Autism Spectrum Disorder:

Parents' Medication Guide

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Introduction

What is ASD? Autism spectrum disorder (ASD) is a developmental disorder characterized by problems with social communication, unusual behaviors such as fixed interests, being inflexible, having repetitive behaviors, or abnormal responses to sensations. Communication problems include difficulty understanding and responding to social cues and nonverbal communication such as gestures and tone of voice, which can result in challenges in making or keeping friends. Although people with ASD may want to make friends, difficulties in understanding social norms or correctly interpreting language and facial expressions can get in the way.

In recent years, it has become clear that individuals with ASD, despite sharing some behavioral challenges, can be quite different from one another. Some people with ASD may be very intelligent, while others may have cognitive challenges. Some may have advanced vocabularies and others may speak very little or not at all. Previous attempts to subdivide the population on the basis of language and cognitive ability have not been supported by research. Thus, people in the same family with autism or who share the same genetic risk factor(s) can end up with very different symptoms and outcomes.

Why consider medication in ASD? People with ASD often experience a host of difficulties that can be as problematic as the symptoms of ASD itself. Anxiety, mood instability, impulsivity, hyperactivity, sleep problems, and even aggression and self-injurious behavior can occur in some people. Just as it would be for other medical problems, medication may be helpful in treating some of these difficulties. The use of medication is more often aimed at treating the symptoms of these associated conditions, which we can characterize as emotional and behavioral challenges, than for core symptoms of ASD itself, as no medications have shown clear benefit for social communication impairment or restricted, repetitive behaviors.

Sitting down with an expert to discuss whether it is a good idea to try medication for certain troublesome symptoms in your child with ASD is reasonable. Although the best approach to addressing those symptoms may not include medication, it can be helpful to learn about various options and/or begin to gather information on the frequency and intensity of behaviors that may ultimately be targets for medication treatment.

Assessment of the Child with ASD Experiencing Emotional or Behavioral Problems

When a challenge presents itself, it is time for an assessment. The first step in helping a child with ASD to get assistance with an emotional or behavioral challenge is to have him or her evaluated by an expert or team of experts. Since many factors may contribute to these emotional and behavioral problems in a child with ASD, it is ideal to have the child assessed by a team whose members can consider different causes and approaches. In reality, most children will only have access to a single provider, or the child's emotional or behavioral problems are severe enough that there is a need to act quickly. Even in these situations, it is important for the clinician who evaluates the child to consider multiple sources for the problem, and refer the child for further assessment if needed.

A thorough assessment of emotional or behavioral problems will take into account the possible role of communication, family functioning, factors that contribute to or exacerbate the behavior, physical health, co-existing mental health disorders, sensory factors, and daily living skills. The child's ability to communicate should be considered and a speech and language pathologist can perform more formal assessments of language and social communication abilities. Mental health providers can assess the functioning of the family and how family relationships could relate to problems, as well as evaluate for co-existing mental health disorders in the child such as anxiety or ADHD. Psychologists and other experts in behavior can assess factors that may maintain or reinforce the problem behavior(s), and can use applied behavioral analysis techniques, as outlined below. The possibility of a medical issue underlying the emotional or behavioral symptoms can be assessed by a physician or other medical provider. Finally, an occupational therapist can assess the role of over or under sensitivities and challenges in daily living and self-help skills, such as dressing, bathing, and eating.

Primary Non-Medication Treatment Strategies for Emotional and Behavioral Challenges

Applied Behavioral Analysis (ABA)

As demonstrated in a number of well designed research studies, Applied Behavioral Analysis (ABA) has been shown to be effective for addressing and often reducing challenging behaviors, as well as teaching many skills and routines. Parents frequently have questions about how ABA works and how it will help their child.

Children with ASD often have difficulty learning. Applied Behavior Analysis (ABA) is an educational and therapeutic approach that involves breaking down tasks and skills into their smallest parts, then teaching them slowly while encouraging, shaping, and reinforcing functional behaviors and discouraging harmful or disruptive behaviors. ABA focuses on the relationship between a certain behavior, the factors that were present before the behavior ("antecedents") and the results of the behavior ("consequences"). ABA has been successful in helping children with ASD improve communication, academic performance, social behavior, and adaptive living skills as well as addressing specific problem behaviors.[1]

Social skills are verbal and non-verbal behaviors necessary for positive and effective social interactions, and include eye contact, smiling, and asking and responding to questions.

Communication supports

While speech is generally the preferred method of communication in our society, not all children with ASD can use speech effectively. For children who have limited or no verbal ability, alternative methods of communicating have been developed to improve communication.

Communication supports are tools to help children with ASD communicate. A non-electronic method that has been shown to increase communication in children with ASD is the Picture Exchange Communication System (PECS), where the child uses pictures to communicate.[2] Electronic assisted communication devices include speech generating devices (SGD), which can produce an electronic voice that communicates words. These SGDs come in two main forms, dedicated devices (e.g. DynaVox, AlphaSmart, DynaWriter) or software (e.g. Proloquo2Go or Touchchat) that can be used on personal computers, tablets, or mobile phones.

Speech-language pathologists can recommend an assistive communication system after a careful evaluation of the unique abilities, needs, and communication goals of the child. Preliminary studies have shown that assistive communication devices are generally liked by users and may improve functional communication in children with ASD.[3]

Cognitive Behavioral Therapy

Cognitive Behavioral Therapy (CBT) is a type of psychotherapy in which a person's negative thoughts are challenged in order to reduce associated troubling emotions and behaviors. CBT is "problem-based," meaning that it is used to address the specific concerns of a patient. CBT has been shown to be an effective treatment for anxiety in individuals with high functioning ASD (HF-ASD), and it may also be helpful in addressing disruptive behaviors, like aggression, and in improving social and communication skills.[4] CBT is typically administered by a therapist, but parents and teachers may also access books or web-based CBT guides.

Social Skills/ Social Cognitive Training

Social skills are verbal and non-verbal behaviors necessary for positive and effective social interactions, and include eye contact, smiling,

and asking and responding to questions. The value of developed social skills is well-documented and can boost academic performance, mental health, and positive developmental outcomes.[5] Social skills training programs are designed to teach the skills necessary to navigate social environments.[6] There is also preliminary evidence supporting programs that address social cognitive impairments, such as helping children develop the skill of understanding the perspective of others.[7]

Life Skills

The countless tasks of daily living—including dressing, bathing, mealtimes, homework, free time, toileting, and waiting—present many opportunities for challenging behavior each day. As children become adolescents and young adults, new tasks to learn include keeping their own schedules or appointments, asking for help, caring for their own belongings, preparing meals, navigating transportation, and learning a trade. An occupational therapist and other providers can help establish routines and teach these life skills. By breaking tasks into parts, making visual charts outlining steps, presenting rewards for step completion, and implementing this plan consistently, caregivers can teach life skills to children with ASD. Before trying to manage problem behaviors through other means, consideration should be given to whether the child has adequate support to meet the goals being set for them.

Sensory Interventions

Possible contributing causes of challenging behavior in a child with ASD include abnormal sensory responses. Children may avoid sensory input, including certain textures (mushy foods, scratchy labels in clothing), excessive movement (crowded stores, busy city streets), or noises (fire alarms, barking dogs). They may also seek out sensory experiences, such as tickling or deep pressure, or more frequent and intensive movement, such as running, climbing, or spinning in circles. Preventing a child's sensory-seeking or sensory-avoiding behaviors can cause distress and/or tantrums. Interventions for sensory-related problems include weighted vests, swinging, or regular sessions of jumping or bouncing, and applying deep pressure, especially to the shoulders. The evidence for such interventions is not convincing so far, however, due to problems with study methods and research design. Occupational therapists can assess the child's sensory system and direct these interventions to help address sensory factors.

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Treatment of Medical Problems

Prior to starting any therapy for a behavioral or emotional problem in ASD, consideration should be given to a possible medical cause. The extent of a medical evaluation should be decided in collaboration with an experienced medical provider. A sudden or drastic change in behavior may warrant a more thorough evaluation. The medical problems mentioned here do not represent an exhaustive list, but are often causes of behavioral problems in children with ASD.

- ***Sleep problems*** are present in many children with ASD. Inadequate sleep can certainly contribute to behavioral problems and should be considered prior to more rare causes. Poor sleep patterns should be initially addressed with good sleep hygiene, such as removing television and video screens from the bedroom, having a set bedtime and a bedtime routine, and learning to fall asleep without a parent present.
- ***Medication side effects*** themselves can contribute to problem behaviors. Possible medication side effects include changes in sleep, sedation, cloudiness of thinking, constipation, and agitation, among others.
- When a child experiences ***pain***, yet is unable to express clearly the nature or source and intensity of the pain, behavioral changes may result. For

instance, headaches may cause head banging or hitting. Dental problems may go unnoticed if the child will not allow examination of his or her teeth. Bodily injuries can result from a high level of activity and a low pain threshold.

- ***Gastrointestinal discomfort*** may be caused by constipation or diarrhea, acid reflux, food allergies, or inflammatory bowel diseases. Constipation is by far the most common gastrointestinal problem in children with ASD and should always be considered as a possible source of problems.
- ***Seizures*** are more prevalent in children with ASD than in the general population. Symptoms of seizures can include staring spells, involuntary movements, confusion, or headaches. Less common features are sleep changes, behavioral problems, or otherwise unexplained emotional changes or severe emotional shifts.

Family Interventions

Although raising a child with ASD can be fulfilling and rewarding, it can also be an overwhelming experience that can negatively impact the health and well-being of parents and families. Interventions intended to provide support and education for families of children with ASD can provide stress reduction to reduce tension in the home environment, which in turn may positively impact the behavioral functioning of the child.[8]

Comprehensive treatment should attend to the well-being and functioning of the entire family. Parent and sibling support groups can help family members feel less alone. Supportive therapy for parents or families can address the challenge of raising a child with special needs. Family therapy aims to create new interactions or awareness that highlight the family's strengths and successes. At the same time, family therapy changes the interactions among family members that may accidentally encourage unwanted behaviors.

The most researched parent interventions are those that help parents to manage the child's behavior (e.g. parent management training (PMT)) and those that enhance skill-based therapies (e.g. parent ABA training). Although less researched than PMT or ABA, there are also treatments that foster parent-child emotional connections in order to improve communication, skills, and emotional balance. Families should be encouraged to talk with other families and their providers about different treatment options. They should also consider the first meeting with a new therapist as an evaluation in which they learn what can be offered and whether there is a good fit between the family's difficulties and the therapist's skills.

Medication as a Treatment Tool for Emotional or Behavioral Challenges

In addition to the interventions outlined in the previous chapter, medication is another tool that may play a role in the treatment of the child with ASD. It is important to recognize, however, that the medications currently used to treat symptoms and behaviors associated with ASD have not at this point in time been shown to improve the core features of autism. In other words, there is no medication to treat the autism itself.

Medication may be recommended to reduce symptoms of an emotional or behavioral disorder in a child with ASD. These co-occurring disorders are more common than once thought, and include ADHD, anxiety, and depression, among others. The symptoms and findings that lead to these diagnoses are the same as those for children without ASD, but may require a provider with experience in ASD to recognize them.

Armed with this knowledge, it may be easier to understand some of the reasons for use of medication in children with ASD. Use of medication in ASD is common, but the number of children with ASD that are prescribed medications has also raised concerns among some doctors and parents. A study in 2013[9] reported that nearly two out of three children with ASD had been prescribed a psychoactive medication during the three-year study period, and one in seven children had been treated with three or more medications at the same time.

Appropriate use of medication requires an ongoing trusting relationship between parents and providers, and clear information about when to use and not use medication for symptoms in children with ASD. When parents have questions about medication use in their children, they should seek the advice of a professional with training in ASD. Board certified pediatricians and family physicians often see many children with ASD, and many times can appropriately recommend a medication for symptoms. Others with more specialized training include child and adolescent psychiatrists, child neurologists, and developmental-behavioral pediatricians. Parents should feel free to ask doctors about their level of training and experience with patients with ASD, and if they feel comfortable prescribing medication, or if they prefer to seek consultation from more specialized or experienced providers.

Important Factors to Consider for Medication Treatment

- **Informed consent.** A clear and thorough discussion between the parent or guardian and the prescriber should explain the diagnosis, symptoms, non-medication treatment options, and expected duration of treatment. For the child or adolescent taking medication, the provider can obtain his/her permission by offering information about why they are taking medication and the symptoms that the medication is meant to treat. These discussions should take place not just at the beginning of medication treatment, but be ongoing, so that as issues arise and symptoms change, treatment can be modified to meet the child's needs.

- **Risks and expected benefits**. Risks include the known side effects from the product label (if studied in children and adolescents), adult use side effects (may have different side effects than in youth), published research, and the experience of the treating clinician with the medication. Expected benefits would be to reduce the target symptoms. If the medication is effective in reducing target symptoms, other benefits may arise, including improved functioning in school, with peers, and at home.

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There are numerous off-label medications that physicians use to treat problems associated with ASD. The provider should explain to a parent or guardian whether or not a medication is off-label.

- **Which medication will work?** Medication trials are exactly that—trials. Prescribers do not have good enough information to predict which medication will be the best option for each individual child. A medication trial is a time-limited period of testing a medication for the individual child. Most clinicians start at a low dose to minimize side effects and increase slowly to a target dose based on the child's age, weight, and his/her response. Once on the target or maximum tolerated dose, for many medications, the prescriber will then wait four to eight weeks for the full benefit to take effect. If a child does not benefit after that time period, it is time to reassess the situation, taper off the ineffective medication, and consider starting the child on an alternate medication.

- **Level of evidence supporting the use of a particular medication for a particular problem.** When considering which medication to use for a particular set of symptoms, clinicians and families can refer to several sources of information about effectiveness, including the table provided at the end of this guide. Two medications are approved by the Food and Drug Administration (FDA) to treat irritability in autism: aripiprazole and risperidone. Other medications may have been originally studied in youth or adults without autism.

- **Understanding "off-label" uses of medication.** When the FDA approves a medication, it allows a pharmaceutical company to advertise that medication for a specific purpose. When a medication is not FDA-approved for a particular clinical purpose, it is termed "off-label." There are numerous off-label medications that physicians use to treat problems associated with ASD. The provider should explain to a parent or guardian whether or not a medication is off-label. This does not mean the medication should not be prescribed to the child with ASD. The decision to use a certain medication should be based on available research, but when research is limited, it may be based on evidence from studies on children or adults without ASD and clinical judgment.

- **Adequate dose and length of medication trial.** It is important to speak with your child's provider about how long to stay on a medication. Some medications may take effect sooner than others. For example, stimulant medications like methylphenidate may take effect very quickly compared to selective serotonin reuptake inhibitors (SSRIs) like citalopram, fluoxetine, or sertraline, which may take several weeks to take effect. While it can be difficult to predict the duration of treatment needed, addressing this topic can be informative and build an understanding between prescriber and family.

- **Understanding placebo effects.** In general, prescribers, families whose child is being treated with a medication, and often the patients themselves would like medications to be helpful and have a positive response. This is a natural reaction. It is important to understand that even in large, well designed drug studies where families and prescribers do not know if the child is receiving an active drug or a placebo (inactive sugar pill), one in three or four of those receiving placebo will report significant treatment-associated improvement. Clearly, this placebo effect can make it more difficult to understand if a drug is truly providing clinical benefit. Given this fact, it is important to try to be as objective as possible when assessing the impact of a drug on your child. Sometimes it can be helpful to receive input from others who know your child, such as teachers, therapists, or other family members. Families will sometimes ask if they should inform school administrators or teachers about a medication change. This common question is designed to increase the strength of objective or unbiased assessment. Depending on the drug and the need to have others observe the child for adverse effects, this option can be considered. Some providers may ask the parent or caregiver or teacher to complete standardized rating scales to measure changes.

- **When to stop a medication.** First, it is generally a good idea to discuss stopping a medication with the prescriber before

doing so. This is important because some medications may require lowering the dose in gradual steps to avoid potential withdrawal effects. It is also important to have an open dialogue with your prescriber about what criteria will be used to determine success and when to stop a medication. Prior to starting a new drug it is important for families to understand what symptoms and/or behaviors the prescriber is hoping to alleviate with the medication. Families can take an individual approach to defining "success" in response to the medication, and discuss this with the prescriber at the time the medication is started and at follow-up visits.

There can be many reasons for stopping a medication: the medication may have adverse effects on the child, the child's symptoms may not respond to the medication, or the child's family may not be able to pay for the medication. Stopping a medication is a personal decision best made in consultation with the prescriber.

- **Combining medication treatment with other forms of treatment.** We know that combining medication for behavioral issues with interventions such as occupational, speech, physical, and behavioral therapies may provide the best chance for some patients and families to achieve the best outcomes. It would be rare to find that use of a medication completely replaces the need for other types of therapies. In many instances, effective medication use may maximize the benefits patients with ASD receive from other types of therapy.

- **It is important to share information about the use of all natural remedies and/or alternative treatments with your child's clinician.** Certain supplements and alternative treatments can interact with prescription medicines. For instance, St. John's Wort, which some people take as a natural treatment to alleviate depression symptoms, may have a negative interaction with prescribed selective serotonin reuptake inhibitor (SSRI) drugs. Given this fact, it is imperative to provide a complete list of supplements and other alternative treatments your child may be receiving to his or her treating clinician to increase safety and effectiveness.

What if medications fail? ASD is a complex disorder that can be difficult to treat. If a medication fails, it is time to reassess the problem and see if an alternate explanation, therapy, or medication may be helpful. If the child's symptoms do not improve after multiple medications and other treatment trials, other options may be considered, particularly if severe aggressive and/or self-injurious behaviors pose a threat to the child or others.

- There are approximately 10 *specialized child psychiatry hospital units* in the U.S. These specialized psychiatric units for children and adolescents with developmental disabilities typically use a multi-modal approach that combines medication and behavioral treatment with communication and occupational therapy strategies. Although waiting lists for these units may be long, there is preliminary evidence that such an intensive approach can be helpful.[10] There are also many day treatment, specialized school, and residential treatment programs that focus on children with developmental disabilities and emotional and behavioral challenges. While evidence for the effectiveness of these programs is generally not available, programs that use evidence-based practices, such as applied behavioral analysis (ABA), and that take a multi-disciplinary approach are more likely to be beneficial.

- *Electroconvulsive therapy (ECT)* In rare instances, ECT can be considered in the treatment of patients who have very severe aggressive and/or self-injurious behaviors that do not respond to other interventions and are driven by a co-existing psychiatric condition, such as a mood disorder or catatonia (a state of muscle rigidity and stupor or great excitability). While there is no controlled evidence, several case studies have reported ECT to be helpful in a few such individuals, though common side effects of ECT include headache and nausea, and short-term memory loss during the initial course of treatment.

Are there treatments that should not be used? Approximately three-quarters of children with autism have been given alternative treatments. Although there is little evidence supporting the vast majority of alternative therapies (with the exception of melatonin for sleep), many of these popular remedies, such as diet or vitamins, are relatively harmless. It should be noted, however, that any treatment always requires effort and expense, consuming resources that could be used for more evidence-based treatments. There are some treatments, however, that parents should not consider. These treatments not only do not work and are expensive, but may pose serious health risks to the child.

- **Chelation** removes toxic metals from the blood and is used to treat cases of severe lead poisoning and elevated iron associated with particular blood disorders. Scientific tests of chelation as a treatment for ASD have not shown it to be effective and the procedure can have dangerous side effects, including kidney and liver failure, cardiac arrest, and has even resulted in the deaths of at least two children with autism.

- **Hyperbaric oxygen treatment** (HBOT) is the administration of oxygen to a patient in a pressurized chamber, and is used for a handful of conditions, including decompression sickness and different types of soft tissue damage. There is a lack of scientific evidence for using this costly procedure in children with autism, which can cause lung, vision, and sinus damage, as well as rupture of the middle ear.

- **Secretin** is the most studied medication in children with autism, and has repeatedly been shown in multiple scientific studies to have no effect. Side effects can include diarrhea, vomiting, fever and blood clots.

- **Stem cell re-implantation** is a potentially promising therapy for many diseases. However, experts have cautioned that the field is at least a decade away from the development of effective treatments. There is no scientific evidence for the use of stem cell procedures in autism, costs can exceed six figures, and injecting dead or deteriorating stem cells into a person can cause potentially fatal side effects, including stroke and brain inflammation.

Symptoms and Medications

Medications can be used to target a wide range of specific symptoms in children and adolescents with ASD, some of which are listed below. A table summarizing the controlled research evidence for medications in children with autism is located at the end of this guide.

- **Irritability, tantrums, and aggression:** Irritability, tantrums and aggression are common reasons for families to seek treatment for their child with ASD. Children who are irritable are prone to become upset or angry easily, sometimes leading to tantrums, property destruction, or aggression. Irritability can range from mild, where the only noticeable problem is that a child cries more easily than peers when frustrated; to severe, where a child may be so prone to aggression that they need to be hospitalized. Addressing symptoms when a child is young may prevent them from worsening as a child gets older and physically larger. Clinicians should evaluate the potential contributing factors to irritability and aggression in a particular child before prescribing medication, as detailed in the assessment section of this guide.

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Medication can be considered to reduce irritability and aggression when contributing factors do not appear to explain the symptoms or these contributing factors have been addressed without resolving the problem. Two anti-psychotic medications, risperidone (Risperdal) and aripiprazole (Abilify) have been shown to reduce tantrums and aggression in multiple large controlled studies in children with ASD, but each of them can also lead to significant side effects, including increased appetite and weight gain, changes in cholesterol, sedation, and movement disorders. Haloperidol (Haldol), another anti-psychotic, also has evidence of benefit for irritability and aggression, suggesting that this general class of medications may be helpful in children with ASD. Little evidence supports other types of medications; although the side effects associated with antipsychotics can lead parents and physicians to try medications that have single controlled studies to support their use, including clonidine or guanfacine (Tenex or Intuniv).

- **Self-injurious behavior (SIB)** can be a significant and distressing problem for children and their families. Almost 11% of children with ASD in a community survey were stated to have SIB, including hitting, biting, or scratching directed at themselves.[11] SIB can range from mild to very severe. Some children will engage in a mild self-injurious behavior, such as lightly hitting their chin, but may do it so often that over time they eventually produce an injury. Other children may only occasionally engage in self-injury, such as banging their head on an object, but may do it with such force, that even a single episode could cause serious injury. Self-injury that is part of a suicidal episode (such as cutting one's wrists) is less common in children with ASD, though some higher-functioning individuals may engage in suicidal actions.

The best evidence for effective treatment of SIB is with applied behavioral analysis (ABA). In this method, the provider performs an analysis to try to determine the source of the SIB, which is typically escaping from demands, accessing preferred items or activities, attention-seeking, or changing sensory input or pain.[12] Functional communication strategies have also been shown to reduce problem behaviors in ASD, including self-

injury.[13] Medication may play a role in addressing SIB, particularly if the SIB is determined to be related to other mental health problems, such as anxiety or depression.

The atypical anti-psychotics, risperidone and aripiprazole, have been studied for treatment of irritability in children with ASD, which can include self-injury.[14,15]

- **Inattention, hyperactivity, and impulsivity**, the cluster of symptoms referred to as attention deficit-hyperactivity disorder (ADHD), are common in children with ASD and can be a treatable source of challenges. Most recent surveys have identified ADHD symptoms in 30–60% of children with autism.[16] While reduced interest and attention to the social environment is a typical feature of ASD, significant inability to focus on tasks, or high levels of motor activity that are present across different settings, such as school and home, are not typical of ASD alone and could indicate the presence of co-occurring ADHD.

There are a number of reasons a child could be very hyperactive, impulsive, or inattentive across settings besides ADHD. Hyperactivity or impulsivity may occur in younger children who do not have enough structure in their day, or do not have a functional means of communication. Inattention may occur in children who are highly anxious and distracted by their worries or are overly sensitive to stimuli in the environment. In these cases, structuring the environment, providing visual and positive behavior supports, and addressing anxiety may reduce ADHD-like symptoms. As always, a careful consideration of why the child may be hyperactive, impulsive, or inattentive should precede treatment.

For children with inattention, hyperactivity, or impulsivity that do not respond to environmental and/or behavioral approaches, methylphenidate (Ritalin and similar forms) has been shown to be effective in approximately half of children with autism and ADHD.[17] Appetite suppression is common, and headaches, insomnia, or irritability can occur. While it has not been specifically tested in children with autism, a similar type of medication, amphetamine salts (Adderall and similar forms), has been shown to be effective for ADHD in children without ASD, and may be helpful if methylphenidate is ineffective.[18] Atomoxetine (Strattera) has also been researched in controlled studies for treatment of ADHD in children with autism, and showed some improvements, particularly for hyperactivity and impulsivity,[19, 36] and common side effects were nausea and vomiting, decreased appetite, and drowsiness. Guanfacine (Intuniv, Tenex) has also shown benefit in a large study of children with ADHD and ASD.[20] In small single studies of children with autism, naltrexone[21] and clonidine[22] showed possible benefit for children with ADHD.

- **Repetitive behavior and insistence on sameness:** In their play activities and daily routines, children with ASD may display repetitive behaviors and insistence on sameness. These behaviors can manifest as:
  - Repeated motor mannerisms (such as hand flapping)
  - Atypical sensory interests (manifested as touching or rubbing certain textures)
  - Complex body movements
  - Repeating a sound, word, or phrase many times

Interruption of these repetitive patterns or the daily environments of children with autism may cause anxiety or even aggression due to their insistence on sameness and inflexible adherence to specific routines.

It is important to note that repetitive behaviors vary greatly among children with autism, in both types and frequency of behaviors, and while some individuals only engage in repetitive behaviors when feeling anxious, others may do so constantly. Therefore, when considering medication treatment, it is essential to determine whether these behavioral patterns are a problem or not. Repetitive behaviors can be unobtrusive or even adaptive (for example, obsessing about model airplanes and developing a passionate interest in learning how to build them), or can be interruptive and cause difficulties for academic and social functioning.

Because selective serotonin reuptake inhibitor (SSRI) medications have been successful in improving repetitive symptoms of obsessive compulsive disorder (OCD) in children without ASD, clinicians have attempted to treat repetitive behaviors in ASD with SSRIs. However, controlled studies of SSRIs—including fluoxetine, fluvoxamine, and citalopram—have shown little or no benefit in improving repetitive behaviors in ASD.[23–25] The atypical antipsychotics, risperidone and aripiprazole, have shown limited evidence of reducing repetitive behavior in children with ASD.

There are a number of other areas that can be a focus of clinical concern in children with ASD, and practitioners and families may consider medication, though there is little or no controlled evidence for effectiveness. These areas include **anxiety and depression, inappropriate sexualized behavior, insomnia, pica, psychosis, bruxism, and social communication.**

- **Anxiety** or **depression** can occur in children with ASD, and cognitive behavioral therapy has been shown to be helpful for high functioning children with ASD and anxiety. While no medication has been directly studied for anxiety or depression in ASD, most practitioners will consider the use of a SSRI, such as fluoxetine or sertraline, both of which have strong evidence for reducing anxiety and depression in children without ASD. As part of assessing anxiety, the possibility of post-traumatic stress should be considered.

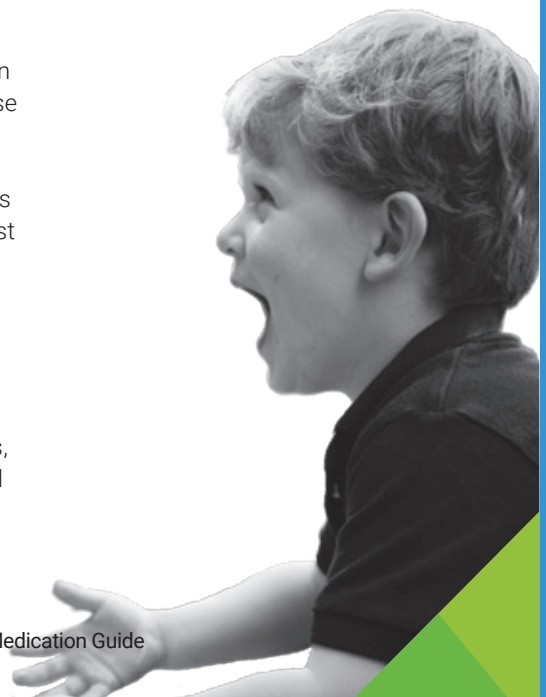
- **Inappropriate sexualized behavior (ISB):** When a person does not follow recognized social rules, socially unacceptable behaviors often occur, and sometimes this includes disinhibited or inappropriate sexualized behavior (ISB). Adolescents with ASD are often discouraged from expressing their sexuality and many are deprived of adequate sexual education. It is also important to note that people with developmental disabilities are particularly vulnerable to abuse, and ISB can be a possible indicator of child sexual abuse.[26] To treat ISB, most clinicians recommend starting with educational or behavioral approaches.[27] There are case reports describing use of mirtazapine (Remeron) to treat ISB in adolescents with ASD, though there is no controlled evidence.[28–30]

Medications such as antidepressants (SSRIs) or antipsychotics may decrease libido, which could be helpful, though this is untested.[31,32] Leuprolide was described in one case report to reduce ISB in a young adult male with ASD,[33] but has potential side effects of depression, seizures, and anaphylaxis, as well as ethical considerations.

- **Insomnia (sleep problems)** appears to be prevalent in children with ASD and should be first addressed by removing electronics and other stimulating activities from the bedroom, developing a consistent bedtime routine, and addressing bed-wetting if needed. For children who continue to have trouble falling or staying asleep, melatonin has been shown in a number of controlled studies to improve sleep in some children with ASD.
- **Social communication** is a core deficit area in ASD and a number of psychosocial treatments have been developed to address this area. Medication is limited to the possible use of methylphenidate, which was shown in one study to potentially improve social communication, perhaps by increasing attention and focus.
- **Pica** is the eating of non-nutritive substances and can have serious medical consequences. Although historically attributed to nutritional deficiencies, many people with pica do not have demonstrable vitamin or mineral deficits, though they are typically evaluated. Nevertheless, iron deficiency is the most common cause of pica, and pica behaviors usually disappear once the deficiency is corrected.[34] Applied behavior analysis (ABA) continues to have the strongest evidence for treatment of pica.
- **Bruxism** is the repetitive clenching and grinding of teeth, often occurs during sleep, and appears to be more frequent in patients with developmental delays, including ASD.[35] To date, behavioral interventions remain the mainstay of treatment.
- **Psychosis** (the loss of reality-based, organized thinking) can occur rarely in children with ASD. Antipsychotic medications that have evidence of benefit in children without ASD are typically used in these cases.

Resource links:

- AACAP practice parameter http://www.jaacap.com/article/S0890-8567%2813%2900819-8/pdf
- Autism speaks https://www.autismspeaks.org/
- CDC website http://www.cdc.gov/ncbddd/autism/index.html
- Others
  - ChildTrends http://www.childtrends.org/?indicators=autism-spectrum-disorders
  - NIMH http://www.nimh.nih.gov/health/publications/a-parents-guide-to-autism-spectrum-disorder/index.shtml
- ATN tool kits https://www.autismspeaks.org/family-services/tool-kits
- Autism Speaks challenging behaviors toolkit https://www.autismspeaks.org/family-services/tool-kits/challenging-behaviors-tool-kit



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CONTROLLED MEDICATION STUDIES IN ASD

	Medication		Participants		Dose (mg/day)	Treatment Response	Side effects Associated with Study Medication		FDA Approval Status	
Target Symptom(s)	Generic Name (Trade Name)	Controlled Trial in ASD	Age Range (years)	Study Duration	Mean Dose (Dose Range)	Target symptom	Side Effects (SEs)	Serious SEs	A=Approved in autism, B=Approved in youth	
	Serotonin Reuptake Inhibitor									
Repetitive behaviors	**Fluoxetine (Prozac)**	Hollander et al., 2005	Youth (5–16)	Short-term (8-week)	10mg ±4 (2.5–20) [once a day]	YES	None (AEs were *less* likely on fluoxetine than placebo)	None		**B** • Major Depressive Disorder (≥8 yo) • OCD (≥7 yo)
Repetitive behaviors	**Citalopram (Celexa)**	King et al., 2009	Youth (5–17)	Short-term (12-week)	16.5mg ±6.5 (2.5–20) [once a day]	NO (Irritability)	97% on study medication experienced AEs: • Insomnia (38%) • Increased energy (38%) • Diarrhea (26%) • Nausea/Vomiting (19%) • Impulsivity (19%) • Hyperactivity (12%) • Stereotypy (11%) • Nightmares (7%)	12% (N=9) on study medication terminated treatment due to AEs: • Seizures (N=2)		
Repetitive behaviors	**Clomipramine (Anafranil)**	Gordon et al., 1993	Youth (6–18)	Short-term (10-week)	152mg ±56 25–250 [in 2 divided doses a day]	YES • Irritability • Hyperactivity	• Insomnia (29%) • Constipation (25%) • Sedation (25%) • Twitching (21%) • Tremor (17%) • Flushing (17%) • Dry mouth (13%) • Decreased appetite (13%)	• Seizure (4%; N=1)		**B** OCD (≥10 yo)
Autism		Remington et al., 2001	Youth + Adults (10–36) Youth [10–18] =27/36	Short-term (7-week)	128mg (100–150) [in 2 or 3 divided doses a day]	NO	NR	38% (N=12) on study medication terminated treatment due to AEs: • Lethargy (13%) • Tremors (6%) • Tachycardia (3%) • Insomnia (3%) • Diaphoresis (3%) • Nausea/ vomiting (3%) • Anorexia (3%)		
	Typical Antipsychotic Agents									
ASD	**Haloperidol (Haldol)**	Anderson et al., 1984	Children (2–6)	Short-term (14-week) [4-week on study medication]	1mg (0.5–3) [in 2 divided doses a day]	YES • Withdrawal • Stereotypies • Relatedness • Hyperactivity • Temper tantrums	• Sedation (78%) • Irritability (28%) • EPS (>25%)	None		**B** • Psychosis • Tourette's Disorder (both ≥3 yo)
		Anderson et al., 1989	Children (2–7)	Short-term (14-week) [4-week on study medication]	0.8 ±0.6mg (0.25–4) [in 2 divided doses a day]	YES • Withdrawal • Stereotypies • Relatedness • Hyperactivity • Temper tantrums	• Sedation • EPS	None		

CONTROLLED MEDICATION STUDIES IN ASD

	Medication		Participants		Dose (mg/day)	Treatment Response	Side effects Associated with Study Medication		FDA Approval Status	
Target Symptom(s)	Generic Name (Trade Name)	Controlled Trial in ASD	Age Range (years)	Study Duration	Mean Dose (Dose Range)	Target symptom	Side Effects (SEs)	Serious SEs	A=Approved in autism, B=Approved in youth	
	Atypical Antipsychotic Agents									
Irritability**	**Risperidone (Risperdal)**	RUPP, 2002	Youth (5–17)	Short-term (8-week)	1.8 ±0.7mg (0.5–3.5) [in 2 divided doses a day]	YES • Hyperactivity • Stereotypies • Repetitive behaviors	• Increased appetite (73%) • Fatigue (59%) • Sedation (49%) • Drooling (27%) • Dizziness (16%) • Weight gain	None	**A** Irritability (5–17 yo)	**B** • Schizophrenia (≥13 yo) • Bipolar Disorder (≥10 yo)
		Shea et al., 2004	Children (5–12)	Short-term (8-week)	1.2mg [once a day]	YES • Anxiety • Hyperactivity • Inappropriate speech • Social withdrawal • Stereotypies	All participants (100%) on study medication experienced AEs: • Somnolence (73%) • EPS (28%) • Increased appetite (23%) • Headache (13%) • Constipation (13%) • Weight gain (10%)	None		
	RUPP Open-label Continuation Trial									
		RUPP, 2005		Long-term (6-month)	2.1 ±0.8mg (up to 4.5)	YES • Repetitive behaviors • Stereotypies • Affectual reaction • Sensory response	• Increased appetite (6%) • Drowsiness (2%) • Weight gain (2%)	• Constipation (N=1)		
		Williams et al., 2006				Adaptive behaviors: • Socialization • Communication • Daily living skills				
Irritability**	**Aripiprazole (Abilify)**	Marcus et al., 2009	Youth (6–17)	Short-term (8-week)	5–15mg	YES • Hyperactivity • Stereotypies At higher dose (15 mg/day): • Inappropriate speech • Repetitive behaviors	88% on study medication experienced AEs: • Sedation (24%) • Fatigue (15%) • Vomiting (13%) • Increased appetite (12%) • Tremors (10%) • Drooling (9%) • EPS (7%) • Weight gain (4%)	10% on study medication terminated treatment due to AEs: • Sedation (N=7) • Drooling (N=4) • Tremor (N=4)	**A** Irritability (6–17 yo)	**B** • Schizophrenia (≥13 yo) • Bipolar Disorder (≥10 yo) • Tourette's Disorder (6–18 yo)
		Owen et al., 2009	Youth (6–17)	Short-term (8-week)	8.5mg (2–15)	YES • Hyperactivity • Inappropriate speech • Stereotypies • Repetitive behaviors	• Weight gain (29%) • Fatigue (21%) • Somnolence (17%) • Vomiting (15%) • EPS (15%) • Increased appetite (15%) • Sedation (11%) • Drooling (9%) • Diarrhea (9%) • Pyrexia (9%)	11% on study medication terminated treatment due to AEs: • Fatigue • Vomiting • Weight gain • SIB • Agitation		

CONTROLLED MEDICATION STUDIES IN ASD

	Medication		Participants		Dose (mg/day)	Treatment Response	Side effects Associated with Study Medication		FDA Approval Status	
Target Symptom(s)	Generic Name (Trade Name)	Controlled Trial in ASD	Age Range (years)	Study Duration	Mean Dose (Dose Range)	Target symptom	Side Effects (SEs)	Serious SEs	A=Approved in autism, B=Approved in youth	
		Marcus et al., 2011a Marcus et al., 2011b		Long-term (52-week)	10mg (1–15)	YES • Hyperactivity • Inappropriate speech • Stereotypies • Repetitive behaviors	87% on study medication experienced AEs: • Decrease in BP (33%) • Weight gain (23%) • Vomiting (19%) • EPS (15%) • Increased appetite (13%) • Pyrexia (12%) • URI (12%) • Insomnia 10%)	11% on study medication terminated treatment due to AEs: • Aggression (2%) • Weight gain (2%) • Suicidal ideation (N=1)		
ASD	**Olanzapine (Zyprexa)**	Hollander et al., 2006	Children (6–14)	Short-term (8-week)	10 ±2mg (7.5–12.5)	YES (in global functioning)	• Sedation (67%) • Weight gain (67%) • Increased appetite (50%) • Constipation (50%)	None		**B** • Schizophrenia • Bipolar Disorder (both ≥13 yo)
	Anti-ADHD Agents									
Hyperactivity/ Impulsivity	**Methylphenidate (Ritalin)**	RUPP, 2005	Children (5–14)	Short-term (4-week)	7.5–50mg [in 3 divided doses a day]	YES	• Decreased appetite (18%) • Insomnia (15%) • Irritability (10%) • Emotional outbursts (10%)	18% on study medication terminated treatment due to AEs: • Irritability (8%)		**B** ADHD (≥6 yo)
				Long-term (8-week)		YES		1 participant discontinued study medication due to AE		
		Ghuman et al., 2009	Pre-schoolers (3–6)	Short-term (1+2-week)	14 ± 4mg (5–20) [in 2 divided doses a day]	YES	50% on study medication experienced AEs: • Increased stereotypy (21%) • Upset stomach (21%) • Sleep difficulties (14%) • Emotional lability (7%)	• Dysphoria (N=1)		
ADHD	**Atomoxetine (Strattera)**	Arnold, et al., 2006	Children (5–15)	Short-term (6-week)	1.4mg/kg/day (divided into 2 doses a day; total of 20–100mg)	YES	• Mood swings/irritability (44%) • Decreased appetite (38%) • Upset stomach (31%) • Nausea/vomiting (31%) • Tiredness/fatigue (31%) • Racing heart (19%) • Insomnia (19%) • Headache (13%) • Rash (13%) • Restlessness (13%) • Constipation (6%) • Diarrhea (6%) • Dry mouth (6%)	• Tiredness (N=1) • Rage outburst with violence and hospitalization (N=1)		**B** ADHD (≥6 yo)
ADHD	**Atomoxetine (Strattera)**	Harfterkamp et al., 2013	Youth (6–17)	Short-term (8-week)	20–100mg (1.2 mg/kg/day) [in 2 divided doses a day]	YES	81% on study medication experienced AEs: • Nausea/vomiting (29%) • Decreased appetite (27%) • Fatigue (23%) • Early morning awakening (10%)	• Fatigue (N=1)		**B** ADHD (≥6 yo)

CONTROLLED MEDICATION STUDIES IN ASD

	Medication		Participants		Dose (mg/day)	Treatment Response	Side effects Associated with Study Medication		FDA Approval Status	
Target Symptom(s)	Generic Name (Trade Name)	Controlled Trial in ASD	Age Range (years)	Study Duration	Mean Dose (Dose Range)	Target symptom	Side Effects (SEs)	Serious SEs	A=Approved in autism, B=Approved in youth	
ADHD	**Guanfacine (Tenex)**	Handen et al., 2008	Children (5–8)	Short-term (4-week)	2.8mg (2–3) [in 3 divided doses a day]	YES	• Drowsiness (50%) • Enuresis (14%)	None		**B** ADHD (6–17 yo)
ADHD	**Guanfacine (Intuniv)**	Scahill et al., 2015	Children (5–14)	Short-term (8-week)	1–4mg/day	YES	• Drowsiness (86.7%) • Fatigue (63.3%) • Decreased appetite (43.3%) • Emotional/tearful (40%) • Dry mouth (40%) • Irritability (36.7%) • Anxiety (30%)	• Verbal and physical aggression requiring police contact and ER visit (N=1)		**B** ADHD (6–17 yo)
ADHD symptoms	**Clonidine (Catapres)**	Jaselskis et al., 1992	Children (5–13)	Short-term (6-week)	0.15–0.20mg (4–10 micro-gm/kg/day) [in 3 divided doses a day]	NO • Irritability	• Drowsiness (38%) • Hypotension (25%) • Decreased activity	None		**B** ADHD (6–17 yo)
	Anticonvulsants / Mood Stabilizers									
Repetitive behaviors	**Divalproex sodium (Depakote)**	Hollander et al., 2005	Youth (5–17) Included participants with ID	Short-term (8-week)	823 ± 326mg (500–1500)	YES	77% on study medication experienced side effects: • Irritability (33%) • Weight gain (22%) • Aggression (11%) • Anxiety (11%)	None		**B** Seizure Disorder (≥10 yo)
Irritability/ Aggression		Hollander et al., 2010	Youth (4–15) Majority	Short-term (12-week)	≥500 (dosed to mean serum level of 90 mg/mL) [in 2 divided doses a day]	YES	• Agitation (13%) • Skin rash (13%) • Polyuria (13%) • Weight gain (6%)	• Irritability & insomnia (N=1)		
Autism	**Lamotrigine (Lamictal)**	Belsito et al., 2001	Children (3–11) NR	Short-term (18-week) [12-week on study drug]	60–200mg (5 mg/kg/day)	NO	• Insomnia • Hyperactivity	• Insomnia (N=2) • Insomnia+ Aggression (N=1) • Stereotypy (N=1)		**B** Seizure Disorder (≥2 yo)
ASD	**Levetiracetam (Keppra)**	Wasserman et al., 2006	Children (5–10) Majority	Short-term (10-week)	863 ±279 mg(350–2500) 20–30 mg/kg/day	NO	• Agitation/Aggression (30%)	None		**B** Seizure Disorder (≥1 yo)
	Cholinergic Agents									
Irritability	**Galantamine (Razadyne)**	Niederhofer et al., 2002	Children (7.4 ± 3.2) Majority	Short-term (Duration NR)	NR	YES Parent-rated (and not Clinician-rated) improvement in: • Hyperactivity • Social withdrawal • Inappropriate speech	None	None		

CONTROLLED MEDICATION STUDIES IN ASD

	Medication		Participants		Dose (mg/day)	Treatment Response	Side effects Associated with Study Medication		FDA Approval Status	
Target Symptom(s)	**Generic Name (Trade Name)**	**Controlled Trial in ASD**	**Age Range (years)**	**Study Duration**	**Mean Dose (Dose Range)**	**Target symptom**	**Side Effects (SEs)**	**Serious SEs**	**A=Approved in autism, B=Approved in youth**	
Core Symptoms	**Donepezil (Aricept)**	Chez et al., 2003	Children (2–10) NR	Short-term (6-week)	1.25–2.5mg	NO (Refer to comments)	• Irritability (22%) • Diarrhea (11%)	• Irritability (N=4) • Diarrhea (N=2)		
Core Symptoms	**Mecamylamine (Inversine)**	Arnold et al., 2012	Children (4–12)	Short-term (14-week)	0.5–5mg	NO	• Constipation 50%	None		
	Glutamate Modulating Agents									
Irritability + Hyperactivity	**Amantadine (Symmetrel)**	King et al., 2001	Youth (5–15)	Short-term (4-week)	168mg (90–200) [5 mg/kg/day] [in 2 divided doses a day]	NO Clinician-rated (and not parent-rated) improvement in: • Hyperactivity • Inappropriate speech	74% on study medication experienced AEs: • Insomnia (21%) • Somnolence (11%)	None		**B** Flu (≥1 yo)
Irritability	**N-acetylcysteine (Mucomyst, Acetadote)**	Hardan et al., 2012	Children (3–10)	Short-term (12-week)	900-2700mg (900 mg once, twice, or thrice a day for 4-week each)	YES • Stereotypies • Social cognition • Social motivation	• Nausea/vomiting (43%) • Constipation (21%) • Diarrhea (21%)	• Irritability (N=1)		
	GABAergic Agents									
Core Symptoms	**Bumetanide (Bumex)**	Lemonnier et al., 2012	Children (3–11)	Short-term (12-week)	1mg	YES	• Hypokalemia (22%)	• Enuresis (N=1) • Hypokalemia (N=1)		
	Miscellaneous Agents									
Core Symptoms	**L-Carnitine (Carnitor)**	Geier et al., 2011	Children (3–10)	Short-term (12-week)	50 mg/kg/day	YES	• Irritability • Stomach discomfort	1 participant discontinued study medication due to AE		
Insomnia	**Melatonin**	Cortesi et al., 2012	Children (4–10)	Short-term (12-week)	3mg (Controlled-release formulation)	YES	None	None		

* Intellectual Disability=IQ<70;

** Behaviors under irritability include aggression, deliberate self-injury, and temper tantrums; NR=Not reported; AEs=Adverse effects; OCD=obsessive compulsive disorder; EPS=Extra-pyramidal symptoms; SIB=Self injurious behaviors; URI=Upper respiratory tract infection; LDL=Low-density lipoprotein; HDL= High- density lipoprotein; TG=Triglycerides; MPH=Methylphenidate;

Medication Tracking Form

Use this form to track your child's medication history. Bring this form to appointments with your provider and update changes in medications, doses, side effects and results.

Date	Medication	Dose	Side Effects	Reason for keeping/stopping

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