

The use of antidepressant medications (ADMs) as a means to manage mood altering life challenges has reached a level of acceptance that probably surprises no one anymore. According to 2005 figures (the most recent available) from the U.S. Centers for Disease Control and Prevention, ADMs are now the most frequently prescribed class of drugs in the U.S., making up about 5% of all prescription medications. For most people, it seems, the fact of the widespread use of ADMs has made it seem unnecessary to question their merits; what's the point of questioning something already so deeply woven into the fabric of our society? It's too much like questioning whether the barn door should be closed after the horse has already escaped.

Many marriage and family therapists (MFTs) routinely encourage medication evaluations for their depressed clients, assuming with little foundation that drugs are the primary intervention, while their psychotherapy is merely secondary. But, several things have happened this year in regard to ADMs that should make every MFT stop in his or her tracks and reconsider the key issues raised by these events. I want to state clearly and explicitly to all MFTs that there are plenty of sound reasons to unapologetically emphasize the merits of teaching skills over taking pills.

My intention is to address some of the legitimate concerns about medications and provide some supportive data in order to make one key point: We shouldn't let the marketing of drugs overshadow the science and art of sound clinical practice. Specifically, I want to draw your attention to the nine domains of concern about antidepressants in Table 1.

For the purposes of our limited space here, I will provide a greatly distilled essence of the various concerns.

Concern #1: The One-Dimensional Nature of a Purely Biological Perspective

Consider your answer to this seemingly simple question: What causes depression? How you answer this question is the single most important determinant of how you will design and deliver

Table 1. Concerns about Antidepressant Medications

- 1. The one-dimensional nature of a purely biological perspective
- 2. The limited definition of client role
- 3. Economic corruption:
 Greed, undue influence
 on the healthcare system
- 4. Pseudoscientific false advertising
- 5. Conflicting data regarding their safety and use
- 6. Over- and under-prescribing issues
- 7. Side effects undermining their effectiveness
- 8. Therapeutic Efficacy: Do they really work
- 9. Ecological issues

treatment... and how you will relate to the points raised in this article.

Is depression caused by:

- Genetics?
- A biochemical imbalance in the brain?
- Psychosocial stressors?
- Cognitive distortions?
- A lack of environmental and social rewards?
- Social inequities?
- Cultural and/or familial influences?
- Mishandling key vulnerable situations?
- Dietary issues?
- A lack of physical exercise?

If you were to review the clinical and research literature, you would find that *each* of the factors above, as well as many others not listed, play significant roles in the onset and course of depression. Thus, the best and most realistic answer to the question of what causes depression is that depression is caused by *many* contributing factors that will vary in degree across individuals. Biology run amok has been overstated as the principal causal factor in depression when *psychological* and *social* factors have been shown to play an even greater role in its onset and course.

The social side of depression, a sensible focus for MFTs, has received too little attention due to the excessive attention paid to biological and drug solutions. I hope to help remedy that with my forthcoming book, due out in September 2009 from The Free Press, called *Depression is Contagious*.

What MFTs Can Do Better: View and treat depression from a multi-dimensional, systemic perspective.

Concern #2: The Passive Definition of the Client's Role

Depression is a disorder built on a foundation of passivity. "Why bother?" is the unofficial motto of depression. It is no coincidence that the therapies with the greatest empirical support all emphasize taking purposeful and sensible **action** in treatment. To merely prescribe an antidepressant is to impart the unhelpful message: You don't have to change your life, you don't have to learn any new skills; you just have to take your medication on time. The problem isn't in your circumstances (tell that to Rachel from the opening vignette)— it's in your brain chemistry. Antidepressants don't make people passive, but they do define people's role in treatment as passive: wait for the drug to "work." If you're trying to empower people to be proactive in managing life skillfully, medication as a sole form of treatment isn't the best means to do so.

What MFTs Can Do Better: Encourage the client to be an active partner in the treatment process by doing skill-building homework and experimenting with perceptions, beliefs and new behaviors.

Concern #3: Economic Corruption and Undue Influence of Pharmaceutical Companies

Researchers, journal editors and clinicians are *not* without greed. Let's start with physicians, too many of whom have essentially defined themselves as regional sales representatives for the drug companies. The American Medical Association (AMA) condones gift-taking from pharmaceutical representatives as long as no single gift is worth more than US\$100. Drug companies find plenty of takers: Spending on marketing to physicians jumped from \$12.1 billion in 1999 to \$22 billion in

2003, \$16 billion of which was in free samples, according to a 2005 Report from the Pharmaceutical Research and Manufacturers of America (PhRMA).

What about the presumed objectivity of our scientific journals attesting to the merits of ADMs? Two reports published in the April 16th issue of the prestigious *Journal of the American Medical Association (JAMA)* raised fresh concerns about how drug companies influence the interpretation and publication of medical research (Psaty & Kronmal, 2008; Ross et al., 2008). The reports claimed that drug manufacturers have frequently paid academic scientists to take credit for research articles prepared by companyhired medical writers, a practice called ghostwriting.

The practice is not uncommon, according to *JAMA*'s editors. In an editorial in the same issue, they urge strict reforms, including a ghostwriting crackdown and requiring all authors to spell out their specific roles. Dr. Catherine DeAngelis, *JAMA*'s editorin-chief, said, "The manipulation is disgusting. I just didn't realize the extent... We're the ones who have allowed this to happen. Now we've got to make it stop" (2008).

What MFTs Can Do Better: Actively resist self-serving forces that attempt to control or manipulate how you do research or provide treatment.

Concern #4: Pseudoscientific False Advertising

The "shortage of serotonin" is a heavily touted hypothesis regarding the cause of depression that has little empirical basis but a growing mass of contradictory evidence. All of us have seen the advertising blitz with ads declaring that "depression *may* be caused by a chemical imbalance and (our drug) corrects this imbalance." The decline of the serotonergic hypothesis of depression was well captured in a recent article in the science magazine *Seed* (Lehrer, 2006, p.63):

For the last 40 years, medical science has operated on the understanding that depression is caused by the lack of serotonin...the theory is appealingly simple: Sadness is simply a shortage of chemical happiness. The typical antidepressant—like Prozac or Zoloft—works by increasing



the brain's access to serotonin. If depression is a hunger for neurotransmitter, then these little pills fill us up. Unfortunately, the serotonergic hypothesis is mostly wrong. After all, within hours of swallowing an antidepressant, the brain is flushed with excess serotonin. Yet, nothing happens; the patient is no less depressed. Weeks pass drearily by. Finally, after a month or two of this agony, the torpor begins to lift. But why the delay?...a range of antidepressants trigger a molecular pathway that has little, if anything, to do with serotonin. Instead this chemical cascade leads to an increase in the production of a class of proteins known as trophic factors. Trophic factors make neurons grow...

It is unknown how antidepressants work. What the new neuroscience highlights, though, is that *psychotherapy changes brains*, just as medication does, although in different ways (Siegel, 2007).

What MFTs Can Do Better: Resist being swayed by misleading advertising by staying current with the scientific literature.

Concern #5: Conflicting Data That Confuses Almost Everyone

Be afraid, we're told, be very afraid. But, we're also told, there's really nothing to be afraid of...

Consider the issue of product safety for children: In the April 18, 2007 issue of *JAMA*, researchers (Bridge et al.) claimed that the suicide threat from

SSRIs for young people was exaggerated and recommended that the "black box" warning be lifted. (A "black box" warning is the strongest warning placed on medication packaging. In the case of ADMs, the warning was about the increased risk of suicidal ideation and behavior in children receiving ADMs.)

On May 2, 2007, just 2 weeks later, the U.S. FDA required drug manufacturers to *expand* their black box warnings! The original warning was for children and adolescents up to age 18. It is now for young adults up to age 24, as well (Friedman & Leon, 2007).

Consider the issue of how long the patient should be on medication: This is a hotly debated issue. Government guidelines say 4-9 months after remission. Magellan Behavioral Health says 4-5 months after remission. Some experts say 1 year, some say 5 years, some say forever. Confused by conflicting data? How do you think your clients feel?

What MFTs Can Do Better: Recognize the subjective biases of "experts" in areas where no such expertise can exist, simply because conclusive data aren't available yet.

Concern #6: Drugs are *Over*-prescribed and, Paradoxically, *Under*-prescribed

Despite the overall increase in the number of people seeking help for depression, estimates are that only HALF of depressed people receive *any* form of

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treatment, and only about *half* of these receive adequate treatment (Kessler et al., 2003). In this sense, the drugs are *underprescribed*. At the same time, you have doctors instantly writing a prescription when they learn someone you love passed away, and there are people who take ADMs for questionable reasons, such as wanting to lose weight or perform better on the job (especially after psychiatrist Peter Kramer promised people they'd be "better than well" in his literary valentine to Prozac, *Listening to Prozac*). In this way, these drugs are *over-prescribed*.

A realistic use of ADMs has yet to develop.

What MFTs Can Do Better: Create and participate in outreach programs to encourage seeking help (e.g., public lectures, national depression screening participation, media participation) for depression, while encouraging people to develop a realistic sense of what the medications can and can't do.

Concern #7: Drug Side Effects Can Be More Than Just An Irritant

In a study by Gandhi et al. (2003), published in the *New England Journal of Medicine*, SSRIs were the class of drug most commonly found in adverse drug events. At the very least, side effects can reduce or prevent participation in treatment, complicate symptoms and serve to **reinforce** depression. The most common side effects include:

- Nausea
- Sedation or agitation/insomnia
- Headache
- Dizziness
- Fine tremor
- Sexual disturbance
- Bone fractures in over 50s

MFTs may appreciate more than most how the sexual side effects, in particular, can exacerbate relationships already strained by depression (Montejo et al., 2001). Sexual side effects jeopardize one's ability to:

- Attract a mate
- Choose a mate
- Fall in love
- Stay in love
- Sustain intimacy in a relationship/ marriage

What MFTs Can Do Better: Highlight at every opportunity that psychotherapy's treatment success rate matches and, in some specific ways, even exceeds ADMs without side effects.

Concern #8: The Arguable Therapeutic Efficacy of Antidepressants

This issue alone makes all the other concerns secondary. If ADMs were highly successful as therapeutic agents, the other concerns might seem less significant. Just how successful are they?

In January 2008, the *New England Journal of Medicine* published an article (Turner et al.) that was staggering in its implications for how science is done and how the results of research studies are published and released to both professionals and the general public. The article documented the fact that research on antidepressant medications was, for years, published selectively. When a study showed a finding favorable to the drug company, it was highly likely (94 % chance) to be published. But, if a study *wasn't* favorable to a drug, that study was very unlikely (only a 14% chance) to be

published. It was essentially hidden from view, never analyzed in order to get a more balanced view of the merits of the drug being tested.

One doesn't have to go very far in one's thinking to wonder why negative studies would be omitted from consideration and who benefits from such exclusion. After including these omitted data to their study of antidepressants' effectiveness, the authors stated, "Our main finding was that antidepressant drugs are much less effective than is apparent from journal articles."

How much less effective? In February 2008, researchers (Kirsch et al.) reported on data they had acquired from the FDA regarding the licensing of the six most popularly prescribed antidepressants approved between 1987 and 1999 (Prozac, Paxil, Effexor, Serzone, Zoloft and Celexa). Their analysis of the data that led to FDA approval of these drugs showed that these drugs had a minimal benefit beyond a placebo effect. The authors concluded, "Metaanalyses of ADMs have reported only modest benefits over placebo treatment, and when unpublished trial data are included, the benefit falls below accepted criteria for clinical significance."

In a remarkable study, the first of its kind, evidence was found to support the hypothesis that much of the therapeutic effect generated by ADMs is attributable to the placebo effect. Dr. Aimee Hunter and her colleagues at the UCLA Neuropsychiatric Institute studied the relationship between EEG changes and clinical outcome on patients taking Effexor and Prozac. Changes in prefrontal EEG patterns were recorded during a placebo lead-in phase, often conducted before randomization to drug treatment in clinical trials. The authors stated: "Brain changes during the placebo lead-in phase may confound apparent medication effects associated with clinical outcomes in medication-treated subjects... Some neurophysiological changes that are associated with endpoint antidepressant outcome reflect nonpharmacodynamic factors" (Hunter

Simply put, brains changed when no active drug was administered, and these changes

predicted response to ADM treatment in depressed patients. Do ADMs provide some benefit? Probably, but perhaps not to the degree or in the way we may have been led to believe.

What MFTs Can Do Better: Recognize that despite people's enthusiasm for medications as a solution, in fact, they can too easily become part of the problem.

Concern #9: Ecological Concerns about Drugs

An Associated Press investigative report released in March raised an unexpected concern: The presence of drugs in our drinking water. Traces of more than 100 different pharmaceuticals, or their byproducts, were found in the drinking water supplies of at least 41 million Americans, including medicines for pain, infection, high cholesterol, asthma, epilepsy, mental illness, and heart problems (Donn, Mendoza & Pritchard, 2008). Human excretions are the major factor in spreading pharmaceuticals through the waste stream. Drugs that are thrown away end up at landfills, where they can slowly seep into the groundwater. Though pharmaceutical sales are rising, plants that cleanse sewage or drinking water are not required to remove drugs; there's no national strategy to deal with them—no effective mandates to test, treat, limit or even advise the public. The unintended consequences for the environment will likely yield long-term effects we can't even imagine right now.

What MFTs Can Do Better: Provide sensible, "green" treatments. Talking doesn't pollute the environment.

Conclusion

You may think I'm against antidepressant medications. No, I'm not that extreme. I simply want people to know the issues are complicated and that the ease with which people put these powerful chemicals in their body on the basis of too little good research and too much exaggerated advertising is a legitimate cause for concern. There's a lot we don't know, and I believe that should concern everyone, especially MFTs who are in positions of authority regarding treatment recommendations.

If I had to choose between "skills or pills," I'd choose **skills**. Suggesting a drug will cure depression misses the inescapable point.....Depression is more a **social** than medical problem.



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