



Treatments for Autism Spectrum Disorder

Endorsed by the American Academy of Pediatrics and the
Society of Developmental and Behavioral Pediatrics

Developed in partnership with
Health Resources and Services Administration
Maternal and Child Health Bureau



Treatments for Autism Spectrum Disorder



Abstract

Kofi is a school-age child with an autism-spectrum disorder (ASD), cognitive impairment, aggressive behavior, and trouble sleeping. His mother comes to you with several concerns about his behavior and possible solutions. You answer her many questions about medications and complementary and alternative medicine (CAM) approaches. Ultimately, you refer Kofi to a specialist for prescription of a psychotropic medication to help with his symptoms of ASD.

Case Goal

Children with autism spectrum disorder (ASD) often present with challenging or maladaptive behaviors that are commonly seen in addition to the core deficits. Pediatricians are often called upon to help evaluate children for underlying medical concerns and to facilitate obtaining appropriate treatment. *After completion of this module, learners will be able to:*

1. Evaluate the etiology of changes to behavior and functioning in children with ASD and describe strategies to analyze these changes
2. Develop knowledge regarding specific options to treat maladaptive behaviors in children with ASD

Three Steps to Prepare - In 15 Minutes or Less!

- 1 Read through the Facilitator's Guide and make copies of the case and learner worksheet for distribution.
- 2 Identify the key topics you wish to address. Consider:
 - Knowledge level of learners
 - Available time
 - Your familiarity with the subject
- 3 Select and prepare the optional teaching tools you wish to use. *Each case provides a variety of **optional** materials to enhance the learning environment, support facilitator style, focus on different themes, or accommodate different time limitations. These materials are optional for facilitators to use at their discretion.*
 - Handouts: select any you wish to use and make copies for distribution
 - PowerPoint: decide if you wish to use and confirm necessary technical equipment
 - Video: review embedded video and video library, decide if you wish to use, confirm necessary technical equipment, and conduct test run

The following case was developed by the authors. It does not necessarily reflect the views or policies of the Department of Health and Human Services (HHS) or the Centers for Disease Control and Prevention (CDC).

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Key Learning Objectives of This Case

1. *Evaluate the etiology of changes to behavior and functioning in children with ASD and describe strategies to analyze these changes.*
 - a. Identify specific causes that can increase maladaptive behavior (Prompt 1.3)
 - b. Describe the components of a functional behavioral analysis (Prompt 1.3)
 - c. Be familiar with rating scales that can be used to assess behavior change in children with ASD (Prompt 1.3)
2. *Develop knowledge regarding specific options to treat maladaptive behaviors in children with ASD.*
 - a. Understand the evidence-based indications for the initiation of pharmacotherapy in children with ASD (Prompt 3.1)
 - b. Become familiar with the classes of drugs used to treat children with ASD (Prompt 1.4)
 - c. Describe the most common complementary and alternative medicine (CAM) therapies used to treat children with ASD (Prompt 2.3 and Handout I: Vitamin and Exercise-Based Therapies)
 - d. Learn strategies to engage families around the use of CAM (Prompt 2.1)

Only Have 30 Minutes to Teach? :30

Focus your discussion on recognizing typical and atypical behavior and development, particularly social and play milestones, as well as the red flags of ASD. Use:

- Handouts II: Treatment Tracking Tool
- Potential Prompts: 1.3, 2.1, 2.3, and 3.1

Materials Provided

- Case Worksheet for Learners
- Case Study: Part I, II, and III (available in Facilitator's Guide and on CD)
- Optional Teaching Tools
 - PowerPoint (available on CD)
 - Handouts (available in Facilitator's Guide and on CD)
 - Handout I: Vitamin and Exercise-Based Therapies
 - Handout II: Treatment Tracking Tool
- Video Library (available on CD)
- References

Case Authors

Cristina Farrell, MD, Einstein College of Medicine, Children's Hospital at Montefiore
Leonard Rappaport, MD, MS, Children's Hospital Boston, Harvard Medical School
Neelam Sell, MD, The Children's Hospital of Philadelphia
Brian Tang, MD, Lucile Packard Children's Hospital, Stanford University School of Medicine

Editors







Georgina Peacock, MD, MPH, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention
Carol Weitzman, MD, Yale University School of Medicine
Jana Thomas, MPA, Porter Novelli

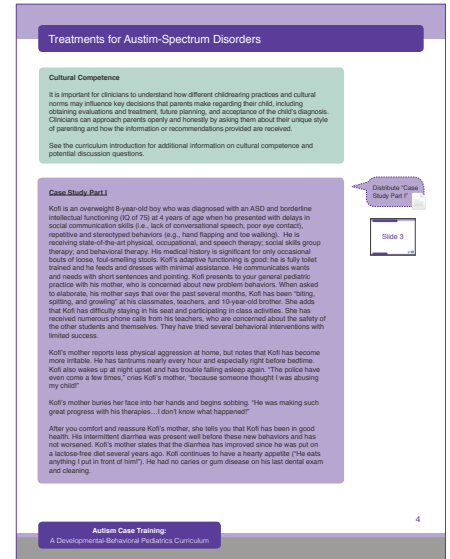
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Getting Started

This case is designed to be an interactive discussion of a scenario residents may encounter in their practices. Participation and discussion are essential to a complete learning experience. This Facilitator's Guide provides potential prompts, suggestions for directing the discussion, and ideas for incorporating the optional teaching tools. It is not designed as a lecture.

Case study icons:

-  Call-out: step-by-step teaching instructions
-  Note: tips and clarification
-  Slide: optional slide, if using PowerPoint
-  Filmstrip: optional slide contains an embedded video
-  Paper: potential place to distribute an optional handout
-  **:30** Digital clock: tips if you only have '30 Minutes to Teach'



The screenshot shows a slide titled "Treatments for Autism Spectrum Disorders" with a purple header. It contains a "Cultural Competence" section, a "Case Study Part I" section, and a footer that reads "Autism Case Training: A Developmental-Behavioral Pediatrics Curriculum". Call-out icons are present: a purple call-out bubble on the left, a yellow note icon on the right, a slide icon on the right, a filmstrip icon on the right, and a paper icon on the right. A digital clock icon is at the bottom left of the slide.

Why is This Case Important?

Autism spectrum disorder (ASD) are characterized by qualitative impairments in social interaction and communication and by repetitive behavior or restricted interests (DSM-IV-TR). Behavioral interventions are often used to address the deficits in these three core domains, but there are no treatments – pharmacological or behavioral – proven to “cure” ASD.

Psychopharmacology has been shown, however, to help with some of the following maladaptive behaviors and psychiatric co-morbidities that are prevalent in children with ASD:

- Harmful/bothersome repetitive behaviors
- Attention problems
- Anxiety
- Aggression/irritability
- Self-injurious behavior
- Sleep difficulties

Many of the medications are used off-label because FDA-approved uses are limited. A primary care physician may encounter a child with an ASD on one or more of these medications in the course of his/her practice. It is important to be aware of side effect profiles, contraindications, and health monitoring in children on these medications. While side effects should be monitored by the prescriber, the primary care provider also needs to make sure these are monitored, be aware of the possible drug interactions with other medications prescribed, and know the side effects so they can be considered in the differential diagnosis of symptoms brought to the primary care office for treatment.

Introduce the session goal and format of the case study

Slide 1-2

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Cultural Competence

It is important for clinicians to understand how different childrearing practices and cultural norms may influence key decisions that parents make regarding their child, including obtaining evaluations and treatment, future planning, and acceptance of the child's diagnosis. Clinicians can approach parents openly and honestly by asking them about their unique style of parenting and how the information or recommendations provided are received.

See the curriculum introduction for additional information on cultural competence and potential discussion questions.

Case Study Part I

Kofi is an overweight 8-year-old boy who was diagnosed with an ASD and borderline intellectual functioning (IQ of 75) at 4 years of age when he presented with delays in social communication skills (i.e., lack of conversational speech, poor eye contact), repetitive and stereotyped behaviors (e.g., hand flapping and toe walking). He is receiving state-of-the-art physical, occupational, and speech therapy; social skills group therapy; and behavioral therapy. His medical history is significant for only occasional bouts of loose, foul-smelling stools. Kofi's adaptive functioning is good: he is fully toilet trained and he feeds and dresses with minimal assistance. He communicates wants and needs with short sentences and pointing. Kofi presents to your general pediatric practice with his mother, who is concerned about new problem behaviors. When asked to elaborate, his mother says that over the past several months, Kofi has been "biting, spitting, and growling" at his classmates, teachers, and 10-year-old brother. She adds that Kofi has difficulty staying in his seat and participating in class activities. She has received numerous phone calls from his teachers, who are concerned about the safety of the other students and themselves. They have tried several behavioral interventions with limited success.

Kofi's mother reports less physical aggression at home, but notes that Kofi has become more irritable. He has tantrums nearly every hour and especially right before bedtime. Kofi also wakes up at night upset and has trouble falling asleep again. "The police have even come a few times," cries Kofi's mother, "because someone thought I was abusing my child!"

Kofi's mother buries her face into her hands and begins sobbing. "He was making such great progress with his therapies...I don't know what happened!"

After you comfort and reassure Kofi's mother, she tells you that Kofi has been in good health. His intermittent diarrhea was present well before these new behaviors and has not worsened. Kofi's mother states that the diarrhea has improved since he was put on a lactose-free diet several years ago. Kofi continues to have a hearty appetite ("He eats anything I put in front of him!"). He had no caries or gum disease on his last dental exam and cleaning.

Distribute "Case Study Part I"

Slide 3

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Kofi's mother reports that she has tried giving Kofi a warm bath, applying deep pressure massage, using his weighted vest, and playing "relaxing" music to help him sleep. In spite of these strategies, Kofi regularly wakes up three to four hours after he falls asleep. "Sometimes Kofi will wake up and just wander around the apartment," explains the mother. "Other times he'll start crying, or worse, screaming." Kofi only falls asleep when one of his parents is in the bed with him. His mother reports no heavy snoring, coughing, or times when he stops breathing briefly while he is asleep.

His mother identifies Kofi's aggressive and irritable behavior as the highest priority. She worries that it will escalate to a point where he will "really hurt someone." She cannot identify any triggers for these outbursts. There have been no stressors or major changes in the family or in Kofi's social and educational settings. "Most of the time it just happens out of the blue," she explains. She and Kofi's teachers have tried time outs and behavior modification plans, including one based on applied behavioral analysis, to little avail.

Your physician and neurological exam reveals no changes since his last exam six months ago. His BMI remains high at 29.3. You observe one of Kofi's outbursts. He has a high-pitched cry and begins tossing your toys against the wall. He screams and kicks on the floor for several minutes until the screensaver of your computer captivates his attention.

Kofi's mother is aware that children with ASD can be aggressive and irritable and have difficulties with sleep regulation. She has read about other parents with similar problems. She says, "My friend's son takes Ritalin for his behavior problems. Do you think medication could help Kofi?"

Case Study Part I: Discussion Question

After reading the case, ask participants, "What stands out to you about this case?"

Case Study Part I: Potential Prompts

- 1.1 What are some strengths of this child and family?
- 1.2 How would you respond to Kofi's mother?
- 1.3 What further information would you like following the mother's disclosure?
- 1.4 How would you prioritize this mother's concern and questions?

:30

Slide 4

Follow up with student responses to encourage more discussion:

- What in the case supports that?
- Why do you think that?
- What makes you say that?

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Supporting Information for Potential Prompts

1.1 *What are some strengths of this child and family?*

It is always important to explore the strengths of a child with an autism spectrum disorder or developmental delays. Parents and clinicians may become so focused on the deficits and, in some cases, the behavioral issues that a child is having that they aren't able to notice what the child does well. By asking a family about what a child is good at, and what their positive traits are, one is able to frame recommendations for intervention and treatment in the context of these strengths. In addition, asking about what a child likes can be used when discussing next steps. Finally, in addition to exploring the strengths of the child, it is helpful to think about the strengths of the family and how these can be used when discussing options and next steps for treatment. If parents are unable to offer strengths and positive attributes of the child, it is important to acknowledge how difficult and stressful things seem for them at this time. It is always helpful for clinicians to take the time to note changes and improvements in functioning and positive features of the child and narrate these observations to parents.

- Kofi is independent with basic self-help skills (e.g. toileting).
- Kofi uses language and pointing to communicate wants and needs.

1.2 *How would you respond to Kofi's mother?*

Very commonly, parents of children with maladaptive behaviors arrive at the office distressed and have many questions and concerns. The first step in such an emotionally charged encounter is to acknowledge the mother's difficulties. It is a moment to empathize. Telling her you are glad she has come to see you **reaffirms her decision to seek help from you** for this type of problem. Explaining that these behaviors are common in children with ASD and can be treated successfully may provide reassurance.

Establishing goals for the visit up front and prioritizing them makes the visit more manageable for both you and the parent. Stating that, together, you will try to unravel the behavioral deterioration, but that it may take several visits and perhaps other consultations, sets realistic expectations. If you feel you must deal with the entire problem at that minute, you'll feel overwhelmed by the time commitment for that first unexpected visit and will be likely to subconsciously give the message that the problem is not solvable.

Knowing what behaviors **are most concerning for Kofi's mother** helps you know where to focus your energies in counseling and treatment. Ask questions about the type of treatments the mother is interested in or has read about. Is the mother looking for a specific behavioral intervention, pharmacologic treatment, or just psychosocial support? **By acknowledging that follow-up visits may be necessary before** successful intervention, you reassure the parent that there is continuity with the clinician, thereby strengthening the therapeutic alliance.

1.3 *What further information would you like following the mother's disclosure?*

Any new maladaptive behaviors in a child with a communication disorder, such as an ASD warrant an **inquiry into possible physical causes**. Gather information about the following at the first visit, at another longer scheduled visit, or over multiple visits depending on the practicalities for you and Kofi's mother:

:30

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- Dental abscesses
- Headache
- Bone fracture
- Constipation
- Diarrhea
- Allergies
- Vision problems
- Dietary history

It is important to remember you may be the only person in the care team who considers medical causes and examines the child thoroughly. Onset, chronicity, potential triggers, and alleviating factors provide important clues. Gather a complete review of systems, including a diet history to determine if there might be an association with the problematic behaviors. Ask detailed questions about appetite, sleep, and energy.

Any variation in history around the time of the onset of these behaviors should be pursued, including a travel history.

- Kofi's history of "loose, foul-smelling stools" suggests the possibility of malabsorption or infection, especially if the timing of the stool and behavioral change coincide. As an aside, there has been controversy surrounding the theory that ASD are caused by malabsorption in the gastrointestinal (GI) tract resulting in excessive levels of opioids in the central nervous system ("leaky gut") and an increased prevalence of GI disorders. There are no rigorously designed studies, however, that support this hypothesis. In a recent long-term, population-based study, the co-occurrence of GI symptoms in children with an ASD was no higher than in normal controls.
- Irritability and insomnia can be symptoms of obstructive sleep apnea or gastroesophageal reflux disease.

All of this information, along with a physical and neurological exam, will guide you in deciding whether to pursue a medical workup and what path to take in that workup.

While pursuing a medical etiology for the behavioral deterioration, gathering **information about the child's environment** can also give you a context for these behaviors. Changes around the time the behavior worsened are particularly helpful. Ask the parent to describe the home and school settings:

- Who lives at home?
- Are there siblings?
- How many students are in the classroom?
- How does their functioning compare with Kofi's?
- How experienced are the teachers and aides in working with children with ASD?
- What are the triggers and alleviating factors for the behaviors?
- Do the behaviors occur less in some settings and more in others?
- Do they occur during transitions?
- Was there a recent stressful event in the family?
- What, if anything, has been done about high BMI?

Investigate any interventions Kofi's mother and school have tried to this point. Details about the quality of these interventions are valuable, although sometimes difficult to determine, because often these interventions have not been applied effectively, consistently, or long enough to work. Direct communication from teachers or other professionals involved with the child provides additional insight into behaviors and

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interventions. Behavioral rating scales or checklists (e.g., Childhood Behavioral Checklist, Strengths and Difficulties Questionnaire, and Aberrant Behavior Checklist) can be useful for categorizing behaviors and quantifying their intensity. They can also be used to establish a baseline and track treatment.

- Kofi's mother has tried approaches based on applied behavioral analysis. This includes a functional behavioral analysis (FBA). A functional behavioral analysis can be a useful way of analyzing and identifying strategies to cope with problem behaviors and the environment(s) they occur in. It is important to recognize that maladaptive behaviors in children with developmental delays are often a means to communicate.
 - An FBA can be performed at home or by the school psychologist to provide more information about behavior in that setting. It involves using direct observation to look at a behavior in the context of what occurs before and after. This approach can be used to identify triggers and reinforcers of problem behaviors and to evaluate the communicative intent of the behavior.
 - The ABCs of a functional behavior analysis include:
Antecedent > Behavior > Consequence

Before treating any child with a behavioral problem, **ask questions that enhance your understanding of the parent's perspective of the problem.**

- What does Kofi's aggression and irritability mean to the mother?
- To whom does she attribute these behaviors?
- Does she blame herself or others?
- Does she think an ASD has anything to do with these behaviors?
- How worried is the mother about her safety or the safety of others?
- Is she concerned that these behaviors are disruptive to the family and class?
- How much do these behaviors impair Kofi's ability to learn or have meaningful relationships?

Information about how a parent sees or feels about the problem allows you to discuss the treatment plan in a sensitive manner.

1.4 *How would you prioritize this mother's concerns and questions?*

The most pressing behavior is Kofi's aggression and irritability, followed by sleep dysregulation and hyperactivity. Several pharmacologic agents can be used to treat aggression and irritability. Risperidone has the strongest evidence for efficacy. Unfortunately, risperidone has been shown to cause weight gain and somnolence. Aripiprazole, another atypical antipsychotic approved by the FDA in 2009, is favored by some clinicians because it may be associated with less dystonia, smaller increases in prolactin levels, and less QTc prolongation. Risperidone will be discussed in further detail later on in this case.

Several off-label medications are used to target aggression and irritability:

- **Alpha2-adrenergic agonists (guanfacine and clonidine)**
 - Indications: Aggression, oppositionality, hyperactivity, inattention sleep disturbances
 - Side Effects: Hypotension, sedation, dry mouth, headache, constipation

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- **Opioid antagonist (naltrexone)**
 - Indications: Irritability, repetitive/self-stimulatory behaviors, hyperactivity
 - Side Effects: Insomnia, headache, decreased appetite, bitter taste
- **Psychostimulants (e.g., methylphenidate, mixed amphetamine salts)**
 - Indications: Aggression, irritability, inattention, impulsivity, hyperactivity
 - Side Effects: Appetite loss, insomnia, headache, irritability, withdrawn behavior, tachycardia, hypertension (not recommended in children with preexisting heart disease or defects), growth retardation (chronic use)
- **Serotonin reuptake inhibitors (e.g., fluoxetine, sertraline)**
 - Indications: Aggression, impulsivity, mood lability, irritability, sleep disturbances
 - Side Effects: Sedation, dry mouth, constipation, suicidality (black box warning)

Compared with risperidone and aripiprazole, these medications are not as well studied in children with ASD. Some argue these medications are less efficacious and have a higher propensity to cause adverse effects in children with ASD. An extensive review of the evidence behind the use of these medications is beyond the scope of this discussion. However, the following resources provide more information:

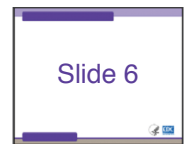
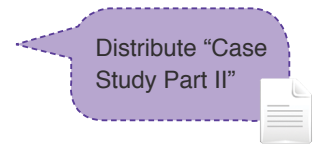
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Many general pediatricians are inexperienced in prescribing and managing psychotropic medications, especially in children with ASD. Regular monitoring, sometimes as frequently as weekly in the initial stages of starting a medication, is warranted. Weight, height, blood pressure, and heart rate are important measurements to document at each visit for certain medications; for others (e.g., atypical antipsychotics), laboratory tests, such as fasting lipids, liver function tests, and serum glucose, are recommended. Because these medications are not well studied in this population and carry a high potential for adverse side effects, consultation with, or referral to, a mental health specialist is recommended. Typically, child psychiatrists, developmental-behavioral pediatricians, and pediatric neurologists are formally trained to treat children with ASD with psychotropic medications and can assist with dosing and titration schedules.

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Case Study Part I: Discussion Question

Before moving to Part II, ask participants, “What would you do next?”



Case Study Part II

Kofi's mother returns for a follow-up visit. She is awaiting consultation with the developmental-behavioral pediatrician. You ask her how things are going. She gets teary eyed. "I'm so frustrated with Kofi's behaviors," she cries. "He used to be such a nice child!" Kofi's mother then tells you that she has been reading up on complementary and alternative medicine (CAM) therapies on the Internet. She has also spoken with several parents whose children with ASD are on CAM therapies. "I couldn't just sit at home and do nothing while I wait for this appointment," she explains. "Besides, many parents in the parent support group I go to have told me how well these therapies work." Kofi's mother is now planning to start Kofi on CAM therapy, but was hesitant to tell you before because she didn't think you would approve.

You ask Kofi's mother what she has looked at, and she mentions chelation therapy, antifungal medication to treat yeast overgrowth in his GI tract, and vitamin supplements. She says, "I was hoping you wouldn't laugh at me, but I really would like your opinion – there is so much information on the Internet and it's hard to know whom to trust." She then looks away sheepishly. "Actually, I've been giving Kofi vitamin supplements I learned about on a website for the past month. I didn't tell you before because I thought you would tell me to stop giving them to him." Kofi's mother then pulls out a folder full of advertisements and articles printed from prominent parent advocacy websites and blogs. She would like your opinion on which treatments are safe for Kofi.

After discussing these issues with Kofi's mother and ensuring her you understand, you say, "Let's talk about vitamin supplements first. Kofi has no chronic illness that might affect his ability to process vitamins, so I don't think we would do any harm by giving him supplements in moderation. Let's just make sure his kidneys and liver are healthy with a few lab tests. I will add these to my records of medications that Kofi is taking. Be careful about adding other sources of the same vitamins that you may not be aware of, such as drinks and other foods that are vitamin fortified."

You continue, "Although I feel that supplements will not harm Kofi, I don't feel the same way about chelation therapy. As we already discussed, chelation therapy hasn't been shown to be effective at helping with the symptoms of ASD in a way that I find convincing. Given the risks, high costs, and potential disruption for Kofi and your family's quality of life, I strongly recommend against starting chelation therapy. On the other hand, one over-the-counter therapy that many people use to help children with trouble sleeping is melatonin. Melatonin is one of the best proven of all the CAM therapies used for children with ASD, with improvements in sleep duration and decrease in the amount of time it takes to fall asleep, with no proven risks. It might really improve everyone's quality of life. Have you looked at it?"

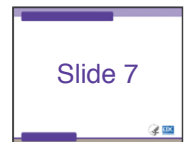
His mother nods her head and tells you that she was meaning to ask you about melatonin.

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Kofi's mother agrees to see the specialist before making any decisions on treatment. She agrees to keep you informed of any additional practitioners or treatments she decides to enlist. You thank her for that and ask her to call you once she has seen the developmental-behavioral pediatrician.

Case Study Part II: Discussion Question

What stands out to you about this discussion?



Case Study Part II: Potential Prompts

- | | | |
|-----|---|-----|
| 2.1 | How would you address the issue of CAM in your practice? | :30 |
| 2.2 | How would you respond to the mother's concerns about disclosing that she already started giving Kofi vitamin supplements? | |
| 2.3 | How do you address questions about selecting or recommending CAM? | :30 |
| 2.4 | How would you respond to the mother's interest in melatonin? | |

Supporting Information for Potential Prompts

- | | | |
|-----|---|-----|
| 2.1 | <i>How would you address the issue of CAM in your practice?</i> | :30 |
|-----|---|-----|

The National Center for Complementary and Alternative Medicine (NCCAM), part of the National Institutes of Health, defines CAM as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional Western medicine.” Complementary therapies are used in addition to conventional, Western medical practices, while alternative therapies replace them. Surveys estimate that among children with chronic diseases and disabilities, an estimated 70% have used CAM, and among these, children with autism spectrum disorder (ASD) are one of eight subgroups reporting the most use of CAM.

Generally, people use CAM for a multitude of reasons, including:

- Eagerness to try anything that might help their child
- Culture/philosophy
- Dissatisfaction with the nature of the conventional medical system
- Concern about adverse effects of “unnatural” medications

ASD present particularly compelling reasons for parents to seek alternate or complementary treatments. Parents often feel a desperate need to take quick action. Conventional medicine has identified relatively few treatments to help with the symptoms of ASD and nothing to cure it. Faced with feelings of lack of control, lack of explanation

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for a devastating illness, and media saturation with enticing promises of “miracle cures” from unproven therapies, many parents are willing to try CAM for their children with ASD.

Pediatricians are in a critical position to initiate and maintain dialog with parents about the role of CAM in treatment for children with ASD, as many parents might be hesitant to bring this up. Although most children who use CAM also use the conventional medical system, few parents inform their pediatricians about CAM use. Encourage parents to discuss CAM with you, but also educate parents on how to navigate the vast amounts of information available regarding CAM therapies.

Ask about CAM regularly and in specific terms to prompt parents’ memory of things they may not consider “treatments” or may be embarrassed to admit (“Have you used any vitamins or supplements or gone to any other practitioners?”). It is essential to convey objectivity and encourage open communication. Emphasize safety and quality of life for not only the child, but also for the entire family, noting that this includes financial considerations, safety, stress on the child, and stress on siblings and parents.

2.2 *How would you respond to the mother’s concerns about disclosing that she already started giving Kofi vitamin supplements?*

First, provide enthusiastic, positive reinforcement about her disclosure to create an atmosphere in which she will continue to feel like she can be completely open with you about her use of CAM therapies. You must convey that you wish to partner with her to help her navigate through the information to make a well-informed decision about what is best for Kofi and for the family. Emphasize that you wish to help her keep Kofi and the whole family as safe, healthy, and happy as possible, and that **you will not judge her decisions or values**. To do this, it is critical for you to know everything he takes, including prescription medications, over-the-counter medications, dietary supplements, vitamins, and any other preparations, such as teas, aromatherapy, or hands-on therapies (such as acupuncture, massage, Reiki, music therapy).

Many parents may not realize the importance of this disclosure because they do not realize that “natural” substances can be harmful or that teas and supplements can have interactions with each other, with foods, and with medications. Parents also may not realize that **vitamins and foods are regulated by different laws than medications**. They are not subject to the same stringent regulations about composition, so there can be impurities and inconsistency in dosage. Furthermore, vitamins and dietary supplements do not undergo the same pre-market testing for adverse reactions that prescription medicines must.

2.3 *How do you address questions about selecting or recommending CAM?*

It is most critical to communicate that some therapies are potentially dangerous.

- **Chelation therapy**, based on the tenet that an ASD mimics symptoms of heavy metal (mercury) poisoning, is a prime example. Chelation is an established treatment for decreasing heavy metal levels in patients with documented toxic exposures to such metals. However, mercury toxicity has not been causally linked to ASD, and chelation as a treatment for ASD is often conducted in the absence of laboratory evidence of mercury toxicity. In other cases, the evidence used is a hair sample, the accuracy of which is unproven. The effects of chelation on children who do not harbor toxic levels of heavy metals are unknown. At least one child has experienced fatal complications related to intravenous chelation therapy for ASD. Furthermore,

I. Vitamins & Exercise
Base Therapies



:30

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safe chelation therapy requires frequent blood testing, which impacts the child's quality of life.

- Many children are prescribed **anti-fungal medication, vancomycin, or antiviral medication**, based on the assumption that they have fungal, viral, or bacterial intestinal overgrowth or occult infection contributing to the development of ASD. These theories have not been adequately substantiated, and parents may not realize that anti-fungals, antibiotics, and antiviral medications all have potentially serious side effects, including liver damage and allergic reaction, and some require frequent blood sampling.

Other therapies show promise, but are expensive and unproven. **Hyperbaric oxygen therapy** is a timely example. Hyperbaric oxygen therapy is an established treatment for forms of disease involving decreased perfusion and/or inflammation, such as burns and carbon monoxide poisoning. The theory behind using it as a treatment for ASD is that ASD are caused by occult inflammation and/or hypoperfusion of the brain. While this treatment has received media attention, there has not been adequate proof of effect to justify its very high cost (ranging from \$100 to \$850 per session) or substantial time commitment.

Dietary modification is a popular and longstanding CAM therapy for ASD that involves significant lifestyle change and may lead to nutritional deficiencies if not conducted properly. The Feingold Diet, popular in the 1970s, eliminates artificial food additives and naturally occurring salicylates. Also in the 1970s, protein malabsorption theories became the basis for the gluten-free, casein-free diet, suggesting that malabsorption of these proteins led to inflammation and absorption through the “leaky gut,” followed by opioid-like neurotransmitter release into the central nervous system that led to behaviors typical of ASD. These theories are based, in part, on the presence of increased peptides in the urine of children with ASD. These laboratory tests have not been shown to be effective biomarkers due to inconsistency and unclear significance. The “leaky gut” theory has never been scientifically proven.

While many parents place their children on such diets and report subsequent improvements in their children's social behaviors, many children have no response, and scientific evidence has not been established. Other popular but unproven dietary modifications include selective elimination diets and ketogenic diets. When talking about dietary intervention, it is important to weigh all the potential risks and benefits, including expense, effects on the family and child's quality of life, and possible nutritional deficiencies/need to supplement that could arise from a strictly limited diet.

It is important to **teach parents how to distinguish valid scientific evidence** from information presented as evidence, but achieved through less rigorous methods. In 1999, several double-blinded, placebo-controlled studies failed to show a significant difference between patients with ASD treated with the pig-derived neuropeptide secretin and those given placebo. These studies came after a media frenzy and development of a black market for secretin based on three case reports citing incidental improvement in symptoms of ASD after receiving secretin for a gastrointestinal procedure. In February 2009, Andrew Wakefield's claims regarding a possible link between ASD and MMR vaccination were discredited when Wakefield's original paper, which spawned a large international anti-vaccination movement, was found to contain falsified data. Wakefield's reported results have not been replicated by other investigators, despite several attempts.

Treatments for Autism Spectrum Disorder

Although some CAM treatments are unproven because they do not work, there may be others that work, but are difficult to prove through high-quality (i.e., controlled, blinded, replicable), peer-reviewed research. Several CAM therapies (e.g., probiotics, massage therapy, guided imagery, mindfulness-based meditation, acupuncture) have entered the realm of “conventional” treatments for diseases other than ASD based on convincing, replicable evidence. Thus, it is important to maintain objectivity and create a collaborative relationship with parents interested in CAM, helping them to navigate the evidence and weigh risks and benefits rather than strictly saying “no” to all CAM treatments based on lack of evidence.

A simple rule of thumb is to **strongly discourage therapies that are disproven and possibly harmful, encourage therapies that are proven and safe, and tolerate therapies that are unproven, but safe.** Dietary supplements and modifications are generally thought to be safe in established therapeutic doses, but show varying degrees of validity in research. When treating a child with an ASD for whom CAM therapies make up part of the treatment regimen, it may be helpful to maintain a list of reported treatments, dates or doses/frequency, and either observed or reported effects.

2.4 *How would you respond to the mother’s interest in melatonin?*

A major issue for Kofi’s mother is sleep problems. **Many families with children with developmental disabilities and sleep problems give their children synthetic melatonin to help them sleep.** It is considered a relatively safe CAM treatment.

- Melatonin is an endogenous substance produced by the pineal gland that **helps regulate the sleep-wake cycle.** Synthetic melatonin has been shown to be effective in children with neurodevelopmental disabilities in helping with sleep onset and maintenance. It is available as a controlled-release tablet. Although one study cited increased seizure activity in children with severe neurodevelopmental disabilities on melatonin, another similarly-designed study showed the opposite. Other than that, there have been no reports of significant adverse effects of melatonin. In addition to telling Kofi’s mother that you would support her decision if she were to try melatonin, you should discuss the importance of **adding one new treatment at a time** to monitor for adverse or positive effects, which should be done in an organized fashion so that ineffective therapies can be stopped.

It is also important to **discuss what parameters you will use to see if this treatment is effective for treating Kofi’s sleep disturbance.** In this case, you could decide together that after one week you will follow up with Kofi’s mother over the phone and discuss whether Kofi is falling asleep faster or having fewer night awakenings since starting the melatonin.

At this point, treatment of Kofi’s behavioral problems is beyond the scope of a primary care physician. Kofi needs an evaluation by a specialist who can provide expertise in the management of maladaptive behaviors in a child with an ASD and recommend treatments. As Kofi’s primary care pediatrician, however, you should remain the central figure who coordinates and advocates for Kofi’s health. Kofi’s mother has clearly identified you as someone she trusts and looks to first for professional advice in her decisions about Kofi’s care. This relationship cannot be emphasized enough in its importance for treatment compliance and monitoring.

Treatments for Autism Spectrum Disorder

Case Study Part III - Epilogue

Kofi's mother calls you with an update after seeing the developmental-behavioral pediatrician. She was advised to try a medication called risperidone. The doctor raised concerns about Kofi already being overweight. The decision, however, was made to start Kofi on risperidone because these extreme behaviors had such a profound impact on his functioning. The doctor prescribed a gradually increasing dose schedule. Blood work was obtained at baseline and after one month of treatment to monitor effects on Kofi's lipids and fasting blood sugar. BMI and vital signs will also be monitored regularly. While Kofi's mother was initially hesitant because of the side effect profile, she agreed that the benefits outweighed the risks.

Kofi was started on a dose of 0.5 mg. He showed no improvement in aggressive and irritable behavior and had gained a few pounds.

The developmental-behavioral pediatrician had given her the name of a nutritionist who helps manage the increased appetite of children with ASD who are placed on risperidone, but she had not yet contacted him. You encourage her to follow through with that plan, and she agrees to do that.

Distribute "Case Study Part III - Epilogue"



Case Study Part III - Epilogue: Discussion Question

How would you apply the information in this case?

What did you learn through this case?

Slide 9

Case Study Part III - Epilogue: Potential Prompts

3.1 What would you recommend following the mother's inquiry into risperidone?

:30

Supporting Information for Potential Prompts

3.1 *What would you recommend following the mother's inquiry into risperidone?*

To put a child with an ASD on a pharmacologic medication that specifically targets maladaptive behaviors is a big decision for parents. It requires a physician who is familiar with the therapeutic and adverse effects of the medication, committed to monitoring the child regularly, and comfortable counseling the parents while the child is on medication.

II. Treatment Tracking Tool



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Treatments for Autism Spectrum Disorder

Any conversation with parents who are considering medication for a child with an ASD must begin with the following statement: “Medications can alleviate some of the associated symptoms of ASD, but they do not treat the core symptoms (i.e., qualitative impairment of social interaction, qualitative impairment of communication, and restricted and repetitive behaviors).”

- Associated symptoms of ASD include aggression, self-injury, oppositionality, hyperactivity, impulsivity, inattention, irritability, emotional lability, depression, anxiety, unusual responses to sensory stimuli, irregular appetite, sleep problems, and gastrointestinal disturbances.

Emphasize to parents that the most studied and effective of ASD treatments are behavioral management and intensive, sustained education. There are certainly limitations to these treatments: they take time to see incremental benefits, they are labor-intensive and expensive, and they are difficult to take to scale.

Pharmacologic medications are appealing because effects can be seen almost immediately. Kofi demonstrates several associated symptoms that have not improved with behavioral intervention. It appears they are severely interfering in multiple settings and potentially harmful. A serious discussion about medication as an adjunct treatment is appropriate. All involved in the care of the child (parents, teachers, and clinicians) should agree on measurable target behavioral outcomes.

Risperidone is an FDA-approved atypical antipsychotic medication used for the treatment of behavioral problems in children ages 5 to 17 years with ASD (www.fda.gov, 2006). These behaviors include irritability described as tantrums, aggression, and self-injurious behavior.

- **Side effects of risperidone** include weight gain and increased appetite, sedation, constipation, and fatigue. There can also be effects such as prolactinemia, insulin resistance, elevated lipids, movement disorders (e.g., tremors), seizures, and dry mouth.

As a primary care physician, you should know that health monitoring of children on risperidone includes a baseline exam measuring BMI as well as lab testing including lipid profile, liver function tests, and fasting blood sugar or hemoglobin A1C. This testing should be repeated at regular intervals. Clinical trials have confirmed that risperidone is a useful medication for the short-term treatment of irritability associated with an ASD.

Next Case: “Autism Spectrum Disorder - Specific Anticipatory Guidance”

Case Goal

Children with autism spectrum disorder (ASD) present with similar developmental issues and challenges to typically-developing children, but special consideration may be needed when evaluating these issues and providing anticipatory guidance to families.

After completion of this module, learners will be able to:

- 1 Recognize some of the common developmental issues that present in children with ASD and how to evaluate them.
- 2 Identify management approaches and strategies for the common developmental issues seen in children with ASD

Case Worksheet for Learners

Case Goal

Children with autism spectrum disorder (ASD) often present with challenging or maladaptive behaviors that are commonly seen in addition to the core deficits. Pediatricians are often called upon to help evaluate children for underlying medical concerns and to facilitate obtaining appropriate treatment.

Key Learning Points of This Case

1. *Evaluate the etiology of changes to behavior and functioning in children with ASD and describe strategies to analyze these changes.*

a. Identify specific causes that can increase maladaptive behavior. _____

b. Describe the components of a functional behavioral analysis. _____

c. Be familiar with rating scales that can be used to assess behavior change in children with ASD. _____

2. *Develop knowledge regarding specific options to treat maladaptive behaviors in children with ASD*

a. Identify key red flags for ASD. _____

b. Recognize the difference between a typical temper tantrum and one of a child with an ASD. _____

c. Describe the most common complementary and alternative medicine (CAM) therapies used to treat children with ASD. _____

d. Learn strategies to engage families around the use of CAM. _____

Post Learning Exercise

Talk with a family who has a child or adolescent with an ASD. Discuss the challenges in managing symptoms, such as aggression, obsessions, and other issues.

Case Study Handout Part I

Kofi is an overweight 8-year-old boy who was diagnosed with an ASD and borderline intellectual functioning (IQ of 75) at 4 years of age when he presented with delays in social communication skills (i.e., lack of conversational speech, poor eye contact), repetitive and stereotyped behaviors (e.g., hand flapping and toe walking). He is receiving state-of-the-art physical, occupational, and speech therapy; social skills group therapy; and behavioral therapy. His medical history is significant for only occasional bouts of loose, foul-smelling stools. Kofi's adaptive functioning is good: he is fully toilet trained and he feeds and dresses with minimal assistance. He communicates wants and needs with short sentences and pointing. Kofi presents to your general pediatric practice with his mother, who is concerned about new problem behaviors. When asked to elaborate, his mother says that over the past several months, Kofi has been "biting, spitting, and growling" at his classmates, teachers, and 10-year-old brother. She adds that Kofi has difficulty staying in his seat and participating in class activities. She has received numerous phone calls from his teachers, who are concerned about the safety of the other students and themselves. They have tried several behavioral interventions with limited success.

Kofi's mother reports less physical aggression at home, but notes that Kofi has become more irritable. He has tantrums nearly every hour and especially right before bedtime. Kofi also wakes up at night upset and has trouble falling asleep again. "The police have even come a few times," cries Kofi's mother, "because someone thought I was abusing my child!"

Kofi's mother buries her face into her hands and begins sobbing. "He was making such great progress with his therapies...I don't know what happened!"

After you comfort and reassure Kofi's mother, she tells you that Kofi has been in good health. His intermittent diarrhea was present well before these new behaviors and has not worsened. Kofi's mother states that the diarrhea has improved since he was put on a lactose-free diet several years ago. Kofi continues to have a hearty appetite ("He eats anything I put in front of him!"). He had no caries or gum disease on his last dental exam and cleaning.

Kofi's mother reports that she has tried giving Kofi a warm bath, applying deep pressure massage, using his weighted vest, and playing "relaxing" music to help him sleep. In spite of these strategies, Kofi regularly wakes up three to four hours after he falls asleep. "Sometimes Kofi will wake up and just wander around the apartment," explains the mother. "Other times he'll start crying, or worse, screaming." Kofi only falls asleep when one of his parents is in the bed with him. His mother reports no heavy snoring, coughing, or times when he stops breathing briefly while he is asleep.

His mother identifies Kofi's aggressive and irritable behavior as the highest priority. She worries that it will escalate to a point where he will "really hurt someone." She cannot identify any triggers for these outbursts. There have been no stressors or major changes in the family or in Kofi's social and educational settings. "Most of the time it just happens out of the blue," she explains. She and Kofi's teachers have tried time outs and behavior modification plans, including one based on applied behavioral analysis, to little avail.

Your physical and neurological exam reveals no changes since his last exam six months ago. His BMI remains high at 29.3. You observe one of Kofi's outbursts. He has a high-pitched cry and begins tossing your toys against the wall. He screams and kicks on the floor for several minutes until the screensaver of your computer captivates his attention.

Kofi's mother is aware that children with ASD can be aggressive and irritable and have difficulties with sleep regulation. She has read about other parents with similar problems. She says, "My friend's son takes Ritalin for his behavior problems. Do you think medication could help Kofi?"

Case Authors

- **Cristina Farrell, MD**, Einstein College of Medicine, Children's Hospital at Montefiore
- **Leonard Rappaport, MD, MS**, Children's Hospital Boston, Harvard Medical School
- **Neelam Sell, MD**, The Children's Hospital of Philadelphia
- **Brian Tang, MD**, Lucile Packard Children's Hospital, Stanford University School of Medicine

Case Study Handout Part II

Kofi's mother returns for a follow-up visit. She is awaiting consultation with the developmental-behavioral pediatrician. You ask her how things are going. She gets teary eyed. "I'm so frustrated with Kofi's behaviors," she cries. "He used to be such a nice child!" Kofi's mother then tells you that she has been reading up on complementary and alternative medicine (CAM) therapies on the Internet. She has also spoken with several parents whose children with ASD are on CAM therapies. "I couldn't just sit at home and do nothing while I wait for this appointment," she explains. "Besides, many parents in the parent support group I go to have told me how well these therapies work." Kofi's mother is now planning to start Kofi on CAM therapy, but was hesitant to tell you before because she didn't think you would approve.

You ask Kofi's mother what she has looked at, and she mentions chelation therapy, antifungal medication to treat yeast overgrowth in his GI tract, and vitamin supplements. She says, "I was hoping you wouldn't laugh at me, but I really would like your opinion – there is so much information on the Internet and it's hard to know whom to trust." She then looks away sheepishly. "Actually, I've been giving Kofi vitamin supplements I learned about on a website for the past month. I didn't tell you before because I thought you would tell me to stop giving them to him." Kofi's mother then pulls out a folder full of advertisements and articles printed from prominent parent advocacy websites and blogs. She would like your opinion on which treatments are safe for Kofi.

After discussing these issues with Kofi's mother and ensuring her you understand, you say, "Let's talk about vitamin supplements first. Kofi has no chronic illness that might affect his ability to process vitamins, so I don't think we would do any harm by giving him supplements in moderation. Let's just make sure his kidneys and liver are healthy with a few lab tests. I will add these to my records of medications that Kofi is taking. Be careful about adding other sources of the same vitamins that you may not be aware of, such as drinks and other foods that are vitamin fortified."

You continue, "Although I feel that supplements will not harm Kofi, I don't feel the same way about chelation therapy. As we already discussed, chelation therapy hasn't been shown to be effective at helping with the symptoms of ASD in a way that I find convincing. Given the risks, high costs, and potential disruption for Kofi and your family's quality of life, I strongly recommend against starting chelation therapy. On the other hand, one over-the-counter therapy that many people use to help children with trouble sleeping is melatonin. Melatonin is one of the best proven of all the CAM therapies used for children with ASD, with improvements in sleep duration and decrease in the amount of time it takes to fall asleep, with no proven risks. It might really improve everyone's quality of life. Have you looked at it?"

His mother nods her head and tells you that she was meaning to ask you about melatonin.

Kofi's mother agrees to see the specialist before making any decisions on treatment. She agrees to keep you informed of any additional practitioners or treatments she decides to enlist. You thank her for that and ask her to call you once she has seen the developmental-behavioral pediatrician.

Case Authors

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- **Leonard Rappaport**, MD, MS, Children's Hospital Boston, Harvard Medical School
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Case Study Part III – Epilogue

Kofi's mother calls you with an update after seeing the developmental-behavioral pediatrician. She was advised to try a medication called risperidone. The doctor raised concerns about Kofi already being overweight. The decision, however, was made to start Kofi on risperidone because these extreme behaviors had such a profound impact on his functioning. The doctor prescribed a gradually increasing dose schedule. Blood work was obtained at baseline and after one month of treatment to monitor effects on Kofi's lipids and fasting blood sugar. BMI and vital signs will also be monitored regularly. While Kofi's mother was initially hesitant because of the side effect profile, she agreed that the benefits outweighed the risks.

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- **Neelam Sell**, MD, The Children's Hospital of Philadelphia
- **Brian Tang**, MD, Lucile Packard Children's Hospital, Stanford University School of Medicine

Handout I: Vitamins/Dietary Supplements and Exercise-Based Therapies

Vitamin Therapies and Dietary Supplements

Carnosine	Thought to have antioxidant activity, as well as a role in production of the inhibitory neurotransmitter GABA.; may lead to hyperactivity.
Dimethylglycine (DMG)	Given on the basis of a theory of decreased inflammation and increased immune function. An earlier study reported improvements in language when children with disabilities were given DMG; more recent studies have been unable to replicate these findings.
Melatonin	Pineal gland hormone given to help with sleep. Synthetic melatonin has been shown to be effective in children with neurodevelopmental disabilities in helping with sleep onset and duration but not necessarily maintenance. Generally thought to be safe.
Omega-3 fatty acids	Thought to have a variety of health and neuroprotective benefits. Preliminary studies have shown mixed, but promising results for improving behavior in children with ASD. Generally thought to be safe.
Probiotics	Given to counteract GI bacterial and fungal overgrowth. Beneficial effects of probiotics have been shown in irritable bowel syndrome (IBS), acute gastroenteritis, urinary tract infections, and other conditions, but meaningful research has not been done on the use of probiotics in children with ASD. Generally thought to be safe in the absence of immunodeficiency and assuming intact gut.
Vitamin A (cod liver oil)	Thought to improve immune function and vision (some groups theorize that ASD have to do with immune or auto-immune dysfunction). Can cause hepatotoxicity, increased intracranial pressure.
Vitamin B6 (pyridoxine)-magnesium	Given on the basis of B6's role in neurotransmitter production plus magnesium's supportive effect. Research has been suboptimal, but pediatricians should advise parents of the risk of B6 toxicity (peripheral neuropathy) and magnesium toxicity (changes in mental status, GI upset, muscle weakness, respiratory depression, hypotension, and arrhythmias).
Vitamin B12 (cobalamin)	Given intramuscularly, in conjunction with oral folinic acid, to counteract decreased plasma antioxidant concentrations identified in a study of 20 children with ASD. Initial research showed positive results, but attempts to replicate the findings were unsuccessful. Low risk of B12 toxicity but requires injection.
Vitamin C (ascorbic acid)	Shown to decrease stereotypic behaviors in double blind, placebo-controlled study that was never replicated. Toxicity causes nephrolithiasis and GI upset.

Exercise-Based Therapies

Many activity-based therapies are also believed to help with symptoms of ASD. The following are popular, safe, but unproven and often expensive therapies:

- Sensory integration therapy
- Aromatherapy
- Massage
- Hippotherapy (horseback riding)
- Yoga
- Water therapy (swimming)
- Craniosacral massage
- Music therapy

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Handout II: Treatment Tracking Tool

:30

Clinical Approach to Psychopharmacologic Management

Clinical Approach to Psychopharmacologic Management

Identify and assess target behaviors

Parent/caregiver interview

Intensity

Duration

Exacerbating factors/triggers (time, setting/location, demand situations, denials, transitions, etc.)

Ameliorating factors and response to behavioral interventions

Time trends (increasing, decreasing, stable)

Degree of interference with functioning

Consider baseline behavior-rating scales and/or baseline performance measures/direct observational data

Include input from school staff and other caregivers

Assess existing and available supports

Behavioral services and supports

Educational program, habilitative therapies

Respite care, family psychosocial supports

Search for medical factors that may be causing or exacerbating target behavior(s)

Consider sources of pain or discomfort (infectious, gastrointestinal, dental, allergic, etc.)

Consider other medical causes or contributors (sleep disorders, seizures, menstrual cycle, etc.)

Complete any medical tests that may have a bearing on treatment choice

Consider psychotropic medication on the basis of the presence of

Evidence that the target symptoms are interfering substantially with learning or academic progress, socialization, health and safety (of the patient and/or others around him/her), or quality of life

Suboptimal response to available behavioral interventions and environmental modifications

Research evidence that the target behavioral symptoms or coexisting psychiatric diagnoses are amenable to pharmacologic intervention

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Treatments for Autism Spectrum Disorder

Choose a medication on the basis of

- Likely efficacy for the specific target symptoms
- Potential adverse effects

- Practical considerations such as formulations available, dosing schedule, cost and requirement for laboratory or electrocardiographic monitoring

- Informed consent (verbal or written) from parent/guardian and, when possible, assent from the patient

Establish plan for monitoring of effects

- Identify outcome measures

- Discuss time course of expected effects

- Arrange follow-up telephone contact, completion of rating scales, reassessment of behavioral data, and visits accordingly

- Outline a plan regarding what might be tried next if there is a negative or suboptimal response or to address additional target symptoms

- Change to a different medication

- Add another medication to augment a partial or suboptimal therapeutic response to the initial medication (same target symptoms)

- Add a different medication to address additional target symptoms that remain problematic

- Obtain baseline laboratory data if necessary for the drug being prescribed and plan appropriate follow-up monitoring

Explore the reasonable dose range for a single medication for an adequate length of time before changing to or adding a different medication

Monitor for adverse effects systematically

Consider careful withdrawal of the medication after 6-12 months of therapy to determine whether it is still needed

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