# New Developments in Autism

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## **KEYWORDS**

- Autism 
  Diagnosis 
  Psychopharmacology 
  Etiology
- Treatment Epidemiology

The dramatic increase in the prevalence of autism within the past decade has been accompanied by an abundance of new research and treatment strategies. Although there is still no known cause or cure, the substantial progression of knowledge about the disorder in such a short period has left many professionals without adequate training on how to recognize and deal with the many cases suddenly presenting in their practice. This article is designed to provide basic information on the disorder to help equip the practicing physician with tools needed to identify early signs of autism, work with families of affected individuals, and implement optimal treatments.

Autism is characterized by a spectrum of abnormal behaviors that include marked impairment in reciprocal social interaction; communication difficulties; and restricted, repetitive, and stereotyped patterns of interests and activities.<sup>1</sup> Although the prognosis for children with autism is variable, most children with an early diagnosis of autism are not completely independent as adults<sup>2</sup> and the disorder generally has lifelong effects on a child's ability to be social, to care for himself or herself, and to participate in the community.<sup>3</sup> Autism often has a devastating impact on the affected child and his or her family members, who may experience associated anxiety, stress, mental illness, and lost productivity.<sup>4</sup> There is no effective means of prevention, no fully effective treatment, and no cure. Improved early diagnosis and a growing body of research are leading to the development of promising treatments and improved outcomes for affected individuals, however.

The increase in the prevalence of autism from 1 in 2500 in the 1980s to 1 in 150 in the past decade has raised great concern.<sup>5,6</sup> Substantial controversy exists as to whether this is attributable to the more frequent emergence of the disorder from an increase in potential triggers, such as environmental toxins, or is simply the result of evolving

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diagnostic practices and a heightened attention to the disorder that have led to more sensitive diagnostic measures and more frequent diagnoses.<sup>7</sup>

Demographic findings on the disorder have been slim and varied. Autism is four times more likely to emerge in boys compared with girls, although the reasons for this are not fully understood.<sup>8</sup> Although most studies have not identified differences in race among affected individuals,<sup>9</sup> some have revealed variations. Most studies report a higher incidence of autism among immigrants when compared with natives.<sup>10</sup> Additionally, a recent study identified lower rates of autism in Latino populations when compared with non-Latino populations, with comparably similar rates in other ethnicities. The same study also identified lower rates of autism in populations with lower socioeconomic status.<sup>11</sup> It is unclear whether this represents a true difference in prevalence or whether it reflects fewer diagnoses being made in underserved and less educated populations, however. No well-established studies have consistently identified differences in the rates of autism across ethnicities or demographic backgrounds. Therefore, most professionals maintain a belief that the occurrence of autism is not influenced by economic, social, racial, or ethnic background.<sup>12</sup>

## DIAGNOSIS Characteristic Features of Autism

In the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), autism is classified as one of the five pervasive developmental disorders (PDDs) and is characterized by impairments in the three domains of social interaction, communication, and repetitive behaviors.<sup>1</sup> Autism is often referred to as autism spectrum disorder (ASD), because the severity and manifestation of these symptoms vary widely, ranging from modest social ailments to severe developmental and behavioral challenges.<sup>13</sup>

Impaired social interactions may include but are not limited to poor eye contact, difficulty in understanding and relaying appropriate social gestures, trouble in interpreting facial expressions, lack of joint attention, and limited or inappropriate facial expressions. Poorly developed empathy and lack of reciprocity are also characteristic traits of the disorder. Many children with autism express the desire to have friends but do not know how to initiate or maintain relationships, and often do not have a clear understanding of what friendship involves.<sup>14–16</sup>

Nonverbal and verbal communication is often impaired in autism. The development of language is delayed in most affected children. Thirty percent of children with autism experience regression, usually before 36 months of age, wherein they frequently lose any previously acquired language.<sup>17</sup> Although many are able to reacquire verbal skills, some never develop language. Individuals with autism who do exhibit adequate speech usually have difficulty in initiating and sustaining conversations outside of their focused interests. Their speech is often repetitive and rote, echoing phrases from surrounding individuals, movies, video games, or books. Children with autism also typically have difficulty in understanding and integrating abstract concepts, focusing their discord on concrete ideas. Nonverbal communication is also impaired in autism, because these children typically use inadequate or inappropriate gestures, which may include failing to point or to shake their head for "yes" or "no".<sup>18</sup>

In addition to impaired social interaction and communication, children on the spectrum display repetitive behaviors or stereotyped patterns of interests. This may include a wide range of behaviors involving excessive circumscribed preoccupations, inflexible mannerisms, and preoccupation with parts of the whole. For example, children who have autism may have their interest overly focused on parts of toys as opposed to the toy as a whole or may be interested in objects of a more unusual nature, such as pipes, fans, or vents. These children may have a strong desire to read the same book incessantly or to watch the same movie. Some of these behaviors, called self-stimulatory behaviors or "stimming," may arise from the child's unusual sensory integration, which may be satisfied by behaviors, such as spinning, flapping arms, or repetitive blinking.<sup>18</sup>

#### Differentiating Autism from Other Pervasive Developmental Disorders

In the DSM-IV, autistic disorder, Asperger's disorder, and PDD not otherwise specified (PDD-NOS) are the most commonly diagnosed disorders, and perhaps the most difficult to differentiate within the PDD category. When the symptoms of autism are present without significant language or cognitive delay, a diagnosis of Asperger's disorder is often assigned. The diagnostic assignment of autism is also often appropriate, however, because language delay is usually present but not required for a diagnosis of autism, although impairment is.<sup>19,20</sup> Such extensive overlapping criteria between the disorders have created substantial debate as to whether Asperger's disorder is on the continuum of ASD as an equivalent to high-functioning autism (HFA)<sup>20</sup> or whether it represents a separate disorder.<sup>21</sup> Individuals with Asperger's disorder and those with HFA may be obsessed with certain topics; may have learning disabilities in reading, writing, and mathematics; may have an unusually accurate memory for certain information and facts; may exhibit peculiar referencing during conversations; and may be hypersensitive to loud sounds, lights, and odors. Studies conducted by Szatmari and colleagues<sup>22</sup> and Fine and colleagues<sup>23</sup> suggest that children who have HFA have more frequent echolalia, pronoun reversal, and difficulty with conversation and intonation compared with children who have Asperger's disorder. Contradictory studies have found no difference in the frequency of these symptoms between the two disorders, however.<sup>24</sup> Conversely, a diagnosis of PDD-NOS is often assigned to children who exhibit subthreshold symptoms, when repetitive behaviors are not present, or when language develops late. Rett's syndrome and childhood disintegrative disorder, the other two diagnoses within the PDD category, are much less common and are associated with characteristic neurologic regression, making them more easily differentiated from ASDs.

## Diagnostic Tools

An autism diagnosis is best made by an experienced clinician using the DSM-IV. A reliable diagnosis may also require the addition of the Autism Diagnostic Observation Schedule (ADOS), an interactive assessment with the child using one of four modules, which is selected based on the amount of language the child has developed.<sup>25</sup> The Autism Diagnostic Interview, Revised (ADI-R) is the other main diagnostic tool, consisting of an extensive interview with the caregiver that focuses on details of the child's development between the ages of 3 and 4 years.<sup>26</sup> Diagnosis is most accurately confirmed when both tests are used, providing an extensive parent-reported history of the child along with a clinician's objective evaluation through a standardized test.

Although the ADOS and the ADI-R are the most reliable assessments to diagnose autism, they require extensive training, certification, and time to administer and were designed to be used for research studies. Other assessments that may be used include the Social Communication Questionnaire (SCQ), Childhood Autism Rating Scale (CARS), Autism Behavior Checklist (ABC), Checklist for Autism in Toddlers (CHAT), Modified Checklist for Autism in Toddlers (M-CHAT), and Pervasive Developmental Disorder Screening Test (PDDST). Although these assessments do not provide definitive diagnoses, they may serve as valuable screening tools that may help a clinician to determine whether a referral for more extensive evaluation is indicated.

#### Early Identification

Although periods of developmental delay may be observed in typically developing children, they are often among the earliest presenting symptoms in children who have ASDs. Primary care practitioners (PCPs) are often the first professionals to whom parents turn when they are concerned about their child's development. It is therefore important that PCPs be sensitive to early diagnostic signs and that they be familiar with referral resources for diagnostic confirmation and behavioral, speech, and pharmacologic treatment so as to provide affected children with the earliest possible intervention.

Characteristic emerging symptoms of autism may be identified in children only a few months old. Autism may be reliably diagnosed around the age of 2 years. The hallmark symptom for evaluation is delayed or abnormal development of speech. Many other characteristic symptoms, including absent or impaired joint attention, affect sharing, eye contact, interest in other children, simple pretend play, and responding to name, may present before obvious disturbances in language development, however. Social referencing, the process of understanding others through observation and changing one's behaviors accordingly, is also limited in autism. These behaviors reliably distinguish children with early-onset autism from those with other developmental disorders.<sup>27,28</sup> Therefore, the first indication of these behaviors warrants close monitoring, and the maintenance and progression of these symptoms necessitate diagnostic evaluation.<sup>27,28</sup> Indications for an immediate evaluation include no babbling or gesturing by 12 months of age, no single word by 16 months of age, no two-word phrases by 24 months of age, and any loss of language or social skills at any age.<sup>29</sup> Other red-flag concerns include sensory issues, such as being hyperreactive or hyporeactive, in addition to problems with sleep, feeding, and coordination.<sup>28</sup>

Before assigning a diagnosis of autism, other causes of developmental disturbances ought to be ruled out. If pica is present, lead poisoning should be assessed, which can present symptoms similar to those of autism. Genetic disorders that need to be ruled out include fragile X syndrome, neurofibromatosis, tuberous sclerosis, velocardiofacial syndrome, 15 q duplications, and Angelman's syndrome. Audiologic and visual examinations also need to be conducted, because hearing loss may account for the presentation of some emerging autistic behaviors.<sup>30</sup>

#### PATHOPHYSIOLOGY

#### Genetic Susceptibility to an Environmental Trigger

Autism is thought to involve a complex interaction between multiple and variable susceptibility genes,<sup>31</sup> epigenetic effects,<sup>32</sup> and environmental factors.<sup>33</sup> Many believe that autism results when a genetically susceptible child is exposed to an environmental trigger. Research into the pathophysiology of autism suggests multiple potential mechanisms, further supporting the likelihood of different groups of autisms. Although no consistent biomarkers have been identified, results from these studies suggest a role of inflammation, abnormal immunity, and neuronal disconnect in at least some types of autism.

A genetic basis for autism is well accepted among most researchers in the field. There is an increased risk for autism among siblings, with a 4% to 10% risk for subsequent offspring developing the disorder.<sup>1</sup> Identical twins share a 36% to 96% likelihood of having ASD compared with fraternal twins, who have up to a 30% risk for sharing the disorder.<sup>34</sup> In addition, one study reported that men 40 years of age or older are almost six times more likely to father a child who has autism than men younger than 30 years of age.<sup>35</sup> Although a specific gene for autism has not been identified, several potential genetic factors have been linked to autism, suggesting that susceptibility to the disorder may involve a combination of various genes. Specific genes implicated in ASD include genes at the loci 2q, 7q31 to 7q36, 15q11 to 15q13, and 16p13.<sup>34,36,37</sup> One recent study showed a strong association of the mesenchymalepithelial transition factor (MET) receptor gene at the locus 7q31 with ASD, suggesting an immune gut-brain connection.<sup>38</sup> These studies and others provide compelling evidence for a genetic contribution to the development of autism.

The nature of the environmental trigger, proposed to be the next step in the development of autism, is more controversial. Documented environmental factors associated with autism include prenatal or early postnatal exposure to viral infections, valproic acid (Depakote), or thalidomide (Thalomid).<sup>39</sup> There is substantial controversy regarding the potential role of mercury, lead, and other heavy metals, in addition to vaccines and chemicals, in the etiology of autism. Although some studies have found high levels of heavy metals, such as mercury, in children with autism, it is unclear whether or not they are etiologically related to the disorder. A potential mechanism of heavy metal influence is the induction of oxidative stress.<sup>40</sup> Similarly, the role of vaccines in the disorder is heavily debated, with many parents reporting regression in their child immediately after vaccination. No causative link has been found between vaccines and autism,<sup>7</sup> and it is vastly important for children to continue to be immunized to prevent the emergence of other diseases. Some studies have shown a higher incidence of autism with increased exposure to mercury from Thimerosal-containing vaccines, however, warranting the continued removal of Thimerosal from vaccines.<sup>41</sup> A safe suggestion for parents hesitant to vaccinate their child may be to spread out their vaccines over a period of several months instead of administering all vaccines during one visit, especially if immune deficiencies are suspected.

Research to date has identified immune, oxidative stress, neurotransmitter, and epileptiform abnormalities in many affected individuals, although consistent biomarkers for these potential pathogeneses have not been identified.<sup>34</sup> Although there is evidence for depressed immunity in some affected individuals, as supported by their frequent infections and other findings, such as low lymphocyte numbers, substantial research has also shown an overactive immune system in many individuals who have the disorder. High levels of leukocytes, autoantibodies, and inflammatory cytokines support a hyperimmunity and an overall inflammatory process that may be influential in the development of ASD. An inflammatory process might also explain the common gastrointestinal symptoms and frequent allergies seen in many affected children.<sup>42</sup> Although approximately 30% of children who have autism have seizures, as many as 65% have abnormal electroencephalographic activity, suggesting potential dysfunctional neuronal connectivity.<sup>43,44</sup> This is further supported by findings of high levels of glutamate in children who have autism, creating an environment known to cause excitoxicity.<sup>45</sup> All these abnormalities can be antagonized by, and contribute to, oxidative stress. This finding has been noted in many children with autism who have been identified as having high levels of reactive oxidative species, such as nitric oxide, xanthine oxidase, and thiobarbituric acid reactive substances,<sup>46,47</sup> and low levels of antioxidants, such as glutathione (GSH)<sup>48</sup> and superoxide dismutase.<sup>49</sup>

Although brain abnormalities in autism are complex and not consistently identified,<sup>50</sup> studies have discovered an intriguing pattern of brain growth. This research indicates that infants with autism have the same or slightly smaller sized brains than typically developing children,<sup>51</sup> which then rapidly enlarge until the age 4 years, after which growth slows during subsequent stages of development.<sup>52–54</sup> By adolescence, most children with autism have a similar overall brain size as typically developing children but with varying abnormalities, which often include enlarged white matter and decreased Purkinje cells.<sup>55,56</sup> This pattern exemplifies one finding that is consistent with the theories of inflammation, oxidative stress, and underconnectivity. Nevertheless, it is difficult to ascertain whether these abnormalities are primary mechanisms in the pathogenesis of autism or whether they are secondary to the disorder.

## Many Different Autisms?

The spectrum of symptoms and their severity, variety of associated symptoms, inconsistent physiologic findings, and varying response to treatment strongly support the presence of subgroups within the disorder, each of which may have a somewhat different etiology and response to treatment. An excellent example of this is fragile X syndrome, a genetic mutation that accounts for approximately 2% of autism cases through a unique etiology. Children with fragile X syndrome possess clinical features that are distinct from those of other autisms (see the article by Solomon elsewhere in this issue).<sup>57</sup>

Although we do not yet know the causes of the other "autisms," many clinicians cluster cases into groups based on commonly associated symptoms. Thirty percent of children with autism exhibit regression.<sup>58</sup> An additional 30% of children have seizures, and up to 65% display abnormal electroencephalograms.<sup>43,44</sup> Mental retardation is found in 70% of children with autism, according to the DSM-IV Text Revision (TR), whereas few affected children possess savant skills.<sup>59</sup> Frequent infections, allergies, and chronic gastrointestinal symptoms are also often associated with the disorder.<sup>60–62</sup>

Commonly associated behaviors include inattention, aggression, impulsivity, hyperactivity, excessive compulsions, affective instability, and, occasionally, psychosis. Studies report widely varying comorbidities of autism with attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder, Tourette's disorder, bipolar disorder, and schizophrenia, however.<sup>63</sup> Additionally, many children exhibit subthreshold symptoms of these disorders, which makes it difficult to discern whether or not these symptoms are simply variations in the autism spectrum or represent full comorbid diagnoses. Regardless of whether the children are diagnosed with a full comorbidity, treatment needs to be targeted to address their symptoms.

### TREATMENT

The abundant anecdotal reports of promise with early intervention are increasingly supported by studies demonstrating substantial cortical plasticity during early development<sup>64</sup> and positive outcomes from many early educational and behavioral intervention programs.<sup>65</sup> Therefore, routine screening and diagnostic evaluation of children exhibiting early signs of the disorder, along with more studies focused on early identification, are crucial in the path toward a better prognosis. Better outcome is associated with higher IQ, language ability and the ability to perform cognitive shifts.<sup>66</sup> Although core features of autism may not dramatically change, behavioral and medical intervention often substantially improves adaptive skills, showing most promise when implemented in conjunction with each other.

# **Behavioral Interventions**

Applied behavior analysis (ABA), an in-home or school one-on-one behavioral intervention program, is one of the most studied treatments for autism and is often effective in helping the child to develop adaptive functioning skills.<sup>65</sup> Such behavioral programs may include up to 40 hours per week of intervention, with younger children usually assigned more treatment hours. The Denver Model is a promising expansion of ABA and other more child-centered approaches, which integrate developmental, behavioral,

and relationship-based interventions.<sup>67</sup> Other approaches are often used during in-home programs, including Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH), which targets characteristic traits of autism, such as impaired visuospatial skills, need for structure, and strengths in visual over verbal communication,<sup>68</sup> and pivotal response training, which involves using child-centered reinforcers and motivational factors to teach communication, self-help, academic, social, and recreational skills.<sup>69</sup> Parent training is often also incorporated to provide consistency with the implemented program and to help parents learn how to meet the needs of their child most effectively.

Occupational therapy (OT) can also be extremely beneficial by addressing the child's unique sensory integration needs and by providing learning skills to obtain sensory input for more effective self-regulation independently and appropriately. Regular sessions with a speech therapist or the use of assistive technologies, such as pictures and computers, also often helps to address the language delays experienced by most affected children.

## Pharmacologic Treatments

Although pharmacologic treatments do not target the core symptoms of autism, many medications are available to ameliorate associated symptoms, which often prove to be the most disturbing in the lives of affected children and their families. When considering pharmacologic treatment, it is important to identify the potential target symptom and its likelihood of response. Some medications used to address these symptoms are briefly discussed here but are also thoroughly elaborated on elsewhere.<sup>70</sup>

Aggression, self-injurious behavior, and irritability are the only associated symptoms of autism that have a pharmacologic treatment approved by the US Food and Drug Administration with the atypical antipsychotic risperidone. Clinical findings also support the use of risperidone for rigidity and transitions, in addition to cognitive disorganization. Children who do not respond to risperidone, or who experience side effects from the medication, may benefit from another medication in this class, such as aripiprazole (Abilify) or quetiapine (Seroquel), which have also been found to be effective in treating these symptoms. Weight gain and sedation are the most common side effects of the atypical antipsychotics, although akasthia and extrapyramidal symptoms do rarely occur.<sup>71</sup>

Repetitive and compulsive behaviors, in addition to cognitive rigidity and anxiety associated with autism, are often improved by selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine. Starting at low doses with slow upward titration often dramatically reduces common side effects, such as activation and decreased appetite.<sup>72</sup> For example, when prescribing fluoxetine for a child with autism, beginning with a dose of 2 mg/d and titrating up by 2 to 4 mg every week may reduce potential side effects and also often identifies a lower optimal dose than might typically be considered. Irritability stemming from extreme cognitive rigidity and self-injurious behavior rooted in compulsions may also be improved by SSRIs, although they are not as frequently prescribed for this use.

ADHD symptoms of distractible inattention, hyperactivity, and impulsivity may be treated with stimulants, including amphetamines and methylphenidate. Frequent side effects include irritability, increased stereotypies, insomnia, and aggression.<sup>73</sup> If stimulants are ineffective or induce unacceptable or unmanageable adverse effects,  $\alpha$ -agonists, such as guanfacine and clonidine, may also be used. Side effects include sedation and hypotension.<sup>74,75</sup> The norepinephrine reuptake inhibitor Strattera is often an effective alternative that may help with inattention and hyperactivity. The most common side effects of Strattera are fatigue and nausea.<sup>76</sup>

Symptoms of mood dysregulation and affective instability may be improved by mood stabilizers, such as divalproex sodium. A retrospective pilot study of 14 patients with ASDs, including autism, Asperger's disorder, and PDD-NOS, demonstrated improvement in mood instability, impulsivity, and aggression after treatment with divalproex sodium for an average of 10 months.<sup>77</sup> Seventy-one percent of patients who completed a trial of divalproex sodium were rated as having a sustained response to treatment.<sup>77</sup> A more recent double-blind placebo-controlled study comparing divalproex sodium with placebo found significant improvement in repetitive behaviors as measured by the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) scale with 13 patients in an 8-week trial.<sup>78</sup> Therefore, divalproex sodium is a potentially promising treatment for mood dysregulation and repetitive behaviors in patients who have ASD. Because as many as 68% of children with autism have been found to exhibit epileptic abnormalities, which some studies have shown to be normalized by divalproex sodium, the efficacy of divalproex sodium for treating autism is thought by some to be, in part, attributable to its antiepileptic properties.<sup>44</sup> Along with most of these medications, however, larger double-blind controlled studies need to be performed to draw any steadfast conclusions about their efficacy in treating autism and their mechanisms of action in ameliorating these symptoms.

#### **Biomedical Treatments**

Biomedical treatments, also called complementary and alternative medical (CAM) treatments, are commonly used by individuals with autism. Recent surveys reveal the prevalence of CAM use in children with autism to be between 30% and 95%. Although this variability is likely related to the substantial differences in survey design and the populations studied,<sup>79–81</sup> these studies clearly demonstrate the common use of CAM treatments among individuals with autism. Numerous anecdotal reports from parents and clinicians have indicated CAM benefits ranging from slight improvement to claims of cure.

A group of physicians, referred to as Defeat Autism Now (DAN) doctors, strongly believe in CAM treatments (so-called because they are scientifically unproved), and many have reportedly developed systems to treat subgroups of autism effectively by targeting their biologic dysfunction. Examples of CAM treatments include hyperbaric oxygen therapy<sup>82</sup> and omega-3 fatty acids<sup>83</sup> to target an inflammatory process, methyl B<sub>12</sub><sup>48</sup> and GSH to target oxidative stress, and chelation to target heavy metal toxicity.<sup>84</sup> Other popular nutritional CAM approaches include the gluten- and casein-free (GF/CF) diet,<sup>85</sup> based on the theory that some children on the spectrum develop gut inflammation. Some hypothesize that this may involve compromised permeability of the intestinal mucosa, which may allow digestive products to enter the blood, a condition referred to as "leaky gut".<sup>86</sup> Many parents report substantial benefits from the GF/CF diet and describe substantially exacerbated autistic symptoms on the child's reintroduction to milk products or wheat. Other innovative treatments include using pharmaceutic drugs to target potential mechanisms. Examples include peroxisome proliferator-activated receptors gamma (PPARg) agonists, which are approved to treat diabetes and to target inflammation in autism,<sup>87</sup> and the Alzheimer's disease drug memantine to treat the core symptoms of autism by potentially minimizing excitotoxicity.<sup>88</sup>

Despite the vast number of individuals using CAM treatments and the frequently reported benefits to children with autism, few studies have been conducted to evaluate their efficacy scientifically. Additionally, many of the CAM treatments come at a cost to affected families, requiring varying investments of time, energy, and money. CAM treatments with a plausible mechanism of action and a surplus of positive anecdotal reports need to be subjected to double-blind studies to determine their efficacy in treating the symptoms of autism objectively. Furthermore, because there are many autisms, each of which may respond differently to treatments, these studies need to be approached by identifying a subgroup of responders with corresponding improved biomarkers. This is in contrast to putting a broad group of subjects with autism in a treatment study, which is unlikely to show significance, assuming that many autisms exist. Therefore, it is essential that good double-blind studies are conducted and analyzed in a manner that does not wash out an effective treatment for a subgroup of autism.

Because of the large number of families using CAM treatments, it is important that the practitioner be aware of the various treatments. Some families seem to be pressured to commit to strictly CAM treatments or to strictly pharmacologic treatments, depending on whether they see a traditional doctor or a DAN doctor. When working with families interested in CAM treatments, however, it is important to provide them with accurate information about the likelihood of response and potential side effects of CAM and traditional treatments. For example, families ought to be informed that these alternative treatments are available, used by many children with autism, and maintain positive anecdotal reports but are not proved effective by any well-done published studies. So that they can ultimately make the best informed decision for their child, families ought to be educated about the placebo effect that may contribute to the positive anecdotal reports in autism, and they need to be aware of the benefits and potential side effects that they might expect from any treatment.

#### Strategy for Implementing Treatments

The complexity of the disorder frequently requires complex treatment strategies, which may include the integration of many treatments that may need to be altered throughout the child's development. Principles to guide such treatment include the following: (1) identify and monitor target symptoms, (2) maximize each medication dose before adding or discontinuing an agent, (3) change and adjust only one drug at a time, (4) monitor medication side effects carefully, and (5) discontinue the drug of least benefit. Pharmacologic treatment of individuals who have autism should always be part of a comprehensive treatment program that includes behavioral, psychosocial, speech, and language therapy in addition to treatment of medical comorbidities. Maintaining strong rapport and treatment partnerships with patients and families is essential if one is to be able to guide decision making, monitor side effects, and provide guidance and referral to educational and support groups effectively.

#### WORKING WITH FAMILIES

Once you have confirmed a diagnosis of autism, you ought to begin to work with the child's family members to provide them with the support and resources that lead to the optimal outcome for the child and family. They ought to be advised that although there is not a cure for autism, many behavioral and pharmacologic treatments are available with the potential to improve their child's adaptive functioning and quality of life vastly. As a physician, you may also want to inform parents of some of the controversies surrounding the diagnosis of autism, ranging from extremes from groups claiming that autism should not be treated to other extremes suggesting a devastating prognosis for all affected individuals. Instead, parents ought to be encouraged that their child may have unique and special qualities resulting from the disorder, but they also need to be prepared for the challenges they are going to face.

Many services are available to children with autism, although locating and obtaining them often require dedication and persistence. On diagnosis, an individual family service plan for preschool children and an individualized education plan for schoolaged children are required by law.<sup>89</sup> Many services are often covered by the local regional center, including in-home behavioral therapy, OT, and speech therapy. A parent-based advocate society for children who have autism, called Families for Early Intervention and Treatment (FEAT), offers excellent support and resources for families to help them obtain services and overcome the everyday challenges of caring for a child with autism, such as finding a dentist who is able to accommodate their child's behaviors. The Autism Society of America<sup>90</sup> and Autism Speaks<sup>91</sup> also provide a large amount of Web-based information and resources.

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