Op-Ed/Editorials: Antiaddiction Medicine and the Future of Addiction Treatment: A Discussion

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The following editorial was written by Dr. McPeake. The pages that follow contain two responses (by Dr.

Dodes and Dr. Potenza, respectively) to this editorial. The last page contains Dr. McPeake's final response.

John D. McPeake, Ph.D., C.A.S
President, Cypress Hill Associates, Inc.

Knowledge-based fields of endeavor, like addiction treatment, proceed within a "taken-for-granted"
frame of reference or paradigm which accommodates instances of new knowledge by incorporating them into the existing paradigm. Twelve-Step-oriented models of addiction treatment, for example, the dominant addiction treatment framework in the U.S., has had little difficulty incorporating cognitive behavioral, stage change analysis and motivational enhancement strategies into its approach. This has enriched the treatment process but left the field of addiction treatment essentially unchanged.

At particular points in the history of any field, however, the accumulation of certain types or
certain amounts of new knowledge can no longer be incorporated into the existing paradigm and
create the circumstances that lead to a paradigm shift. Two brief examples from the history of
behavioral health may suffice to illustrate this process.

Until a decade ago some gastric ulcers were regarded as a condition produced in part by faulty
response to stress. Psychotherapeutic approaches that identified and treated the stress
predominated but were only marginally successful. Then it was discovered that

many gastric ulcers
were caused by h. pylori that could be effectively treated with a course of antibiotic medicine. This
resulted in a reassessment of the treatment of psycho-physiological disorders. Similarly, until approximately 1960 the dominant understanding of mood disorder and psychosis involved psychodynamic treatment. The successful use of the phenothiazines, the monoamine oxidase inhibitors and the tricyclics in the treatment regimen led to a dramatic shift away from psychodynamic models and methods and ushered in the era of psychopharmacology and biological psychiatry.

The field of addiction treatment is about to undergo a dramatic paradigm shift. During the last
twenty-five years the cortical locus of addiction has become clear in the mesolimbic structures of
the ventral tegmentum connecting with the limbic system and the nucleus accumbens. Dopamine
the central mesolimbic neurotrasmitter interacts with serotonin, opioids, GABA, NDMA and perhaps
other neurotransmitters in a molecular dance. Alcohol and other drug use alter the balance in
these structures, which genetics may already have made vulnerable.

Enter antiaddiction medicines, even now a dissonant locution, which will soon proliferate and become as common as antidepressants. Antiaddiction medicine is thought to treat the functional and structural changes caused by addictive use. The integration of these new medicines into the treatment of the addictions will produce dramatic changes in the way addiction treatment is carried out. Addiction treatment professionals need to become educated and sophisticated about these medicines or risk
becoming obsolete. The example of recent work on ondansetron (Zofran) is a harbinger of the future. Bancole Johnson et al in a recently-published article in JAMA note that early onset alcoholism, alcoholism developed at 25 years of age or younger, is marked by greater serotonergic abnormality and antisocial behaviors. Specific serotonin receptors mediate alcohol’s rewarding effects by regulating dopamine release in the mesolimbic cortex, the “brain reward” center. Thus, blockade of serotonin receptors blockade that would subsequently reduce dopaminergic release should reduce alcohol consumption.

Ondansetron (Zofran) is a selective serotonin 5HT3 receptor antagonist (N.B., versus a selective serotonin reuptake inhibitor such as fluoxetine (i.e., Prozac)) which to date has been utilized to prevent nausea and vomiting associated with repeat courses of cancer chemotherapy, prevention of nausea and vomiting in radiotherapy to the abdomen and in the prevention of postoperative nausea and vomiting. In this study, ondansetron was employed to provide such selective serotonergic blockade in early onset alcoholics and controls. Compared to patients administered placebo, early-onset alcoholic patients administered ondansetron, but not late-onset alcoholics, had significantly fewer drinks per day, fewer drinks per drinking day, increased percentage of days abstinent and increased total days abstinent. Ondansetron was well-tolerated by the study patients and ondansetron's adverse event profile was similar to placebo. The authors conclude: "Our results suggest that ondansetron ... is an effective treatment for patients with early-onset alcoholism, presumably by ameliorating an underlying serotonergic abnormality."

How will the presence of efficacious antiaddiction medication change the field of addiction treatment
in general and gambling treatment in particular? First medication will become a treatment of choice for all addicted individuals. Therapists will therefore need to understand and be able to explain the mechanisms of action, the benefits, the potential side effects and adverse reactions. Second, the psychiatrist, psychopharmacologist or addiction medicine physician will play a more prominent role in treatment. Third, treatment team interaction will become more important to ensure an integrated treatment process. Fourth, evidence-based individual and group therapy strategies will need to accommodate medication and will need to be employed vigorously so their usefulness will not be undermined by a wave of biological psychiatric interest. Fifth, therapists will have to learn fast and work hard to assure that they are not pushed aside in what will be a rush to use these new medications.

Paradigm shifts are often met with skepticism. In attempts to preserve and protect standard practice
patterns in addiction there will be those who will attempt to discount or disparage this pharmacological approach. While challenge and academic debate are important, necessary and the core of scientific research the new knowledge about treatment with antiaddiction medicine is compelling and demands the attention and careful scrutiny of all treatment providers.

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Lance M. Dodes, M.D.
Director, The Center for Problem Gambling Mount Auburn Hospital
Assistant Clinical Professor, Harvard Medical School

Dr. McPeake's editorial correctly observes that new medications may prove to be effective in affecting
certain addictive behaviors by reducing the biological response to particular drugs. However, I believe that his description of these drugs as "antiaddiction medicines" and his idea that they should usher in a paradigm shift in treatment contains several critical errors in understanding the nature of addiction.

Interdicting the biological response to drugs, including altering serotonergic transmission, as occurs with the SSRI's as well as the new receptor antagonist ondansetron, in itself is not new. Opioid antagonists which block the response to heroin and other narcotics have been available for a long time, and their newer use in alcoholism (Revia ®) has been with us for a number of years. These medications do not work very well to treat addiction, however, because they are not "antiaddiction" drugs at all.

Addictions are fundamentally a psychological, not a biological phenomenon, as is easily shown by the
fact that detoxifying people from their drugs of abuse unfortunately solves only their physical
addiction, but does not cure their risk of returning to the same or a different addictive behavior even
years later. Likewise, people regularly shift their addictive behavior from one drug to another, or
from drug to non-drug behaviors such as compulsive gambling or compulsive sex, or even to compulsive behaviors that are often not considered to be addictions at all – such as cleaning, running or working. These shifts can occur because the psychology driving them remains the same, regardless of the form of the

behavior, or the specific biological activity of one drug or another.

When Dr. McPeake notes that "selective serotonin receptors mediate alcohol's rewarding effects" he
illustrates the problem with his view. People do not become addicts because of the rewarding
effects of alcohol, or any drug. As is well-known, addiction is not a matter of seeking to be high —
indeed this is the old, discredited idea that addicts are merely pleasure-seekers. On the contrary, addiction is a compulsive activity, an action which must be repeated for psychological reasons, even
though many addicts, and almost all those seeking treatment, dearly wish to be able to stop.

Blocking the physical effects of a drug may decrease the use of that drug, but will not address the need to perform a behavior designed to solve an internal emotional problem — it will not address the cause of addiction. Dr. McPeake states this himself when he says that "antiaddiction medicine is thought to treat the functional and structural changes caused by addictive use." Treating the changes caused by drugs is a very different matter from treating the causes that lead to such use. If one wants to treat addiction, therefore, it is necessary to understand the nature of the compulsion to repeat this behavior. The most widely known formulation of this mechanism is of course the "self-medication hypothesis," but a number of people have made more specific contributions to understanding the psychology of addiction (Wurmser 1974, Khantzian 1985, Krystal and Raskin 1970, Dodes 1990, 1995). This is the area that I believe deserves our closest attention if we want to keep up with the newest knowledge of the causes — not the effects — of addiction.

I would also note that Dr. McPeake's assertion that there has been a "dramatic shift away" from psychodynamic approaches to depression with the advent of antidepressant medication is similarly inaccurate. Rather than replacing psychodynamic therapy, very frequently these medicines are combined with therapy, at least in the hands of those trained to do psychodynamic work. Experience over many years has shown that while symptom relief from the newer antidepressants is common, this does not replace the need to resolve the emotional issues that lie behind the tendency to become depressed.

To conclude, I hope that we can be sophisticated enough about human psychology to recognize that our patients suffer with human problems which they manifest in part through addictive behaviors. Attempting to treat these behaviors by a narrowly focused effort to block the biological action of certain drugs may be a helpful adjunct but is no more an “antiaddiction” treatment than painkillers are an “anticancer” treatment. New adjunctive medicines should be welcomed, but they will only produce a paradigm shift for those who prescribe them without understanding the nature of addiction.

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Marc N. Potenza, M.D., Ph.D.
Assistant Professor
Director, Problem Gambling Clinic
Division of Substance Abuse
Department of Psychiatry, Yale University

It was with great interest that I read the editorial by Dr. McPeake describing his vision of the future
of addiction treatment. Dr. McPeake raises important issues that warrant further discussion. It is particularly exciting that over the past several decades (including the 1990’s "Decade of the Brain") significant advances have been made in our understanding of brain function in healthy and disordered states. The importance of utilizing knowledge of brain function in designing and testing for efficacious

and well-tolerated treatments for mental health disorders, including addictive disorders, cannot be understated.

Although the article by Johnson et al. (2000) describing the efficacy of ondansetron (Zofran) in the short-term treatment of individuals with early-onset alcohol dependence (AD) represents a significant contribution to the treatment of individuals with AD (Kranzler, 2000), it is not the first report of a drug therapy for AD. Other investigators have reported the utility of disulfiram (Antabuse) (Hald, Jacobsen, 1948) and naltrexone (ReVia) (O'Malley, Jaffe, Chang, Schottenfeld, Meyer, Rounsaville, 1992) , (Volpicelli, Alterman, Hayashida, O'Brien, 1992) in targeting core and related symptoms of AD. Despite the availability (for many years) of these drugs for the treatment of AD, many would argue, as Dr. McPeake has, that 12-step programs remain, "the dominant addiction treatment framework in the United
States" (McPeake, 2000). If this is the case, it is important to try to understand why there has not been the rapid shift to pharmacotherapies and away from 12-step and other behavioral modalities that Dr. McPeake suggests could happen in the wake of the recent ondansetron study.

One factor potentially related to a hesitancy to move directly into pharmacotherapeutic treatment for addictive disorders is that we remain in the midst of an evolution of the conceptualization of
addictive disorders. Addictive disorders historically have been associated with greater stigma than
arguably any other group of disorders. Over time, the conceptualization of addiction has been
shifting from sin to vice to habit, and only recently has addiction been viewed as a disorder or an
illness. A recent article by McLellan (McLellan, Lewis, O'Brien, Kleber, 2000) describes data
supporting the conceptualization of drug dependence as a chronic medical illness. As the authors indicate in their article, the general acceptance of drug dependence as a chronic medical illness has multiple important implications for treatment, insurance parity, and evaluation of outcome. Many features of their arguments seem applicable to other addictive disorders, including pathological gambling.
Although it seems doubtful that an immediate shift will occur to solely pharmacotherapeutic modalities

of treatments for addictive disorders, it appears we are in the midst of a paradigm change.

Increasing data supporting biological determinants of addictive disorders, with some of the strongest
data coming from genetic studies in which it is not unusual for 30% to 70% of the variance of
substance use disorders in specific populations to be attributable to genetic factors (Goldman,
Bergen, 1998). Similar studies also provide some of the strongest data supporting a biological
commonality between behavioral and substance use addictive disorders – namely, in a group of
males with gambling and alcohol use problems, shared genetic factors were implicated in the
expression of the illnesses (Slutske, Eisen, True, Lyons, Goldberg, Tsuang, 2000). Data from these
and other studies will likely be important components in moving addictive disorders, including substance use and gambling disorders, into a framework in which they are viewed similarly to other chronic, biologically-based, behaviorally-influenced, medical illnesses. In this movement, it will be important, as Dr. McPeake states, that effective treatment components not be discarded but instead incorporated and evaluated in evidenced-based manners. For example, many of the pharmacotherapy trials demonstrating drug efficacy in the treatment of AD have utilized a behavioral therapy platform, (Anton, Moak, Waid,
Latham, Malcomb, Dias, 1999), (Swift, 2000) including the recent ondansetron study (Johnson et al, 2000) The same ondanstron study also demonstrates that biological differences between groups of individuals with AD can have an influence on choice of treatment, a consideration likely to become increasingly important over time as knowledge of the underlying biologies of addictive disorders advances. The data supporting a biological basis for addictive disorders provide a powerful armamentarium in arguing to patients, clinicians, physicians, insurance representatives, politicians, and the general public the necessity to view addictive disorders as chronic medical illnesses that require the use of empirically-tested interventions for short- and long-term treatment.

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In Response…

John D. McPeake, Ph.D., C.A.S

President, Cypress Hill Associates, Inc.

Dr. Potenza identifies the marked and persistent stigma associated with addictive disease as one
barrier to the new treatment paradigm that seeks to integrate evidenced based pharmacological and
psychosocial approaches. An additional barrier he notes is the lack of acceptance of the addictions as
chronic medical illnesses. Dr. Potenza references some of the voluminous data, particularly the
genetic data, supporting common biological determinants for these illnesses. He argues
cogently for evidence based pharmacologic and psychosocial interventions in the addictions.

Dr. Dodes on the other hand reminds us not to omit psychological variables in addiction
treatment. Twelve Step approaches and more recently cognitive behavioral, stage change and
motivational enhancement strategies have demonstrated efficacy and of course respond to
the psychological needs of drug dependent persons in treatment.

Alone, these psychosocial approaches all leave something to be desired. Several decades of neuroscience research identifying the biological determinants of addictive disease offer new medicine based approaches that enhance outcomes, particularly when integrated with the treatment approaches named. Addiction treatment professionals are encouraged to move to an approach that integrates medical and psychosocial approaches.