

Possible Link Between Attention-Deficit/Hyperactivity Disorder and Reproductive Complications

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Background: Initially conceptualized as a disorder of childhood, attention-deficit/hyperactivity disorder (ADHD) is now emerging as a chronic disorder that may present in adolescence and persist into adulthood. Failure to recognize this common disorder in childhood may lead to disabling comorbid symptoms and a poor long-term prognosis in adulthood. Young adults with undiagnosed ADHD experience significant psychiatric comorbidity, including high rates of drug dependency and lower levels of global functioning. The public health consequences of poor impulse control (e.g., delinquency, criminal activity, drug use, risky sexual behaviors, high-risk pregnancies) are emerging, and a link between ADHD and poverty seems highly probable.

Case Report: I explore the sexual behaviors, and their consequences, of a young adolescent female. Her reproductive complications led me to consider undiagnosed ADHD.

Conclusion: The long-term prognosis when ADHD is unrecognized and untreated in the adolescent is discouraging: maternal and perinatal morbidity may be anticipated and are biologically plausible. The actual assessment of risk in the setting of pregnancy and unrecognized ADHD remains largely unknown, and the benefits of timely diagnosis and appropriate treatment of ADHD during pregnancy have yet to be addressed. The following case presentation suggests an association between undiagnosed ADHD and reproductive complications.

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Adult attention-deficit/hyperactivity disorder (ADHD) is a major clinical and public health problem in the United States.¹ Failure to recognize this common disorder in childhood may lead to disabling comorbid symptoms and a poor long-term prognosis in adulthood.¹ The adolescent who is inconsistently attentive, easily distracted, impulsive, and overactive will have problems with education, vocational training, and interpersonal relationships. An evolving conduct disorder, delinquency, and inevitable school failure will produce an adult with no job skills and little interest in a healthy lifestyle.² The resultant poverty and associated high-risk behaviors (smoking, drinking, unsafe sex, obesity) predict poor health and premature death.²⁻⁶ Rates of sexually transmitted diseases, teenage pregnancy, substance abuse, and academic failure are disturbingly high in young women with ADHD.⁷ However, since current research has dealt little with the specific female manifestations of this disorder, a large pool of undiagnosed women may pose significant public health problems.⁸ The following case presentation suggests an association between undiagnosed ADHD and reproductive complications. Moreover, a review of the literature supports the plausibility of this heretofore unrecognized association.

CASE PRESENTATION

Unrecognized ADHD in a sexually active adolescent may present to the family physician in a number of ways; the following is the true story of Miss A. She presented for contraceptive counseling at the age of 13, unaware that she was already pregnant by her 18-year-old boyfriend. She was the oldest of 3 children, and her mother was a recovering alcoholic. A smoker, Miss A delivered prematurely at 23 weeks and was discharged on treatment with deponedroxyprogesterone. Her firstborn was admitted for failure-to-thrive, and Miss A was noted to have difficulty perceiving her baby's needs. Over the next year, she was treated for recurrent pelvic and urinary tract infections, used contraception inconsistently, and presented at age 15 with her second pregnancy. She was found to have cervical dysplasia, and treatment was deferred until after delivery. Her pregnancy was complicated by recurrent episodes of preterm labor, positive gonorrhea and chlamydia cultures, continued smoking, and an assault by her boyfriend in

mid-pregnancy. She delivered at 37 weeks, and a postpartum colposcopy confirmed moderate cervical dysplasia, vulvar warts, and vulvar dysplasia. By the time Miss A returned for definitive treatment, she was found to be pregnant again at age 16. Cervical cryocautery was nonetheless performed following gynecologic consultation, and excision of the vulvar lesion revealed vulvar carcinoma in situ. This third pregnancy was complicated by recurrent uterine irritability requiring tocolytic therapy and culture-positive herpetic skin lesions and was followed by a surprisingly uneventful vaginal delivery at 38 weeks' gestation.

Prior to discharge, the author interviewed both Miss A and her mother. Miss A was enrolled in the local alternative high school for young women with children and hoped to attend community college following graduation. Her mother was recently diagnosed with ADHD and started on treatment with methylphenidate. For the first time, Miss A's mother had not only remained on the job long enough to receive a raise, but was promoted to assistant manager. Miss A's mother described her daughter as undisciplined, poorly organized, easily angered, self-centered, and immature. Never "overactive," Miss A had been persistently inattentive since early childhood. Unsafe sex, poor medical compliance, smoking, and educational failures characterized her turbulent adolescence. This additional history confirmed the diagnosis of ADHD, predominantly hyperactive-impulsive type. Follow-up was arranged with her personal family physician.

BACKGROUND

Is there biological plausibility to the hypothesis that Miss A's perinatal complications and her ADHD are linked? ADHD is a neurobiological condition affecting the 3 developmental areas of attention, impulse control, and activity regulation. Recent studies summarized by the National Institutes of Health Consensus Development Conference provide convincing evidence that the frontal lobes and basal ganglia are reduced in size in individuals with ADHD and that a deficiency of the neurotransmitter dopamine is corrected by stimulant therapy.⁷ An estimated 3% to 5% of schoolchildren, or 2.5 million children, have ADHD.⁸ The prevalence of ADHD in the adult population is unknown. Earlier studies have noted persistence of symptoms into adulthood in as few as 10% to as many as 60% of hyperactive children.^{9,10} Despite substantial differences in methodology among these various studies, the number and intensity of ADHD symptoms are noted to decline as these children mature.¹¹

Recent revisions in the DSM-IV text have sought to modify the wording of previous diagnostic criteria so that each might apply equally as well to either the adult or the child.¹² Consideration is given to broadly similar maladaptive symptoms: regardless of age, there must be sig-

nificant interference with social, academic, and/or occupational functioning. The diagnosis of ADHD is unlikely if a profound disability is noted in a single setting only.¹² However, gender differences remain largely unknown and therefore unmeasured. Male-to-female ratios ranging from 3:1 to 9:1 were derived from studies that favored the referral of boys with comorbid conduct or oppositional disorders. Even after correcting for comorbidity, referral bias favors the referral of boys over girls, who have lower rates of inattentiveness and hyperactivity. Nonetheless, girls diagnosed with ADHD suffer more serious cognitive and language impairment than boys and must endure more peer rejection. Anger and low self-esteem may explain the increasing prevalence of conduct disorders and ADHD noted in young female prisoners.⁷ Would Miss A have been more likely to use birth control and practice safe sex if her ADHD had been diagnosed when she was younger? One can only speculate.

DIAGNOSIS OF ADHD

The diagnostic criteria by which ADHD is defined are outlined in the DSM-IV. Both inattention and impulsivity-hyperactivity contribute to the morbidity of this disorder.¹ Table 1 outlines the 3 ADHD subtypes recognized by the DSM-IV: a predominantly inattentive type, a predominantly hyperactive-impulsive type, and a combined type.¹² The diagnosis of ADHD is more difficult to make in children who are not hyperactive and in women, who typically are less hyperactive and impulsive at any age.⁷ However, there is little doubt that ADHD affects both sexes. A diagnosis of ADHD cannot be determined by physical features, laboratory tests, or psychological tests.⁷ Symptoms are easily overlooked in a busy office practice unless actively elicited using the DSM-IV symptom list. The diagnosis is suggested when patients relate a history of academic underachievement or learning disabilities, although there is no pathognomonic neuropsychological profile in ADHD.¹ Sex-specific thresholds have been suggested as a way to identify girls in a more timely manner, but use of such thresholds may falsely label girls as having the disorder who are not impaired in the usual sense and has never been tested.⁸

Although the classic triad of inattention and distractibility, impulsivity, and hyperactivity is found in 3 of 4 children with ADHD, hyperactivity is the symptom most likely to remit by adulthood.¹¹ Diagnosing ADHD in the adult presents 3 additional concerns:

1. At least some symptoms must have been noted in childhood,
2. Other diagnoses or comorbidity may confuse the diagnosis, and
3. Many features of adults with ADHD mimic those seen in other disorders.⁹

Table 1. DSM-IV Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder^a

- A. Either (1) or (2):
- (1) Six or more of the symptoms of inattention persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level
- Inattention**
- (a) Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
 - (b) Often has difficulty sustaining attention in tasks or play activities
 - (c) Often does not seem to listen when spoken to directly
 - (d) Often does not follow through on instructions and fails to finish work
 - (e) Often has difficulty organizing tasks and activities
 - (f) Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
 - (g) Often loses things necessary for tasks or activities
 - (h) Is often easily distracted by extraneous stimuli
 - (i) Is often forgetful in daily activities
- (2) Six or more of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level
- Hyperactivity**
- (a) Often fidgets with hands or feet or squirms in seat
 - (b) Often leaves seat in classroom or in other situations in which remaining seated is expected
 - (c) Often runs about or climbs excessively in situations in which it is inappropriate
 - (d) Often has difficulty playing or engaging in leisure activities quietly
 - (e) Is often on the go, or acts as if "driven by a motor"
 - (f) Often talks excessively
- Impulsivity**
- (a) Often blurts out answers before questions have been completed
 - (b) Often has difficulty awaiting turn
 - (c) Often interrupts or intrudes on others
- B. Some hyperactive-impulsive or inattention symptoms that caused impairment were present before the age of 7 years
- C. Some impairment from the symptoms is present in 2 or more settings
- D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning
- E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder

^aAdapted with permission from the American Psychiatric Association.¹²(pp92-93)

A history of inattention and/or hyperactivity occurring before the age of 7 is required and often difficult to obtain. There is poor agreement between the patients' and their parents' recollection of ADHD behavior and symptoms. Parent information appears to more accurately predict a favorable response to treatment, suggesting that parental recall is a more valid measure of childhood ADHD.⁹ The adult who presents to the physician with problems at work, at home, and in personal relationships may poorly recall distant events, prior mood shifts, and childhood behaviors. Even those with documented childhood hyperactivity may forget, while others may exaggerate inattention

problems in childhood. Patient responses during a focused physician visit may at best only suggest the diagnosis.

COMORBIDITY

Much easier to diagnose are the comorbid conditions. The ADHD child with an oppositional defiant or conduct disorder and/or a learning disability may present as an adult with an antisocial personality, substance abuse, and/or a dismal occupational history. Miss A's pervasive pattern of unstable interpersonal relationships, low self-esteem, sexual impulsivity, inappropriate anger, and non-compliance suggests the presence of an underlying borderline personality disorder as well as ADHD. Whether or not a personality disorder evolves from inattentiveness and hyperactivity or is the result of a continuous conduct and learning disorder remains unclear.⁹

Family genetic data presented by Biederman et al.¹³ confirm that children with ADHD are at increased risk for developing depression or a bipolar disorder, particularly those individuals with a family history of mood disorders. The presence of pervasive mood lability and cycling, irritability, and psychotic symptoms¹⁴ suggests bipolarity rather than ADHD. The overlap of ADHD symptoms with mood and borderline disorders has led some to propose that the diagnosis of ADHD in these adults is an artifact of overlapping symptoms.¹⁴ Milberger et al. present data to suggest that the diagnosis of ADHD remains intact even when the overlapping symptoms of major depression, bipolar disorder, and/or generalized anxiety disorder are subtracted.¹⁴ Depression from unrecognized ADHD is more common in women than in men, and the correct diagnosis often is considered only after numerous medication failures.⁸

In summary, although there is little doubt that ADHD is a valid diagnosis in adults, the correct diagnosis is rarely considered when a high-school dropout presents with her third unplanned pregnancy, recurrent sexually transmitted diseases, and vulvar cancer. Perhaps this behavior, and the resultant complications, is a more common presentation for undiagnosed ADHD in adolescence than is recognized.⁷

DISCUSSION

Miss A is easy to characterize as another welfare mother fallen through the cracks. She is irresponsible, erratic, undependable, poorly organized, undisciplined, angry, a problem student, and often unaware of the needs of those around her. Yet these are the very symptoms of undiagnosed ADHD. Hallowell and Ratey¹⁵ have compiled a list of symptoms commonly found in their young adult patients with ADHD. If 15 of the 20 behaviors are present, they suggest that the diagnosis of ADHD be considered. Although these "criteria" remain untested, the full range of ADHD symptoms is considered, and the diagnosis may be

Table 2. Suggested Diagnostic Criteria for ADD/ADHD^a

- A. Symptoms (at least 15 of 20)
1. A sense of underachievement, of not meeting one's goals—regardless of how much one has actually accomplished
 2. Difficulty getting organized
 3. Chronic procrastination or trouble getting started
 4. Many projects going simultaneously; trouble with follow-through
 5. Tendency to say what comes to mind without considering the timing or appropriateness of the remark
 6. Frequently searches for high stimulation or something new
 7. Intolerant of boredom
 8. Easily distracted, trouble focusing attention, a tendency to tune out or drift off in the middle of a page or conversation—while often able to “hyper focus.” This seeming paradox is usually noted, and implies that ADD is a syndrome of attention *inconsistency* rather than attention *deficiency*
 9. Often creative, intuitive, highly intelligent. Flashes of brilliance are often noted in the midst of disorganization and distraction
 10. Trouble going through established channels or following “proper” procedures. Bored with routine ways of doing things, prefers the novel approach—a risk taker
 11. Impatient, low tolerance for frustration
 12. Impulsive, either verbally or in action (impulsive spending, sudden change in plans, new schemes)
 13. Tendency to worry endlessly, needlessly, and to scan the horizon for the next disaster or crisis. Alternating inattention to or disregard for actual dangers at hand
 14. Sense of insecurity
 15. Mood swings, often over the space of a few hours, but never as pronounced as those in manic-depressive illness or depression
 16. Restlessness, nervous energy—pacing, tapping fingers, shifting position, or feeling edgy while at rest
 17. Addiction—current or recovering—to a substance (eg, alcohol, tobacco, illicit drug) or a behavior (eg, eating, gambling, shopping, working)
 18. Chronic problems with self-esteem: “I must be lazy, stupid, or crazy”
 19. Poor self-observer. Impact upon others is not appreciated, and actions or statements are often misunderstood
 20. Family history of ADHD, bipolar disorder, depression, substance abuse, or other disorders of mood or impulse control.
- B. Childhood history of ADHD
- C. Situation not explained by other medical or psychiatric conditions

^aReprinted with permission from Hallowell and Ratey.¹⁵
 Abbreviations: ADD = attention deficit disorder,
 ADHD = attention-deficit/hyperactivity disorder.

suspected in the absence of hyperactivity (Table 2)—an advantage over older rating scales.

Concern has been raised that “labeling” these adolescents with the diagnosis of ADHD may miss an underlying and more pervasive bipolar disorder.¹⁶ Although there is overlap in DSM-IV diagnostic criteria, an adolescent bipolar disorder is differentiated from ADHD by mood elevation, grandiosity, a decreased need for sleep, racing thoughts, and hypersexuality.¹⁶ Self-administered tests may help the physician differentiate ADHD from more serious comorbid conditions. The Child Behavioral Checklist¹⁷ has been standardized on children aged 4 to 18 years and was recently shown to discriminate between ADHD and other comorbid diagnoses. If ADHD is suspected but the primary care provider is uncomfortable making the diagnosis, referral to a psychologist or psychiatrist experienced in the care of adolescents is essen-

tial. However, the DSM-IV diagnostic criteria are presented in such a way as to help the family physician make the correct diagnosis in all but the most obtuse cases.

It is well documented that females diagnosed with ADHD have significantly higher rates of learning disabilities than do their peers.¹⁸ To achieve success in school, which promotes self-esteem, these girls require a unique educational experience. They must acquire the underdeveloped social skills that have disrupted relationships with family, peers, and teachers. These young women must learn to control anger and impulsive behavior before success in the classroom is possible. Their special educational needs include training in organizational skills and time management if successful job placement is to occur after graduation. The ideal school setting for Miss A would require that childcare be provided by the young mothers themselves. The acquisition of parenting skills is essential if the children raised by these young women are to thrive. School nurses and educators—working with each mother and her extended family in a culturally sensitive fashion—must provide an appropriate level of sex education and an awareness of birth control options to limit family size.

ADHD AND PREGNANCY OUTCOME— ARE THEY LINKED?

Any association between undiagnosed ADHD and perinatal morbidity does not prove causality, but such an association is biologically plausible. A few key points that suggest plausibility are as follows. First, untreated ADHD leads to self-medication with tobacco, alcohol, and cocaine—all known causes of perinatal morbidity.¹⁹ Second, being poor and from a lower socioeconomic class is associated with a worse pregnancy outcome.²⁰ Furthermore, men with ADHD are poorer than their peers,²¹ although studies on women are limited. Gender differences are poorly understood and generalizations are not always accurate.²² Women with ADHD are less likely to graduate from high school than their peers, and high school dropouts are less likely to seek timely prenatal care—another strong predictor of reproductive complications.²³ The largest study of ADHD girls to date (1999)²⁴ confirms that recently diagnosed females aged 6 to 18 years suffer negative psychological, educational, social, and vocational sequelae as the result of school failure, family dysfunction, and failed peer relationships. Will the more timely diagnosis and treatment of these young women with ADHD alter the poor birth outcomes and maternal morbidity associated with these known psychosocial risk factors?

CONCLUSION

In summary, ADHD—initially conceptualized as a disorder of childhood—is now emerging as a chronic disorder.

der that may present in adolescence and persist into adulthood. There is an evolving consensus that abnormalities in dopamine function are responsible for the inattentiveness, distractibility, impulsivity, and hyperactivity that characterize the ADHD patient. Young adults with undiagnosed ADHD experience significant psychiatric comorbidity, including high rates of drug dependency and lower levels of global functioning. The public health consequences of poor impulse control (e.g., delinquency, criminal activity, high-risk pregnancies) are emerging, and a link between ADHD and poverty seems highly probable. The long-term prognosis when ADHD is unrecognized and untreated in the adolescent is discouraging: maternal and perinatal morbidity may be anticipated and are biologically plausible. However, the actual assessment of risk in the setting of pregnancy and unrecognized ADHD remains largely unknown. Finally, the benefits of timely diagnosis and appropriate treatment of ADHD during pregnancy have yet to be addressed.

Drug names: medroxyprogesterone (Depo-Provera), methylphenidate (Ritalin, Concerta, and others).

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