CHAPTER 1

Historical Perspectives on Child and Adolescent Psychopharmacology

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The psychiatric treatment of children with drugs was essentially taboo until the 1990s, possibly due to the still major influence of psychodynamic views. This attitude presented a double-sided problem: there was a disinclination to administer pharmacotherapy to children who needed it and would benefit from it and, equally concerning, there was a vocal movement for mass treatment, underscoring a profound cultural shift. The media reported this widely, for example, in the article "Paxil, Prozac, Ritalin—are these drugs safe for kids???" [1]. It was thus commonplace to read that parents and schools were just searching for a quick fix for behaviors that fell outside the "norm." Ritalin had been available since 1954, and so perhaps the acceptance of psychopharmacology as an intervention sped the clock on the acceptability of pharmacological agents to deal with behaviors outside the new cultural norms. These treatment options claimed to offer the possibility for any child who fell outside these behavioral "norms" to be "improved." Thus, a market force developed that underpins the efforts of pharmaceutical companies to develop their products. Although controversial, these concepts have expanded recently to suggest that early diagnosis of psychiatric disorders such as schizophrenia and bipolar disorder may warrant the initiation of pharmacotherapy at the earliest manifestation of "prodromata" of these conditions.

Stimulants may well have been the first entrants into child pharmacotherapy. Amphetamine was resynthesized in the US in the 1920s and had been employed as a respiratory stimulant for narcolepsy and as an appetite suppressant. By 1937 it was shown to be an effective treatment for hyperactivity in children by Charles Bradley [2]. Later others also reported on the efficacy of Ritalin in children with hyperactive states. Its

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effectiveness led to the acceptance of the concept of minimal brain dysfunction, which in 1980 in DSMIII was categorized as attention-deficit hyperactivity disorder (ADHD).

Psychopharmacological treatments have been introduced in large part as the result of serendipitous events. The earliest agents included lithium, chlorpromazine, and imipramine. They gradually developed a role in the treatment of adult patients and then were tried in pediatric patients by deduction of the possible similarity of these behaviors to those established in adults. There are many assumptions in this last step to the treatment of children. For example, imipramine and related compounds were indeed quite effective for major depressive disorder in adults. However, their translation to children implied an essential assumption that the depression seen in children was analogous to that seen in adults, and that the underlying substrate would respond similarly. Whatever the assumptions, the outcome belied these assumptions, as the careful studies of Ryan et al. [3] clearly demonstrated. Here we had a cautionary tale and we have not fully explained this outcome and the assumptions inherent therein. Thus we must move cautiously before we presume such simple projections from adults to children.

Then there developed a period of major enthusiasm for two new classes of psychotropic agents: the selective serotonin reuptake inhibitors (SSRIs) and the atypical second-generation antipsychotics (SGAs). As before, their usage was explored initially in adults with the SSRIs becoming widely employed for depressive disorders and pretty much completely displacing the tricyclics. Both classes of drugs were then extensively prescribed for children and adolescents. Following the FDA's warnings, with black-box and bold-print cautions, there has been a significant reduction in their prescriptions. Associated with this is the hotly debated issue of suicidality associated with these antidepressants.

Some of the SGAs have also caused serious concern because of the increased risk of metabolic syndrome with significant weight gain and the concurrence of type-II diabetes. These adverse effects produce a very special risk in developing children. These few instances provide adequate warning about a transfer of psychopharmacological drug prescribing from adults to children. There is now clearly the need, which has been recognized, for the careful clinical evaluation of new agents for specific indications in children.

The prevention and treatment of emotional and behavioral problems affects about one in five children and is the major mental health problem in the United States. Most major mental health problems begin during adolescence. Therefore, this is the critical period for their identification, prevention and often their treatment. Suicide among the young has become an increasing concern over the past several decades. It is important

to consider, within this context, the high rate of suicide in the young inductees in the armed forces. Another aspect of this issue has come up over the past 10 years and that has been the possible effects of administering antidepressant drugs to children and adolescents and the concerns that were raised about possible increase in suicidal outcomes. All these questions have increased the importance of the optimal methods of treatment of depression in these populations.

This third edition of pharmacotherapy for child and adolescent disorders is being published 10 years after the first edition. Although the field has advanced considerably, the fact that we are dealing with a still-developing nervous system presents both special options and serious cautions. The use of psychotropic agents in adults has become well established since the 1960s and the picture of their clinical indications and side effect profile has become much clearer. These issues are still not so well defined in children, as their diagnostic entities are still being delineated and thus specific therapies are also under debate. The social and cultural background for the acceptance of psychotropic interventions has altered over the years. Initially, they were considered inappropriate, dangerous and treatments of last resort for children. Society has changed its attitude dramatically and now there is a serious concern of overmedication of children. Thus, although the field has progressed significantly, the appropriate administration of psychoactive medications to children requires training, skill and ongoing interaction with the patient and family throughout the course of treatment.

This is especially the case as many more drugs have been introduced and their indications and profile of actions are still in progress. The basic research studies on their mode and site of action will continue to provide the field with knowledge, which will help considerably in their more targeted usage. The question of early usage of therapeutic interventions in some of these conditions has been raised, offering the possibility of preventive value. This early and possibly long-term usage raises new and important questions in regard to short- and long-term possible adverse effects on developing systems.

Early intervention for all medical or psychiatric disorders is essentially always considered beneficial. However, with psychiatric disorders in children, especially in the younger age groups, the prospective identification of prodromata has been and still is problematic. Various investigators have presented studies on this problem, such as the proposal of "ultra high risk" (UHR) criteria [4]. One still unresolved problem is the potential effects of the various psychotropic drugs on the developing nervous system and other organ systems, especially if administered long term, as is often necessary in a number of disorders. Adverse neurocognitive effects of psychotropic medications have been reported [5, 6]. For example,

GABAergic agonists have been demonstrated to interfere with both mood and memory, as well as attention and psychomotor speed.

Thus, there is a debate about early psychopharmacologic intervention in children. Specifically, it concerns the issue of whether the impact and consequences of lack of treatment outweigh the potential for prematurely labeling children with emotional disturbances. In this population of children and adolescents, early clinical features can also be difficult to distinguish from benign conditions and normal experience. These concerns cannot easily or speedily be resolved. The question of the diagnosis of these psychiatric disorders is still being evaluated for DSM V. Good data on the long-term use of psychotropic agents both on body organs and the central nervous system are still incomplete in young developing systems. Therefore, we believe we can only raise a cautionary note and await further data on both aspects of this question. Hopefully we will have a resolution by the time we come to the fourth edition of this volume.

All of these activities in the field have contributed to the creation of this third edition. It is hoped that this volume will serve as a valuable guide to the treatment of patients 18 years of age and under with psychiatric disorders. This volume is presented as a practical guide to the clinical psychiatrist. The book also provides valuable material for other health care professionals in the management of children and adolescents with psychiatric conditions. The material presented here is in a format readily available for psychologists, social workers, therapists, nursing staff and students, as well as medical students, pediatricians and family practitioners. We felt that a brief historical review of the background of the development of psychopharmacological interventions in children could provide a frame of reference for the developments and practices in the field today. It should also provide a perspective that the field is and should be changing. We have delineated what is known currently on the basis of a critical review of controlled trials available. We have also attempted to integrate the basic neuroscience available to help guide clinical decision making.

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