Commentary by a Child Psychiatrist Practicing in a Community Setting

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HOW HAVE THE RELATIONSHIPS between the pharmaceutical industry, academic medicine, and the Food and Drug Administration (FDA) affected the clinical practice of child psychiatry? To address the question, I have selected two major problems that affect psychiatrists who, like me, practice in a community-based setting.

Problem 1

The first problem is the publication in trusted journals of inaccurate or premature data may lead child psychiatrists to prescribe medications that can be deleterious to their patients.

Several studies have indicated that industry-financed drug trials tend to support the efficacy of the drug under investigation (Safer 2002; Als-Nielsen et al. 2003). Longer-term effects of medications on children are often unknown when the drug enters the market (Greenhill 2003) and await wider usage and longer exposures for safety to be fully assessed. In 1999, as a psychiatric consultant to a public mental health clinic, I evaluated an 8-year-old with significant anxiety, including avoidant behaviors, obsessive ruminations, and increasing explosiveness under stress. There were many psychosocial stressors, and several months of therapy with a school-based therapist-in-training were clearly inadequate. After attempting unsuccessfully to address the stressors and increase support, I initiated a cautious dose of

paroxetine based on then-current prescribing practice. Two weeks later, the child's foster mother called me in the evening to report that the child, who had never been suicidal, was sitting on the second-story window ledge and was "out of it." Luckily, the child was pulled to safety, but the relationship with me was over. I was never able to obtain follow up to learn the specifics of this episode.

Five years later, I learned that Glaxo Smith Kline had been aware of the potential for suicidality in children taking paroxetine (Paxil), but had hidden the information from the public (Office of the N.Y. State Attorney General 2004). The FDA was aware of this in 1996, but failed to reveal it. An internal safety review was withheld from the public advisory hearings of 2004 (Rosack 2004). Even more discouraging for me was the possibility that the weak risk/benefit relationship of the serotonin-selective reuptake inhibitors (SSRIs) in children could have been publicized had the clinical journal policy of rejecting negative studies not been in effect (Zito et al. 2004). In the 2006 American Academy of Child and Adolescent Psychiatry (AACAP) meeting session on ethical issues in pediatric psychopharmacology, which I chaired, data were presented summarizing clinical trials evidence that did not support SSRI efficacy for young children with depressed mood states (Zito 2006). Despite the weak evidence, SSRIs continue to be used at increasing rates even in children (Hunkeler et al.

2005). Whether this practice pattern changes since the negative evidence has become more widely promulgated remains to be seen.

Nonetheless, we clinicians continue to minimize the impact of adverse drug events (ADEs) associated with the SSRIs, both the psychological and behavioral type ADEs, as well as akathisia and activation in children, where rates are as frequent at 20–30% of youth (Wilens et al. 2003). I am surprised by the number of my colleagues who add a sedating drug for an agitated child on SSRIs, that lacks evidence of benefit or safety (Safer et al. 2003) instead of reconsidering the medication or a less complex regimen (Kratovich et al. 2006).

During this same period, I treated 3 young adults with very severe developmental delays, whose caregivers sought help for their impulsive, destructive, and intractable behavior. On the basis of the prevailing view, I initiated treatment with risperidone or olanzapine. All three experienced benefit, but rapidly gained weight. The appetite-increasing effects of the atypical antipsychotics were commonly known, but the caregivers were unable to enforce environmental or behavioral interventions to decrease the young peoples' binge eating. It was not until a few years later that I became aware of the profound metabolic changes associated with these medicines (Correll and Carlson 2006).

These experiences left me feeling intensely guilty for having so negatively affected my patients. They temporarily drove me out of community mental health, in spite of my long commitment, because I began to question the value of treatments for which I was ultimately responsible and would be held to as the current standard of practice. They left me disillusioned with academic institutions I had previously trusted and anxious about the quality and meaning of a profession I had spent many years learning. While teaching and lecturing, I have spoken to many with similar concerns and doubts. It is very possible that the difficulty that child and adolescent psychiatry is having recruiting new trainees is a reflection of the confusion in which the field finds itself (Thomas and Holzer, 2006).

Problem 2

The second problem is that the reduction of psychiatry to a biological psychiatry model has not served child and adolescent psychiatry well.

Current research often attempts to demonstrate the validity of the biological basis of mental illness or the benefit of specific medications to treat these disorders. In the past 25 years, this approach to psychiatric research has narrowed the psychosocial framework for understanding our patients. We are losing the integrated perspective of developmental psychopathology, as we view our patients' distress and struggles as a series of symptoms, diagnosed with a checklist and treated with a medication. It has been suggested that this narrow biomedical model comes directly from our academic thought leaders (Angell 2004). It has shaped the design of research (Safer 2002) and influenced treatment options available to psychiatrists (Fava 1996; Vitiello 2001).

This problem is especially evident in our current approach to children with emotional dysregulation/mood disorders, and specifically bipolar disorder in children (Kowatch et al. 2005; McClellan 2005). The overwhelming evidence from developmental psychopathology is that children's mood states are related to multiple factors besides genetics: Specifically, trauma, neglect, loss, parental mental health and especially maternal mood states, and relationship disturbance (Hammen et al. 2004; Cicchetti and Toth 1995; Rutter 2005). There is a vast literature on attachment disorders and relationship disturbances in children (Sameroff and Emde 1989). Yet these concepts have not yet been integrated into our research on juvenile bipolar disorder, despite the many areas of symptom overlap.

Despite numerous studies documenting the relationship between parental stressors and psychopathology, early trauma and neglect, and subsequent affective and disruptive symptoms (Cicchetti and Toth 1995; Rutter 2005), there are no published clinical epidemiologic studies to further this conceptualization. This hole in our empirical knowledge base substantially weakens our evidence for the validity of

juvenile bipolar disorder, especially in prepubertal children. There is only weak evidence linking childhood syndromes of reactivity, explosiveness, and developmental/behavioral incompetence to the biphasic mood disorder known as bipolar affective disorder in adults. On the other hand, there appears to be more clinical continuity with the Cluster B personality disorders, which require more intensive psychotherapy than the mood disorders of adulthood (McClellan and Hamilton 2006).

In recent years, many publications show the influence of the pharmaceutical industry on professional behavior of physicians (Kravitz et al. 2005), trainees (Sierles et al. 2005), and the FDA (Markel 2005). We accept industry claims of safety and efficacy and are particularly vulnerable to drug company-sponsored educational efforts (Avorn 2004; Healy 2004; Zipkin and Steinman 2005; DeAngelis 2006). The common acceptance among both laypersons and professionals of the validity of the construct of juvenile bipolar disorder as a direct precedent to the more clearly defined adult syndromes of bipolar affective disorder, and the urgency of starting medications may represent successful marketing more than scientific thinking.

Many leading researchers in this area have financial relationships with the manufacturers of the drugs recommended for the treatment of juvenile bipolar disorder. Although such relationships are not illegal, the growing chorus of questions about their appropriateness jeopardizes our credibility with the public. Added to this conflict of interest is the high level of financial support the AACAP receives for their research, education and philanthropic activities from the drug companies (AACAP Annual Report 2006). In addition to the lack of diagnostic validity, the lack of evidence for medications used in juvenile bipolar disorder is a cause for grave concern. In reviewing pediatric anticonvulsant studies, Golden et al. (2006) noted common methodological flaws in studies assessing these drugs in the treatment of juvenile bipolar disorder, as well as a lack of efficacy for several novel antiepileptics. Only valproate (available as a generic) received recommendation level B,

when used in combination with a sedating antipsychotic. Although the newer, expensive brand-name drugs had little demonstrated efficacy, they are routinely prescribed to severely disturbed children (Golden et al. 2006).

By contrast, papers have shown the efficacy of dyadic and family-based and behavioral approaches to severe relationship disturbances contributing to emotional dysregulation (McClellan and Werry 2003; Barrett et al. 2004; Lyons-Ruth and Melnick 2004; Lieberman et al. 2006; McClellan and Hamilton 2006). However, few of us have the opportunity to practice these rewarding techniques due to our limited scope, as dictated by current reimbursement policies (Jellinek 1999).

CONCLUSION

As long as child psychiatric research is so heavily focused on pharmacology, we will lack evidence-based tools for understanding and differentially treating the complex interplay of genetic liability, attachment disturbance, and environmental risk that affects so many of our patients. Medications are indeed often useful for the treatment of many of these children. To support this position better, we require a meaningful framework for understanding the details, namely, medications for which children, with what aim, for how long, and what else is necessary to increase the odds of success.

Despite the wealth of knowledge now available to child and adolescent psychiatry, the profession continues to experience cognitive dissonance, accepting the hopeful promises of the drug advertisements, while ignoring the Surgeon General's call to improve access to services that will reduce the misery of many of our nation's children (U.S. Public Health Service 2000).

DISCLOSURE

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