F
	Age	46	61	55	48	25
[AuQ5]	**Race**	C	B	B	B	C
[AuQ6]	**DSB**	Yes, and due to IFN	No	Remote	Yes	No
	Drug Abuse	Yes	Yes	Yes	Yes	No
	History of Mental Health Problem	Yes	No	No	No	No
	Current Legal Problems	Yes	No	No	No	No
[AuQ7]	**Relative to IFN, and Degree**	Homicidal thoughts on IFN	Anger, homicidal thoughts, irritability, aggression on IFN	Homicidal thoughts on IFN	HI not on IFN	HI not on IFN
	Outcome	Stopped for psychological adverse events	Stopped for psychological adverse events			
	Concurrent Medications	SSRI	Lortab, fosinopril, propranolol, glipizide	Hydrocodone, acetaminophen	Metoprolol	None

Note. HI: homicidal ideation; IFN: interferon alpha2; SSRI: selective serotonin reuptake inhibitor.

TABLE 2. **Some Frequently Used Medications With Serious Central Nervous System Adverse Events**

Medication	Anxiety	Depression	Aggressive and/or Violent Behaviors	Hallucination	Impulsivity	Paranoia	Irritability	Psychosis	Suicidal	Homicidal	DSB	Seizures	[AuQ8]
Accutane		X	X					X	X				
Adderall		X	Restlessness					X				X	[AuQ9]
Antiseizure (Neurontin, Lyrica)										X			
Chantix	X	X	Infrequent	Rare	Agitation		X	And mood swings, abnormal thinking	Rare				
Cymbalta SSNRI	X	X	X and hostility		X			Mania	X				[AuQ10]
Interferon alpha 2		X	X	X				X	X	X	X		
Larium mefloquin	X	X		X and confusion		X		X	rare				
Reglan metoclopramide	X	X		Rare			Restlessness		X			Reports	
Corticosteroids			X				X						
SSRI	X		X and hostility		Agitation		X	Mania	X				

Note. SSRI: selective serotonin reuptake inhibitor.

TABLE 3. Frequency of Specific Adverse Events Appearing in Prescribing Information

Keyword for Adverse Event	Number of Citations in Prescribing Information
Agitation	214
Aggression	22
Hallucination	46
Homicide	1 (prescribing information for Effexor, reports for SSRI, IFN)
Irritability	117
Nightmare	8
Psychosis	84
Restlessness	152
Suicidal	49

Note. IFN: interferon alpha2; SSRI: selective serotonin reuptake inhibitor.

the adverse event keywords listed in Table 3. These specific keywords were chosen because of a potential inciting effect on homicidal ideation.

This directed search revealed that a wide range of medications in varied therapeutic categories was associated with adverse CNS events. Some of these, alone or in combination, can reasonably have relevance to initiating or exacerbating HI. More specifically, the prescribing information for medications in use at Cooper Green Mercy Hospital, including the hepatitis patient population, were searched using the same electronic database, concentrating on those keywords listed in Table 3, and the results are listed in Table 2.

The findings illustrate a wide range of potential CNS adverse events with relevance to the development or exacerbation of SI or HI to patients from medications available in a hospital formulary.

A literature search was also performed of illicit drugs associated with a number of CNS effects that could initiate or exacerbate SI or HI.A number of illicit medications and alcohol, with some prevalence of use in hepatitis patients, can be associated with HI or cause neuropsychiatric effects that might reasonably lead to HI.

DISCUSSION

Recent years have seen increased concern about suicidality induced by prescription medications. Suicidality and violence are closely connected clinically and often occur in the same individual at the same or at different times. This known clinical phenomenon is reflected in the frequent use of the phrase "violence toward self or others."

Paroxetine provides an example of a drug associated with both suicidality and violence. Based on a reanalysis of placebo controlled clinical trials, Kraus (2006) concluded on behalf of GlaxoSmithKline, the manufacturer, that paroxetine caused a 6.4 times increase in the rate of suicidal behavior compared to placebo (11/3,455 [0.32%] versus 1/1,978 [0.0.5%]) in adults of all ages with major depressive disorder. This information was later included in the FDA-approved label (Paxil, 2006, p. 1531).

Violence, including homicide, as a reported adverse event, has a lower reported frequency than suicidality and has more rarely been demonstrated in placebo controlled clinical trials. Nonetheless, aggressive and violent behaviors are often reported in association with drugs such as paroxetine that are more definitively implicated in suicidality. In fact, the class warnings for antidepressants, as illustrated by paroxetine, contain the following FDA-mandated statement (Paxil, 2008; also see Food and Drug Administration, 2005a): **[AuQ11]**

> The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. (Paxil, 2006, p. 1531)

Nearly all of the symptoms described are related to the potential for violence toward *others*, including agitation, irritability, impulsivity, aggressiveness, and hostility. They are commonly found as adverse effects of drugs that cause violence or suicide. In addition, akathisia (American Psychiatric Association, 2000, p. 801) and mania (American Psychiatric Association, 2000, p. 359) are associated with both depression and aggressive behavior.

Atomoxetine (Strattera), a drug with a black box warning that "identified an increased risk of suicidal thinking" (Food and Drug Administration, 2005b), also has been associated with aggressive and violent behavior (Henderson & Hartman, 2004). A review **[AuQ12]** of 153 sequential children treated at two clinics with atomoxetine revealed an extreme amount of disturbed and hostile behavior: "We have observed extreme irritability, aggression, mania, or hypomania induction in 51 cases (33%)" (Henderson & Hartman, 2004). Of the 51 cases, 88% displayed aggression; 49%, physical aggression; and 96%, irritability. The researchers described examples of extreme aggression, including punching, strangling, and brandishing a weapon.

Numerous nonpsychiatric drugs also carry FDA warnings concerning suicidality together with violence. In the warnings section under psychiatric disorders, the Accutane label states "Accutane may cause depression, psychosis, and rarely, suicidal ideation, suicide attempts, suicide and aggressive and/or violent behaviors" (Accutane, 2008, p. 2707).

Levetiracetam (Keppra) is an antiepileptic agent. In placebo controlled clinical trials, **[AuQ13]** "non-psychotic behavior disorders (reported as abnormal behavior, aggression, conduct disorder, and irritability) occurred in 11.4% of KEPPRA-treated patients compared to 3.6% of placebo patients" (Keppra, 2008, p. 3252). This is one of the few demonstrations of medication-induced aggression and aggressive-like behavior in placebo controlled clinical trials. The label also warns about depression and suicidality, once again indirectly linking harm to self and others.

Although not confirmed in placebo controlled clinical trials, many FDA-approved labels include warnings about reported aggression, including the label on Rebetron (a combination of ribavirin and interferon), which describes "rare instances of homicidal ideation" in patients with and without a psychiatric history (Rebetron, 2008, p.). In our patient **[AuQ14]** population, PEG-interferon alpha2 was associated with depression, SI, and HI.

Many researchers and clinicians have noted the association between benzodiazepines and aggression or violence. Dukes (1980) addressed the question of whether the benzodiazepines can unleash violence and pointed to more than a dozen articles confirming the tendency of the drugs to produce irritability, defiance, hostility, aggression, and rage. In an unpublished in-house study utilizing the FDA's spontaneous reporting system, Wise (1989)

found increased reporting rates for hostility on alprazolam, a short-acting benzodiazepine, compared to temazepam and flurazepam, two longer-acting benzodiazepines. The study was conducted in response to six reports to the agency within 1 year concerning rage, agitation, anger, aggression, and similar behavioral disturbances. Five of the six reports involved murderous impulses, some of which were acted upon.

Psychoactive medications produce violence by causing a variety of clinical syndromes that are associated with this behavior, including agitated depression, irritability, dyscontrol, mania, and aggression. Often activation or stimulation is involved.

The findings reported here support the potential for HI arising from the use of a wide range of common therapeutic medications. Violent behavior has been reported to occur as a known adverse effect of certain medications, and, when it occurs in temporal association with treatment, the violence should not automatically be attributed to an underlying psychiatric abnormality or to past criminal behavior. Specifically, if a patient treated with any of the medications listed in Table 4 develops SI or HI, the possibility should always be entertained that these thoughts could arise from an adverse effect of those medications, rather than simply attributed to a manifestation of an underlying psychiatric or personality state. Adverse medication effects one could reasonably associate as potential precursors or exciting factors for HI include anxiety, depression, aggressive or violent behavior, hallucination, impulsivity, paranoia, irritability, psychosis, drug-seeking behavior, or seizures. Persons who develop a substance-induced mood disorder, as described by the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV;* American Psychiatric Association, 1994), may be more likely to develop a new onset of HI or perhaps a destabilization of HI.

[AuQ15] The prescribing information for Pegasys states, "Life-threatening or fatal neuropsychiatric reactions may manifest in patients receiving therapy with PEGASYS and include suicide, suicidal ideation, homicidal ideation, depression, relapse of drug addiction, and drug overdose. These reactions may occur in patients with and without previous psychiatric illness. Patients being treated for hepatitis who develop aggressive behavior, psychoses, hallucinations, bipolar disorders, or mania, all potential precursors of SI or HI, should be questioned (as encouraged by the prescribing information) about the occurrence of SI or HI. Medication dose adjustments, discontinuation, or psychiatric intervention may be needed.

The treating/prescribing physician of medications that have the potential to cause CNS adverse events should perform an adequate medical and psychiatric history and evaluation to ascertain the risk for using these medications in each patient. Professional help should be sought from psychiatrists with a good knowledge of psychopharmacology and substance-induced mood disorder. Consideration should be given to the consequences in each patient of inducing increased anxiety, aggression, agitation, anger, depression, hallucinations, impulsivity, irritability, paranoia, or suicidal or homicidal ideation. It would seem reasonable that all patients who receive these listed drugs and their immediate family and caregivers be given specific caution and warning about the potential for induction of CNS adverse events, including HI. Patients receiving these listed medications should be queried at regular intervals for the development of CNS adverse events, and appropriate follow-up should be performed. If a person receiving these medications develops new or heightened HI, it is important for the treating/prescribing physician to determine whether the medication should be discontinued. Patients developing CNS adverse events should be questioned concerning their degree of risk to themselves and others, and they should be requested to notify anyone who may be at risk from their actions. Professional psychiatric input should be considered. All these actions should be documented in the medical records.

TABLE 4. Some Illicit/Addictive Drugs With Serious Central Nervous System Adverse Events

	Anxiety	Depression	Aggressive and/or Violent Behaviors	Hallucination	Impulsivity	Paranoia	Irritability	Psychosis	Suicidal	Homicidal	DSB	Seizures
Cocaine		X	Agitation insomnia	X				Paranoia	X and homicidal		X	
Heroin		X									X	
Methamphetamine	X		Agitation, violence					X	X		X	
Alcohol		X	X	X	X							

[AuQ16]

Patients undergoing treatment for hepatitis C have a higher background rate of alcohol and illicit drug use. These drugs can be associated with a number of CNS effects that could initiate or exacerbate SI or HI. It is also well characterized that illicit drugs and alcohol could exacerbate CNS adverse events experienced from prescription medications. It is important to take a thorough drug and alcohol history when evaluating CNS adverse events possibly related to therapeutic medications

LEGAL IMPLICATIONS

The potential for prescription medications to cause violence, including suicide, has wide-reaching implications in the law.

First, if a crime is committed as a result of ingesting a prescription medication, many states have statutes that allow for the defense of involuntary intoxication. This has generally been defined as intoxication with a prescription medication without foreknowledge that the medication can cause abnormal behavior.

While *mens rea* or "guilty mind" is usually one of the necessary elements of a crime, states vary regarding the requirements for proving this mental state, sometimes requiring the accused to meet legal criteria for insanity. Some states require negligent prescription of the medication or require the individual to have taken the drug as prescribed in order to qualify for the defense. In most cases, involuntary intoxication can serve as a complete defense to the charges, similar to the insanity defense. Significantly, even if the accused is convicted of the crime, the sentencing judge could and should take into account the fact that the criminal behavior was caused by or aggravated by a prescription medication. As a result, the judge could conclude that the individual does not pose a danger to society absent further exposure to the offending agent.

Just as individuals convicted of crimes while taking psychoactive medications may argue that they are no longer at risk of perpetrating after becoming medication free, individuals adjudicated incompetent while under the influence of a prescribed medication may argue that they are no longer at risk of being incompetent after withdrawal from the agent.

Second, if a patient is injured as a result of ingesting a prescription medication, the prescribing physician may be liable for money damages. In medical malpractice suits against prescribing physicians, the failure to warn a patient that a medication may cause violent and suicidal behavior, particularly if the medication's label directly warns the prescribing physician of this risk, may be grounds for negligence.

Third, if the pharmaceutical manufacturer failed to properly warn physicians of the true risks of suicide or violence associated with a medication, a patient may have a civil claim against the manufacturer in a product liability suit. Specifically, a pharmaceutical company's failure to properly evaluate whether or to warn that a drug can cause suicidal or violent behavior may be grounds for negligence.

CASE EXAMPLES

In several dozen individuals deemed to suffer from involuntary intoxication, none of them repeated their crimes after withdrawal from the offending medication (Breggin, 2008). In

addition to that series, here are three additional cases in which the author testified as a psychiatric expert: **[AuQ17]**

> In the *State of Connecticut v. Christopher DeAngelo,* February 2000, a man with no criminal record committed a series of robberies over a period of a few days, including a bank robbery from which he fled by car amid a hail of police bullets. He was charged with first-degree robbery and larceny. He had been prescribed and was taking fluoxetine (Prozac) for obsessive-compulsive disorder and alprazolam (Xanax) for anxiety disorder. Two psychiatric experts concluded that the combination of drugs caused him to experience a manic psychosis with uncontrollable bizarre behavior. For example, he robbed his wife's bank and the drug store he regularly patronized without wearing a disguise. The defendant waived a jury trial, and the judge found him not guilty by reason of mental disease or defect due to intoxication with the two medications.
>
> In *Commonwealth of Virginia v. Amnulla Khaliqi,* 1997, Mr. Khaliqi, a young adult with no history of violence, was taking multiple psychiatric drugs when he cursed and kicked a policeman who shook him awake from a deep sleep in his bed at home. The judge allowed testimony from a psychiatrist concerning the adverse disinhibiting mental effects of numerous prescribed medications that he was taking simultaneously, including antidepressants, benzodiazepine tranquilizers, and antipsychotic drugs. The defendant was acquitted of assault on the grounds of involuntary intoxication. This was the first application of the involuntary intoxication defense in Virginia.
>
> In February 1998, 60- year-old husband, father, and grandfather Donald Schell, complained of difficulty sleeping. As a result, he went to see his physician, who diagnosed him as having anxiety and prescribed him Paxil. Forty-eight hours later, Mr. Schell shot and killed his wife, his daughter, and his granddaughter before shooting himself. Three years later, in June 2001, a Wyoming federal jury awarded $8 million in damages after finding, by a preponderance of the evidence, that "Paxil can cause some individuals to commit suicide and/or homicide," and "Paxil was a proximate cause of the homicides and suicides involved in this litigation." (*Tobin v. SmithKline Beecham,* 164 F. Supp.2d 1278 [D.Wy. 2001]). This case remains, however, the only civil damage award against a manufacturer of an antidepressant for a suicide/homicide.

CONCLUSIONS

Even though our data concerning interferon alpha2 is preliminary and concerns a small number of subjects, the incidence of IFN-induced HI, as was the case for IFN-induced depression and SI, is very low but real in this treatment population. The rate of HI in IFN-treated patients may be representative of the expected incidence rate for the population in general, although our numbers were too low to allow statistical comparison. It will be of clinical value to practitioners to know more precisely the extent of IFN-induced HI and to predict increased mood disorders. Besides interferon, a wide range of therapeutic prescription medications have been associated with reports of HI, for which there is a dearth of information concerning individual or group causation. Nevertheless, for many of the medications discussed in this article, it is probable, due to the known adverse effect profiles, that sufficient agitation and irritability could cause HI in certain individuals. Indeed, the antidepressants and numerous other drugs report aggression and hostility in association with their use (Food and Drug Administration, 2005a). Further, when considering motive during the sentencing of criminals, it can be instructive to consider the potential role of medication use at the time of homicide. In someone who fits the pattern of as substance-induced mood disorder according to the *DSM-IV* (American Psychiatric Association, 1994), the potential for an element of iatrogenic responsibility may exist.

REFERENCES

[AuQ18] Accutane. (2008). In *Physicians' desk reference* (pp. 2706–2614). Montvale, NJ: Thomson Healthcare.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., Text revision). Washington, DC: Author.

Bostwick, J., & Lineberry, T. (2006). The meth epidemic: Acute intoxication. Managing psychosis,
[AuQ19] agitation, and suicide risk. *Current Psychiatry, 5*(11), 47–62.

Breggin, P. (2003). Suicidality, violence and mania caused by selective serotonin reuptake inhibitors (SSRIs): A review and analysis. *Ethical Human Sciences and Services, 5*, 225–246.

Breggin, P. (2008). *Medication madness: A psychiatrist exposes the dangers of mood-altering drugs*. New York: St. Martin's Press.

Brunton, L., Lazo, J., & Lazo, J. S. (Eds.). (2005). *Goodman and Gilman's the pharmacological basis of therapeutics*. New York: McGraw-Hill.

Catani, M., Cherubini, A., Howard, R., Tarducci, R., Pelliccioli, G. P., Piccirilli, M., Gobbi, G., Senin, U., & Mecocci, P. (2001). 1H-MR spectroscopy differentiates mild cognitive impair-
[AuQ20] ment from normal brain. *NeuroReport, 12*(11), 2315–2317.

Dealberto, M. J., Marino, J., & Bourgon, L. (2006). Homicidal ideation with intent during a manic episode triggered by antidepressant medication in a man with brain injury. *Bipolar Disorders,*
[AuQ21] *10*, 111.

Dukes, M. (1980). The van der Kroef syndrome. *Side Effects of Drugs Annual, 4*, v–ix.

Food and Drug Administration. (2005a). *Class labeling for antidepressants*. Retrieved June 13, 2008, from http://www.fda.gov

Food and Drug Administration. (2005b). *FDA issues public health advisory on Strattera (atomoxetine) for attention deficit disorder*. Retrieved June 13, 2008, from http://www.fda.gov

Healy, D., Herxheimer, A., & Menkes, D. B. (2006). Antidepressants and violence: Problems at the
[AuQ22] interface of medicine and law. *PLoS Med, 3*(9), e372.

Henderson, T. A., & Hartman, K. (2005). Aggression, mania, and hypomania induction associated with atomoxetine. *Pediatrics, 114*, 895–896.

James, C. W. & Savini, C. J. (2001). Homicidal ideation secondary to interferon. *Annals of Pharma-*
[AuQ23] *cotherapy, 35*, 962–963.

[AuQ24] Keppra. (2008). In *Physicians' desk reference* (pp. 3249–3256). Montvale, NJ: Thomson Healthcare.

Khan, A. (2002). Suicide risk in patients with anxiety disorders: A meta-analysis of the FDA database. *Journal of Affective Disorders, 68*, 183–190.

Korn, M. L., Plutchik, R., & Van Praag, H. M. (1997). Panic-associated suicidal and aggressive
[AuQ25] ideation and behavior. *Journal of Psychiatric Research, 31*, 481–487.

Kraus, J. (2006). *Important prescribing information*. Dear Healthcare Provider letter about Paxil. Philadelphia: GlaxoSmithKline.

Marks, D. H. (2004, February 2). Testimony at Food and Drug Administration Psychopharmacologic Drugs Advisory Committee meeting and the Pediatric Subcommittee of the Anti-Infective
[AuQ26] Drugs Advisory Committee.

Marks, D. H. (2005). Evaluation of medical causation. In J. T. O'Donnell (Ed.), Drug injury: Liabil-
[AuQ27] ity, analysis and prevention (2nd ed.). [City]: L&J Publications.

Marks, D. H. (2007). Depression leading to suicide as an adverse effect of metoclopramide. *Inter-*
[AuQ28] *net Journal of Gastroenterology, 5*(2). Retrieved [date], from http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijge/vol5n2/depression.xml

[AuQ29] Marks, D. H. (2008, [month]). *MR imaging of drug-induced suicidal ideation*. Abstract presented at the American Association of Suicidology meeting, Boston, MA.

Marks, D. H., Adineh, M., Wang, B., & Gupta, S. (2007). Use of MRI to predict psychiatric adverse effects of interferon treatment for hepatitis C. *Neuropsychiatric Disease and Treatment, 3*(5), 655–667.

Marks, D. H., & Milby, J. (2008). Interferon and risk for drug-seeking behavior. **[AuQ30]**

Myers, W. C., & Vondruska, M. A. (1998). Murder, minors, selective serotonin reuptake inhibitors, and the involuntary intoxication defense. *Journal of the American Academy of Psychiatry and Law, 26,* 487–496. **[AuQ31]**

Paxil. (2008). In *Physicians' desk reference* (pp. 1529–1538). Montvale, NJ: Thomson Healthcare. **[AuQ32]**

Pope, Jr., H. G., & Katz, D. L. (1990). Homicide and near-homicide by anabolic steroid users. *Journal of Clinical Psychiatry, 51,* 28–31. **[AuQ33]**

Porcerelli, K., & Sandler, B. (1998). Anabolic-androgenic steroid abuse and psychopathology. *Psychiatric Clinics of North America, 21,* 829–833. **[AuQ34]**

Prenzlauer, S., Galynker, II. & Cai, J. (1996) Cocaine-related obsessive homicidal ideation. *Journal of Clinical Psychiatry. 57*(9), 424–425. **[AuQ35]** **[AuQ36]**

Rebetron. (2008). In *Physicians' desk reference* (pp. 3012–3017). Montvale, NJ: Thomson Healthcare. **[AuQ37]**

Schwartz, R. C., Wendling, H. M., & Guthrie, H. K. (2005). Examining anxiety as a predictor of homicidality: A pilot study. *Journal of Interpersonal Violence, 20,* 848–854.

Shaw, E. D., Mann, J. J., Weiden, P. J., Sinsheimer, L. M., & Brunn, R. D. (1986). A case of suicidal and homicidal ideation and akathisia in a double-blind neuroleptic crossover study. *Journal of Clinical Psychopharmacology, 6,* 196–197.

Strattera. (2008). In *Physicians' desk reference* (pp. 1850–1855). Montvale, NJ: Thomson Healthcare. **[AuQ38]** **[AuQ39]**

Tobin v. SmithKline Beecham Pharmaceuticals, 164 F.Supp.2d 1278, 1284.

Whitehead, P. D. (2003). Causality and collateral estoppel: Process and content of recent SSRI litigation. *J Am Acad Psychiatry Law, 31*(3), 377–382. **[AuQ40]** **[AuQ41]**

Wise, B. (1989). *Reports of hostility after exposure to triazolobenzodiazepines.* Rockville, MD: Food and Drug Administration Division of Epidemiology and Surveillance.

Correspondence regarding this article should be directed to Donald H. Marks, MD, PhD, 9340 Helena Road, Suite F-414, Hoover, AL 35244. E-mail: Extant4@hotmail.com

[AuQ1] Is it correct that there is no space between the word alpha and the number 2? Looking up this term, I find various treatments, including interferon-alpha 2 and interferon alpha-2. And in this article, it is presented inconsistently. Please check the preferred format and apply consistently throughout.

[AuQ2] Springer mandates 4 to 6 keywords per article; please delete 3 to 5 keywords.

[AuQ3] Correct that this word is all caps? In the previous sentence, it is not. Please check and correct throughout as necessary.

[AuQ4] Per APA style, all quotes must be from sources listed in the references, and each quote must be cited in text, including page number. Please provide a complete reference, if necessary, for this source and also include an APA-style citation.

[AuQ5] Is race relevant? Can this category/row be deleted from Table 1?

[AuQ6] Please spell out DSB in Table 1.

[AuQ7] In Table 1, are homicidal thoughts the same as homicidal ideation. If not, please explain the difference; if the same, please use term consistently — that is, HI.

[AuQ8] What does DSB stand for in Table 2? Please spell out.

[AuQ9] What does the yellow highlighting indicate in Table 2? Can it be deleted?

[AuQ10] What does SSNRI stand for in Table 2? Please explain in the table notes.

[AuQ11] The reference list and a citation in the previous paragraph give 2006 as the date for Paxil. Please check the date and correct throughout as necessary.

[AuQ12] The reference list gives 2005 as the date for Henderson & Hartman, but this citation and one below give 2004. Please check the date and correct throughout as necessary.

[AuQ13] Should Keppra be in all caps, as it is in the following quote? Please check and treat consistently throughout.

[AuQ14] Please provide the page number for this quote about Rebetron.

[AuQ15] Please indicate where this quote about the prescribing information for Pegasys ends. There is an opening quotation mark but no closing quotation mark. At the end of the quote, please provide a citation, including the page number, and make sure the source is added to the reference list.

[AuQ16] What does DSB stand for in Table 4? Please spell out.

[AuQ17] Descriptions of three cases (not two) follow. Okay to change two to three here? Please clarify and correct as necessary.

[AuQ18] Are there editors or authors of Physicians' Desk Reference? If so, please include them in the Accutane reference.

[AuQ19] Bostwick and Lineberry 2006 is not cited anywhere in this article. Please make sure it is cited somewhere, or delete this entry from the reference list.

[AuQ20] Please make sure Catani et al. 2001 is cited somewhere in the article or delete from the reference list.

[AuQ21] Please cite Dealberto et al. 2006 or delete the reference.

[AuQ22] Please spell out the journal title *PLoS Med* in the Healy et al. 2006 reference.

[AuQ23] Please make sure James & Savini 2001 is cited somewhere in the article, or delete this entry from the reference list.

[AuQ24] If there are editors for Physicians' Desk Reference, please add them to the Keppra 2008 reference.

[AuQ25] Please cite Korn et al. 1997, or delete the reference.

[AuQ26] Marks 2004 is not cited anywhere in the article. Please make sure there is a corresponding citation, or delete this entry from the reference list. Can you provide the city where this testimony took place?

[AuQ27] Please provide the place of publication for Marks 2005.

[AuQ28] Please provide the date of retrieval for Marks 2007.

[AuQ29] Please provide the month of the meeting in Boston for Marks 2008.

[AuQ30] Please make sure Marks & Milby 2008 is cited somewhere in this article. Otherwise, it must be deleted from the reference list. If it is retained, please complete the reference information.

[AuQ31] Myers & Vondruska 1998 must be cited somewhere in the article or deleted from the reference list.

[AuQ32] If there are editors of Physicians' Desk Reference, please provide them in the Paxil 2008 reference.

[AuQ33] Please cite Pope & Katz 1990 or delete this entry from the reference list.

[AuQ34] Please cite Porcerelli & Sandler 1998 or delete from the references.

[AuQ35] Is II coauthor Galynker's initials or a suffix? Please clarify and correct as necessary in the Prenzlauer et al. 1996 reference.

[AuQ36] Please cite Prenzlauer et al. 1996 or delete it from the reference list.

[AuQ37] If there are editors for Physicians' Desk Reference, please provide them in the Rebetron 2008 reference.

[AuQ38] If there are authors of Physicians' Desk Reference, please provide in the Strattera 2008 reference.

[AuQ39] Schwartz et al. 2005, Shaw et al. 1986, and Strattera 2008 all must be cited or deleted from the references.

[AuQ40] Please spell out the title of the periodical in Whitehead 2003.

[AuQ41] Please cite or delete Whitehead 2003.