CASE 8.1
Attention Deficit Hyperactivity Disorder | Level 1

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1. What is the subjective and objective evidence for the diagnosis of ADHD and ODD?

SUBJECTIVE FINDINGS: ADHD—difficulty concentrating at school, frequent careless errors at school, inability to concentrate when spoken to, and trouble completing tasks at home; ODD—anger outbursts and history of starting fights at school and at home

OBJECTIVE FINDINGS: There is no objective evidence to support the diagnosis of ADHD and ODD in this patient. Although ideally one would like scales available to determine efficacy for ADHD (e.g., Conners' Rating Scale, Vanderbilt ADHD Rating Scale) and ODD (e.g., subscales or specific questions from aforementioned scales), they are not always available in clinical practice.

2. What risk and environmental factors may have contributed to ADHD in this patient?

Low birth weight and possible early social deprivation are potential risk factors for the development of ADHD in this patient as his mother had postpartum depression. There is evidence that there may be a genetic component to ADHD. The father appears to display symptoms of ADHD given his history of not completing tasks.

3. How would you assess the current pharmacologic therapy for the patient?

Current therapy is not working and possibly contributing to insomnia. The patient has not experienced an improvement in concentration or disruptive behavior at school. Therefore, the patient requires a dose reduction (to alleviate the insomnia) and the addition of an alternative agent (to treat the unresponsive ADHD symptoms and aggressive behaviors). In this case, the increase in dose led to insomnia, necessitating a decrease in the dose. When this occurs, it is best to reduce the stimulant to the previous dose and add another agent to treat the unresolved symptoms of ADHD and aggression.

In this case, the patient is overweight (BMI greater than 90th percentile) and has an elevated blood pressure (prehypertension as blood pressure is above the 90th percentile) and heart rate; he may benefit from an alpha-2 agonist. With the addition of an alpha-2 agonist, a reduction of the previous stimulant dose may be necessary. For example, studies with clonidine indicated a 15% to 40% decrease in

stimulant doses when clonidine was titrated to effect. Therefore, after one decreases amphetamine/dextroamphetamine XR back to 25 mg daily, further reduction *may* be needed after initiating an alpha-2 agonist. However, this further reduction in stimulant dose would not occur until the alpha-2 agonist is at a therapeutic dose and patient is reassessed.

4. What pharmacologic treatment would you recommend?

Although amphetamines are first-line therapy for the treatment of ADHD, this patient was not able to tolerate an increased amphetamine dose. Therefore, the amphetamine should be reduced to its previous dose (in this case 25 mg daily), which was partly effective. The patient will also require an adjunctive agent for the management of his symptoms.

Start guanfacine extended-release (Intuniv®) 1 mg at bedtime. Titrate by 1 mg at weekly intervals up to 4 mg at bedtime. Although there are many other adjunctive treatments to use, alpha-2 agonists may be preferred in those with ODD, as they are effective in reducing aggression and oppositional symptoms. Unlike other treatment options, alpha-2 agonists may also have a beneficial effect on the patient's blood pressure, which is elevated.

Among the alpha-2 agonists there are two options: guanfacine and clonidine (see **Table 1**). Guanfacine has a couple of advantages over clonidine. Guanfacine can be dosed once daily and has a perceived decreased risk of adverse reactions, due to its higher selectivity for alpha-2 receptors. Guanfacine is available in both an immediate-release and an extended-release formulation. The extended-release formulation may be preferred in this case because the patient displays ODD symptoms throughout the day. Also, once-daily dosing may help with adherence. However, please note that if cost is an issue, the immediate-release formulation can be used.

5. How would you counsel the patient and caregiver regarding the new medication?

Recent studies state that approximately 20% of patients discontinue their ADHD medication within 1 year. From these, over 40% of patients discontinue during the first month largely due to lack of efficacy and the occurrence/possibility of adverse reactions. As such, it is important to stress that alpha-2 agonists take approximately 2 to 4 weeks before benefits are seen. Also, efficacy is usually assumed by a 30% to 50% reduction in symptoms. Therefore, expectations and goals of therapy should be discussed with the patient and family. Goals of therapy for this patient include improved concentration span and a reduction in aggression, while minimizing adverse reactions from the medications. Guanfacine may cause drowsiness and dizziness and, therefore, should be taken at bedtime. The package insert states one can start in the morning; however, reports of sedation by patients occur at high rates (~38%). The patient should let the prescriber know immediately if the medication causes excess dizziness, bradycardia, or syncope (from hypotension). Patients should make sure to drink plenty of fluids to prevent dehydration, which would increase the risk of dizziness. Additionally, it is best to separate the extended-release formulations of guanfacine from high-fat meals, which increase absorption of the medication. Alpha-2 agonists may cause dryness of the mouth. If this occurs, the patient can try using sugarless gum or sugarless hard candy (e.g., xylitol lollipop). Patients should not stop the medication abruptly unless they are at the starting dose or a severe adverse reaction occurs. Discontinuing without

TABLE 1: BENEFITS AND CONSIDERATION OF ALPHA-2 AGONISTS

	Pros	Cons
Clonidine	Absorption not affected by food Available in weekly patch formulation	Extended-release formulations still require twice daily administration
Guanfacine	Higher selectivity for alpha-2 receptors, which may result in a decreased incidence of adverse reactions Can be dosed once daily	Extended-release formulation should be separated from high-fat meals