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## NMS and HIV

**To the Editor:** In their excellent review of neuroleptic malignant syndrome (NMS) published in the September 1998 issue, Pelonero and associates (1) called attention to the role of poorly controlled or treatment-resistant extrapyramidal symptoms as risk factors for NMS. We would like to amplify this point and call attention to the association between HIV infection and increased sensitivity to extrapyramidal symptoms. Several authors have reported on cases of NMS in patients with AIDS, leading us to wonder whether advanced HIV infection may be a risk factor for NMS.

Breitbart and associates (2) reported three cases of NMS in patients with AIDS dementia who were treated with neuroleptics. Rosebush and Stewart (3) reported on 24 cases of NMS occurring in 20 patients, one of whom was a 31-year-old man with AIDS. Swenson and associates (4) reported a case of AIDS and dementia in a man who developed severe extrapyramidal symptoms with many features of NMS while being treated with a phenothiazine, prochlorperazine, as an antiemetic. Vogel-Scibilia and colleagues (5) identified an episode of NMS in a literature review of 13 cases of HIV infection presenting as psychosis, of whom seven were treated with neuroleptics.

These case reports call attention to the possible role of HIV infection as a risk factor for NMS. Several of these authors observe that HIV infection of the central nervous system may increase a patient's susceptibility to extrapyramidal symptoms. If increased sensitivity to extrapyramidal symptoms is a risk factor for NMS, as Pelonero and associates suggest, then it follows that HIV infection may predispose to NMS.

Of note, five of the six cases of NMS reported by the authors cited above occurred in patients with AIDS, and most involved the use of standard, as opposed to atypical, antipsychotics. Some authors have suggested that the increased sensitivity to extrapyramidal symptoms may be a direct effect of HIV on the basal ganglia. At the very least, clinical caution is indicated when using standard antipsychotics in the treatment of patients with advanced HIV infection or AIDS.

**Ewald Horwath, M.D.**  
**Francine Cournos, M.D.**

*Dr. Horwath is associate clinical professor of psychiatry and Dr. Cournos is professor of clinical psychiatry at Columbia University College of Physicians and Surgeons in New York City.*

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**In Reply:** We believe several important issues should be considered regarding NMS and HIV infection. Epidemiologically, one cannot conclude from a series of cases separate

from a defined population that the risks of NMS will be higher in persons with HIV infection. There may also be reporting bias; that is, so many case reports of NMS have appeared in the literature that NMS cases with interesting comorbidities may be more likely to be submitted and published than reports of "routine" cases.

If NMS does occur more often in patients with AIDS, such occurrence might be a nonspecific effect of other recognized risk factors such as dehydration, malnutrition, or organic brain disease. In any case, we certainly agree that clinicians should be on the alert for NMS in patients with AIDS. Fever, altered mental status, and autonomic instability are frequent in AIDS, making NMS more difficult to discern.

**Anthony L. Pelonero, M.D.**  
**James L. Levenson, M.D.**  
**Anand K. Pandurangi, M.D.**

## Physician-Assisted Suicide

**To the Editor:** The November 1998 debate on physician-assisted suicide between Drs. Hartmann and Meyerson (1), followed by the paper from the Netherlands by Dr. Shoenberger and associates (2), raises significant issues about how psychiatrists ought to conduct themselves if asked to assist in suicide.

Unfortunately, the debate between Hartmann and Meyerson ignores the clinical context and concentrates instead on ethical, moral, and philosophical issues. While consideration of these issues is important, we believe the narrow focus on them will not resolve the question of whether legislation should allow physician-assisted suicide. What we are left with is disagreement as to what is ethical and what is not, and a choice between different philosophical versions of the notion of autonomy of the individual. Such questions need to be placed in the clinical context, specifically the way decisions of life and death can be affected by the vicissitudes of the doctor-patient relationship (3).

Whether a physician should assist in a patient's suicide remains fundamentally a question about the framework and boundaries of clinical practice. To draw a parallel, we suggest that whether a physician should engage in a sexual relationship with a patient is less a moral or philosophical issue than one of therapeutic boundaries. The therapeutic framework that implicitly and explicitly forbids a sexual relationship allows the doctor to examine the patient's feelings with the patient. Whether a patient who seeks a sexual relationship with the doctor is "competent" is not the issue. The very presence of the prohibition against a sexual relationship makes it possible for the patient's wishes to be dealt with in a therapeutic manner.

We contend that the same therapeutic framework applies to requests for physician-assisted suicide. Without a framework that prohibits the action, a doctor is not able to carefully examine the possible meanings of such a request in the total context of the patient's life, and indeed in the context of the relationship with the doctor. Such a process of therapeutic engagement is not possible within a legislative framework in which assisted suicide is a potential outcome.

Much of the debate about euthanasia and physician-assisted suicide has as its underlying assumption that doctors will always act in the interests of their patients. This assumption fails to take into account the doctor's unconscious and indeed sometimes conscious wishes for the patient to die and thereby to relieve everyone, including the doctor, of distress. The Dutch authors rightly point to the question of the violation of therapeutic boundaries and the role of countertransference in influencing how doctors behave toward suicidal patients. We suggest that countertransference is also an issue with terminally ill patients, where disgust with disease and decay may operate (4).

Legislation to enable assisted suicide has been designed to provide a safeguard, through psychiatric assessment, that protects patients from

themselves (5). What these laws do not do and cannot do is protect the patient against unconscious factors in the doctor.

**Francis T. Varghese, M.B.B.S.,  
F.R.A.N.Z.C.P.**

**Brian J. Kelly, Ph.D.,  
F.R.A.N.Z.C.P.**

*Dr. Varghese and Dr. Kelly are associate professors in the department of psychiatry at the University of Queensland in Brisbane, Australia. Dr. Varghese is chair of the division of mental health and Dr. Kelly is director of consultation-liaison psychiatry at the Princess Alexandra Hospital and District Health Service in Brisbane.*

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**To the Editor:** Thank you for publishing the articles on physician-assisted suicide by Hartmann and Meyerson and Schoevers and associates in the November 1998 issue. That psychiatrists are considering the issue is a sign of a profound shift in the underlying philosophical assumptions of our culture.

The traditional psychiatric frame of reference about the wish to die evolved at a time when people accepted the sanctity of life as a religious principle. There was no need to explicitly build it into our concept of treatment. When a patient came to the psychiatrist and said, "I want to die," the psychiatrist knew the message was, "Even though my life is

valuable, I have frightening wishes to die. Please help me." Even when psychotherapy and medications didn't work, we protected our patients, expecting that after a while they would no longer be dangerous to themselves. Our expectations were fulfilled. No patient who was placed on suicide precautions remained there until he or she died from old age.

Today we can no longer count on our practitioners' or our patients' belief in the sanctity of life. This shift leaves a dangerous gap in our diagnostic manual. A patient with feelings of hopelessness and suicidal ideation who does not meet diagnostic criteria for any of the disorders can be perceived as making a rational choice for suicide. One of the cases cited by Schoevers and associates and discussed elsewhere by Hendin (1) fell into this category.

If we are willing to consider hopelessness and suicidality as a psychiatric disorder, there is certainly no lack of good treatments. Thanks to the work of Albert Ellis (2) and Aaron Beck (3), we have powerful cognitive techniques that we could offer to far more patients than we currently do (4), and we can hope for future medications to help them as well. Including hopelessness and suicidality as a psychiatric disorder will help us with bedside consultations, where physicians may take our judgment of "no psychiatric disorder" as automatic permission for physician-assisted suicide.

If we do not include hopelessness and suicidality as a psychiatric disorder, then we must make it clear that a doctor cannot offer a biological treatment for it in the form of lethal medication. To do otherwise encourages absurdity. It is ridiculous to treat the nonmedical disorder of suicidality and perceived hopelessness with a medical treatment that causes the patient to die. The medication gets rid of the symptoms, but it has death as a side effect. Since when do we consider that acceptable?

Our psychiatric wards are full of patients with more tragedy in their lives than the cases described by Schoevers and associates. If we do

not educate our psychiatrists to know their professional limits, these patients' lives could be at risk.

**Barbara A. Olevitch, Ph.D.**

*Dr. Olevitch is courtesy assistant professor of psychiatry at the Missouri Institute of Mental Health, School of Medicine, University of Missouri-Columbia.*

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**To the Editor:** Reasoning by analogy can be misleading. In their November 1998 article discussing developments in the Netherlands concerning physician-assisted suicide in psychiatry, Schoevers and associates state that "a comparison with the death penalty may not be as far-fetched as it seems; the death of an innocent person is always one death too many." The authors thus suggest an analogy between the death penalty and physician-assisted suicide in psychiatry, at least as far as it concerns the deaths of "innocent persons." This presumed analogy, however, is defective for a number of reasons.

First, leaving exceptional cases aside, persons who are confronted with the death penalty have no wish to die. Psychiatric patients who have an enduring wish for assistance in suicide, on the other hand, want life to end because they consider themselves to be suffering unbearably, with no prospect for relief.

Second, presume for the sake of argument that the taking of the life of a guilty person by the state can be justifiable under specific conditions. The legal standards of evidence that can justify the death penalty in an individual case are not necessarily the same standards of evidence that ought to be applied to morally or

legally justify physician-assisted suicide. The implication of the analysis by Schoevers and associates seems to be that the standards of evidence in cases of physician-assisted suicide should at least be comparable to the standards for a death penalty sentence. But it is not at all evident what the right standards in physician-assisted suicide should be.

Reasoning by analogy can be dangerous. If such reasoning takes place for rhetorical reasons, we should be particularly cautious. Taking the life of an innocent person who is believed to have committed a serious crime is not comparable to assisting in the suicide of a mentally ill person who is considered incurable, but who might in fact have been curable if his or her life was not ended, perhaps because a new treatment eventually was developed. In the latter case, we will not even be able to make a valid statement about "innocent" patients: in retrospect we can never be sure that the patient would have been curable.

For some, this uncertainty is precisely the ultimate argument for categorically opposing physician-assisted suicide. Indeed, only when certainty is assured will we be able to totally rule out "innocent" candidates for assisted suicide. As a consequence, however, mentally ill but competent patients who suffer severely and hopelessly are left alone.

The morality of physician-assisted suicide in psychiatry needs a different weighing of values, norms, and interests than the morality of the death penalty.

**Ron L. P. Berghmans, Ph.D.**

*Dr. Berghmans is a senior research associate at the Institute for Bioethics in Maastricht and is affiliated with the department of health ethics and philosophy at the University of Maastricht in the Netherlands.*

**In Reply:** Dr. Berghmans rightly draws attention to the differences between the evaluation of a request for physician assisted suicide by a suffering psychiatric patient and the judicial process leading to the death penalty for persons who have com-

mitted criminal offenses, in countries where this sentence exists.

The analogy with the death sentence was used in the context of a discussion of the incurability of psychiatric disorders, in which we asked whether psychiatrists can provide sufficient certainty on the treatment prognosis of their patients to warrant assisting a suicide. The analogy was not based on a literal interpretation, but rather on the fact that decisions on life and death are final and should be carried out only when there is certainty that the decision is right. The need for certainty places a heavy responsibility on those who have to make such decisions, whether judges or physicians, and on the evaluation procedure that is to be followed.

In our paper we underlined the uncertainties and complexities of such an evaluation procedure, applicable to psychiatric patients with a death wish who turn to their psychiatrist for help. We hope we made clear what those complexities are, and how a policy favoring physician-assisted suicide may fundamentally affect clinical practice. By focusing on a "new treatment that may eventually be developed," Dr. Berghmans failed to address some of the key issues we raised.

**Robert A. Schoevers, M.D.**

**Frank P. Asmus, M.D.**

**Willem Van Tilburg, M.D., Ph.D.**

### Medication Compliance

**To the Editor:** The article on criminal victimization of persons with severe mental illness by Hiday and associates (1) in the January 1999 issue is an important contribution. Conspicuously absent, however, is any mention of medication compliance among the 331 study subjects with severe mental disorders. Because they all had been involuntarily admitted and subsequently court-ordered to outpatient commitment after hospital discharge, it seems highly probable that they had not been compliant with their psychiatric medications before admission, since noncompliance is the usual cause for outpatient commitment.

In another paper, the authors indicated that 71 percent of the study group were noncompliant with their medication (2). This finding implies that there is a direct relationship between medication noncompliance and criminal victimization, which many of us have observed anecdotally among our patients.

**E. Fuller Torrey, M.D.**

*Dr. Torrey is president of the Treatment Advocacy Center in Arlington, Virginia.*

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**In Reply:** Dr. Torrey correctly points out that our sample was involuntarily hospitalized and subsequently court-ordered to outpatient commitment, orders generally associated with non-compliance, and, furthermore, that our sample had a 71 percent non-compliance rate, as we reported in another article (reference 2 above). He concludes that these factors indicate "a direct relationship between medication noncompliance and criminal victimization."

It is possible that taking antipsychotic medication may reduce the risk of victimization by ameliorating symptoms such as disorientation, which might cause a severely mentally ill person to wander into dangerous areas, appear more vulnerable, and thus be criminally victimized, or by ameliorating symptoms such as annoying behavior, which might be provocative of abuse from acquaintances and friends. But we believe that the relationship between medication noncompliance and criminal victimization is more complicated.

Victimization reflects exposure to crime and violence in the social environment. Our analysis, along with the analyses of others who have looked at the problem, shows that victimization is associated with a constellation

of problems such as alcohol abuse, drug dependence, homelessness, and mental disorder. Additionally, in our sample and in other samples of persons without mental disorders, victimization is associated with criminal and violent behavior.

Our second paper to which Dr. Torrey refers reported that medication noncompliance has a significant effect on violence only in interaction with substance abuse. As we suggest, medication noncompliance may lead to self-medicating with alcohol or drugs, and the subsequent impairment may impede medication adherence so that focusing on treatment of one without the other is unlikely to lead to effective reduction of violence and victimization. Problems of the social environment, such as homelessness, need to be addressed as well.

**Virginia Aldigé Hiday, Ph.D.**

**Jeffrey W. Swanson, Ph.D.**

**H. Ryan Wagner, Ph.D.**

### A Note on Competition and Profit in Medical Care

**To the Editor:** The exchange between Stone and Blackwell (1,2) in the September and December 1998 issues is far from trivial and deserves wide-ranging discussion. The establishment of medicine as a profession around the turn of the century had salutary influences on the autonomy, power, prestige, and quality of medical practice. The territorial claims and many defensive battles over the boundaries of the profession protected medical practice from the crass competitive commercialism that was rampant at that time. Monopolistic control, securely maintained until after World War II, contributed to both the quality of medical care and the development of the infrastructure of education and research.

For the first 25 years the hospital insurance industry did not challenge the power and prestige of the medical profession. Nor did it challenge the prerogatives of the doctor to make the decisions about clinical events, and so the impossible-to-de-

fine phrase "medical necessity" was invented. But now we can make only empty and impotent claims to those prerogatives and blame managed care because we must compete in a sordid profit-dominated marketplace like any other business or industry. As reprehensible as managed care organizations may be, they did not introduce either competition or the profit motive. Physicians must accept some historical responsibility for our current position.

For example, in 1963 advocacy by the American Psychiatric Association played a major role in the negotiations of the United Auto Workers contract that established the principle that insurance would pay for outpatient psychotherapy. The unintended economic consequence was that such payment presented irresistible financial opportunities for other professions and encouraged the development of new "products." Psychiatrists no longer maintained a monopoly over psychiatric services and were on the unrecognized brink of overexpanding costs of health care to employers. Granted, psychiatry has always been a relatively unimportant but vulnerable player in the health care economy. But managed care didn't even exist.

The profit motive was established in health care by the federal Medicare and Medicaid legislation of 1965. This legislation converted hospitals from charitable institutions into profit-making enterprises. Interestingly enough, organized medicine was not attending to the impact of this legislation on the industrialization and monetization of health care. Instead, organized medicine feared the regulatory influence of government. Compromises were made to accept government-financed health care as long as the medical profession maintained control over clinical decisions, and the doctor-patient relationship was protected. "Medical necessity," meaning "what the doctor said," was promoted to unsustainable importance. Even psychiatrists basked in the glow of expanding funds for health care. Managed care didn't arrive for another 20 years, but the profit motive in

the economics of health care had been unleashed. We were there and profited.

To address the issue of the relevance of information in efficient markets, raised by Dr. Stone, we might note that the technology of many products such as computers, automobiles, airline tickets, and financial operations, has surpassed the information available to the ordinary consumer of these products. Health care products are no longer unique.

**Frank T. Rafferty, M.D.**

*Dr. Rafferty is affiliated with the Gateway Center for Human Development in Brunswick, Georgia.*

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## Placebos in Research

**To the Editor:** In a letter to the editor in the May 1998 issue, McCarthy (1) posed important and potentially disturbing questions about the ability of patients with schizophrenia to fully understand the implications of receiving a placebo in a clinical trial and to provide genuine informed consent.

We fully agree with McCarthy that all necessary measures should be taken to assess and facilitate patients' understanding of the research process and to safeguard their rights. Investigators and other parties, such as institutional review boards, must be vigilant in this regard. Clearly, the good of society—in particular the interests of other patients with the same disorder—cannot be used to justify encroaching on the principles of beneficence and autonomy as they apply to the individual patient.

However, in considering the use of placebos in research, several other issues need to be examined, which we address briefly below.

**Are there viable alternatives to placebo controls for research?** Alternatives to placebo controls include active controls, who receive the stan-

dard drug for the condition, and historical controls, which are based on data from previous placebo-controlled studies with similar patients. Several writers have argued that placebo controls are essential to clinical trials in certain circumstances and that alternative control groups are inadequate. Given the need for placebo controls to permit meaningful conclusions to be drawn from clinical studies, it may be argued that not using placebo controls would be unethical because patients receiving the experimental drug would be exposed to potential risks in a study of questionable scientific benefit.

**What is the potential harm to patients receiving placebo?** Conventional antipsychotics are not uniformly effective in schizophrenia, in particular against negative symptoms. Between 30 and 50 percent of patients are exposed to the risk of troublesome adverse effects for minimal or no benefit (2). Also, contrary to popular belief, as many as 55 percent of patients who receive placebo in the acute phase do not worsen, and up to 25 percent are much improved (2,3).

In addition, some studies have found that patients who relapse while on placebo do not suffer any long-term consequences. For example, Curson and associates (4) followed patients who had participated in a short-term trial of relapse prevention. They found that although in the original trial 66 percent of patients on placebo had relapsed compared with 8 percent of those on the active drug, there were no differences between the two groups in the number of relapses after the end of the trial or in any clinical or social variable over a seven-year follow-up period.

**How well informed is the informed consent of patients with schizophrenia who participate in clinical trials?** Carpenter and associates (3) have cited recent research suggesting that approximately 75 percent of patients with a diagnosis of schizophrenia incorporate information and make decisions much like comparison groups do when dealing with consent issues.

**What can be done to protect the individual patient?** Explicit guidelines, such as those adopted by Loma Linda University (5) or proposed by Carpenter and associates (3) may aid in protecting psychiatric patients, particularly those with a psychotic disorder, who are enrolled in placebo-controlled trials. Although researchers must continue to be very concerned and vigilant about protecting the rights of subjects participating in research, the use of placebos in research has unique scientific benefits. With proper care, it need not be incompatible with concerns for the safety of the subjects.

**Rajnish Mago, M.D.**

**Richard Petty, M.D.**

**Paul Root Wolpe, Ph.D.**

*Dr. Mago is associated with the department of psychiatry at the University of Pennsylvania in Philadelphia. Dr. Petty is clinical director of the neuropsychiatry program and Dr. Wolpe is associated with the Center for Bioethics at the University of Pennsylvania.*

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