CME CREDIT ***EDUCATIONAL OBJECTIVE:*** Readers will recognize the signs of Asperger syndrome in their adult patients

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Is an adult with Asperger syndrome sitting in your waiting room?

ABSTRACT

The prevalence of Asperger syndrome, a mild form of autism, appears to be rapidly increasing. This developmental disorder affects children and adults and can present challenges to providing medical care. In this update on Asperger syndrome, we offer guidance on how to interact with adult patients with the disorder. We also address proposed diagnostic changes scheduled to take effect in 2013.

KEY POINTS

Indicators of Asperger syndrome include lack of eye contact, inappropriate comments, odd posture, high anxiety, and intensely focused interests.

Asperger syndrome is evident in childhood, but it also presents undiagnosed in adulthood.

Physicians should be aware of patients' social differences and increased sensitivities in order to improve health care delivery.

Episodic cognitive behavioral therapy addressing interpersonal skills can dramatically improve quality of life and independence.

Proposed diagnostic changes scheduled to take effect in 2013 involve including Asperger syndrome as an autism spectrum disorder.

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In 1944, Hans Asperger described a subset of children who exhibited "a lack of empathy, little ability to form friendships, one-sided conversation, intense absorption in a special interest, and clumsy movements."[1]

In recent years, Asperger syndrome has become increasingly recognized in the medical community and by the general public. It has been popularized in the media in John Elder Robison's bestselling book, *Look Me in the Eye*; with the television character Sheldon Cooper in *The Big Bang Theory*; and in the 2009 film, *Adam*, a romantic comedy with the title character accurately portraying a young man with Asperger syndrome.

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In this article, we discuss the causes and characteristics of Asperger syndrome, with special focus on adults: how it presents, how to treat it, and how to enhance the delivery of care.

PREVALENCE SEEMS TO BE INCREASING

One in 88 children is diagnosed with an autism spectrum disorder, and the rates of Asperger syndrome and other autism spectrum disorders appear to be increasing.[2] Whether this increase is the result of more thorough assessment and identification or of environmental changes is hotly debated.[3] The rise began before the proposed changes to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-V*) to combine autism, Asperger syndrome, and pervasive developmental disorder not otherwise specified to simplify diagnosis.[4] Asperger syndrome affects males three to four times more often than females.[5] For most patients, the effects persist throughout life.

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BEHAVIORAL IMPAIRMENTS CHARACTERIZE THE SYNDROME

Poor social skills are a hallmark

People with Asperger syndrome struggle with social interaction and face challenges in forming and maintaining relationships. They tend to have less eye contact (often the first indicator), smiling, animated speech, and physical communication such as hand gestures. They tend not to solicit another's attention to something they themselves find interesting. They often lack social and emotional reciprocity and have difficulty understanding another person's thoughts or feelings,[6] and they have marked difficulty reading social cues. Some adults may appear rigid, selfish, or narrow-minded.

Sometimes behavior is in the normal range but is out of context for a particular situation.[7] For example, a preprofessional student with Asperger syndrome might walk into a psychiatric evaluation to assess fitness for duty and take a seat cross-legged on the floor and have a snack. Poor grooming inappropriate for the occasion may also be observed, such as showing up for a formal photo with unkempt hair and in a stained shirt that is half tucked in.

A frequent sign is an intense obsession with numbers and dates

Many adults with autism spectrum disorders are oblivious to their social reputation.[8] They are often unaware that their behavior is out of place and only learn that it is not normal when they are told. Others recognize that they have trouble empathizing with or understanding the perspectives of others, but they are at a loss as to how to improve. The syndrome has a tremendous impact on broader aspects of life, such as employment, functional independence, relationships, and social networks.

Other odd behaviors are common

Repetitive behaviors. Many patients with Asperger syndrome have repetitive behaviors, which can manifest as repeating phrases or expressions, attempting to imitate others, and rocking. They tend to follow routines, do not enjoy spontaneity, and are more inflexible and uncomfortable when their planned regimen is altered.

Gait or balance issues may be observed on physical examination.[9] Uncoordinated motion and clumsiness are common,[10] and some patients may have a bouncy, stilted gait or may walk on their toes, although the latter is more common in children than adults. Many patients have illegible handwriting.[11]

Fixations. Many Asperger patients have unusual and intense obsessions with subjects like numbers, dates, or aerodynamics of planes. Children with such fascinations are described as "little professors" or as having "geek syndrome."[12] Certain obsessions often continue into adulthood, although one area of interest may fade and another may take over. Such "expertise" in adults may gain them respect, even though they may seem very odd in other ways.

Lack of boundaries. Patients with Asperger syndrome tend to have poor spatial awareness and to be unaware of physical boundaries, standing too close for others' comfort or unusually far away. Lack of boundaries may extend beyond the physical, as patients may inappropriately help themselves to food or use an item belonging to another without invitation, being unaware that the behavior may be intrusive or inappropriate.

BEHAVIORAL ASSESSMENTS HELP MAKE DIAGNOSIS

Asperger syndrome is most often diagnosed in early childhood, although it may remain undiagnosed into adulthood. Coexisting depression, attention deficit hyperactivity disorder, or anxiety disorders are also often present.

Establishing the diagnosis is aided by information from family members and others who interact with the patient, from the observations of trained professionals, and from self-reported data. However, self-reported assessments are not always reliable, because the syndrome can affect insight.

The most common assessment tool for autism spectrum disorders is the Autism Diagnostic Interview-Revised (ADI-R),[13] a battery of tests given in a structured interview to identify and quantify symptoms, determine where a patient falls on the autism spectrum,[14] and point toward interventions. The ADI-R also organizes critical developmental history to evaluate if something else is present, such as prodromal schizophrenia. Although the ADI-R can be very useful in the diagnostic process, it is based on parental reporting,

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which is neither always available nor fully reliable.

A specific diagnostic tool for adults is the Adult Asperger Assessment.[15] Patients are asked to complete two screening questionnaires that gauge cognitive function and gather information about thinking, processing, and behavior.

TABLE 1 lists the criteria for Asperger syndrome from the *DSM Fourth Edition, Text Revision* (*DSM-IV-TR*).[16] Asperger syndrome differs from general autism in that it is not associated with language delay. In addition, patients with Asperger syndrome usually have average or above-average IQ scores.[17] Still, determining whether a patient has Asperger syndrome or high-functioning autism is sometimes challenging.[6]

In *DSM-V*, Asperger syndrome will be subsumed under autism spectrum disorder

In 2013, the *DSM-V* will replace the *DSM-IV-TR* and will combine autism, Asperger syndrome, and pervasive developmental disorder not otherwise classified into a single diagnosis: autism spectrum disorder. The new system uses two instead of the previous three clusters of core symptoms, centered on "social reciprocity and communication" in one arm and "restricted interests and repetitive behavior" in the other.[18] There will be less emphasis on play and imagination than in the past. Some authors suggest adding sensory criteria, particularly reduced pain and increased hearing sensitivity.[19]

The proposed system is sensitive and specific for autism spectrum disorders, allows early diagnosis, and indicates degree of severity.[20] It is hoped that the new system, which accounts for the range and severity of symptoms, should help physicians refer patients to the correct level of treatment.

On the other hand, it may be difficult to think of the three disorders as a single diagnosis. Asperger syndrome manifests in distinct ways, and clear behavioral criteria for diagnosis can be invaluable in helping people with the syndrome. Also, the public may continue to refer to it as Asperger syndrome, and parents and patients may feel uncomfortable having it considered to be the same diagnosis as autism.

TABLE 1

DSM IV-TR criteria for Asperger syndrome

Qualitative impairment in social interaction, as manifested by at least two of the following:

- Marked impairment in the use of multiple nonverbal behaviors, such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction
- Failure to develop peer relationships appropriate to developmental level
- Lack of spontaneous seeking to share enjoyment, interest, or achievements with other people, (eg, by a lack of showing, bringing, or pointing out objects of interest to other people)
- Lack of social or emotional reciprocity.

Restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:

- Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus
- Apparently inflexible adherence to specific, nonfunctional routines or rituals
- Stereotyped and repetitive motor mannerisms (eg, hand- or finger-flapping or twisting, or complex whole-body movements)
- Persistent preoccupation with parts of objects.

The disturbance causes clinically significant impairments in social, occupational, or other important areas of functioning.

There is no clinically significant general delay in language (eg, single words used by age 2 years, communicative phrases used by age 3 years).

There is no clinically significant delay in cognitive development or in the development of age-appropriate self-help skills, adaptive behavior (other than in social interaction), or curiosity about the environment in childhood.

Criteria are not met for another specific pervasive developmental disorder or schizophrenia.

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS TEXT REVISION DSM IV –TR 4TH EDITION 2000; WASHINGTON, DC: AMERICAN PSYCHIATRIC ASSOCIATION; 2000; 80–84. COPYRIGHT 2000. REPRODUCED WITH PERMISSION OF THE AMERICAN PSYCHIATRIC ASSOCIATION.

BEHAVIORAL THERAPY CAN HELP ACHIEVE INDEPENDENCE

Although there is no cure for Asperger syndrome, various interventions can dramatically improve quality of life and independence. The

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health care team may include a primary care physician, psychologist, psychiatrist, neurologist, and speech therapist.

Behavioral therapies can help patients with Asperger syndrome learn skills to reduce their symptoms. Occupational and physical therapy can improve dexterity, fluidity, and coordination. Desensitization training may help patients adapt to uncomfortable sights, sounds, or smells that may arise. This can be critical in a job situation. For example, while an average person exposed to a foul odor in public is likely to react tactfully, a person with Asperger syndrome may scream loudly, make inappropriate comments, or run from the room. Social training, especially targeted to the workplace, can provide strategies for promoting typical behaviors and be key to maximizing functional independence.

Speech therapists can teach patients how to sound more relaxed and help them master the natural give-and-take of conversational exchange. Psychotherapy can provide a safe place to work on anxiety, express emotions, and manage restricted interests or repeated behaviors. Group therapy or social training can be a venue for learning improved interactions.

The syndrome has a tremendous impact on employment, functional independence, and relationships

Living independently can be very challenging, and patients with Asperger syndrome may need functional independence training to help with a variety of skills, from handling finances to organizing the home.

Improving quality of life includes determining the best learning environments from childhood into college years and beyond.[21–23] Socialization can be enhanced with additional social support at home or on campus, through family interactions and collaborative learning, and by teaching empathy.[24] Vocational training can be extremely useful.

DRUG THERAPY MAY HAVE A ROLE

Medications are not usually prescribed unless depression or anxiety is also present, but they may also help manage irritability, anger, stereotypical mannerisms, and disturbing movements. Fluoxetine (Prozac) helps reduce repetitive behaviors in adults with Asperger syndrome. Propranolol (Inderal), a well-known antihypertensive, is also used for performance anxiety and improves word fluency, understanding of verbal communication, and verbal problem-solving in patients with an autism spectrum disorder.[25]

Giving oxytocin (Pitocin) intranasally in a spray formulation is currently being tested to enhance social skills. Patients with an autism spectrum disorder were more able to perceive emotions of others and to respond more appropriately.[26] Oxytocin has long been associated with bonding and is believed to enhance mothering skills. It is naturally present in both sexes, but levels are higher in women, which may in part explain the lower rate of autism spectrum disorders in females.[27]

HEALTH CARE REQUIRES SPECIAL CONSIDERATIONS

Medical care for patients with Asperger syndrome is enhanced by understanding the patient's experience. Adults, in particular, may have learned to suppress symptoms of Asperger syndrome to better function in society but still experience stress in situations in which others would not. Patients with Asperger syndrome may struggle with social interactions during medical examinations or procedures, and clinicians may find interaction with the patient challenging.

It is important for health care providers to be calm and patient and to understand that anxiety may prevent people with Asperger syndrome from making eye contact. The clinician should confirm that a patient is engaged but should avoid seeming pushy or invasive.

When anxious, patients may employ strange gestures that they find soothing, such as flapping the hands, rocking, or cracking the knuckles. It is usually easier to allow them to continue unless the activity hinders the examination or treatment.

Patients are likely to respond better to direct requests than to subtle questions: eg, "Open your mouth, please" instead of "Could you open your mouth?" Using clear, specific language and avoiding metaphors, irony, and nonverbal communication are best. It is important to explicitly ask for everything needed, as patients may not volunteer information and may have trouble articulating what they are thinking or feeling. While educating pa-

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tients about their health needs, physicians may need to reiterate guidance several times or approach the same topic from different angles in order for the patient to accept a concern.

All actions, especially touching the patient, should be explained clearly beforehand. If possible, the doctor should demonstrate using visuals or on his or her own body if appropriate. For invasive procedures, anesthetizing the local area is recommended.

People with Asperger syndrome often rely heavily on a regular routine to maintain a sense of organization. By interrupting this routine, a doctor's visit can induce anxiety. Waiting also increases anxiety, so scheduling patients with Asperger syndrome either first or last in the day may help.

Hypersensitivity poses challenges

Many people with Asperger syndrome have abnormal sensitivity to stimuli, with differences in pain sensation and hearing perhaps most prominent. Loud noises, such as beeping equipment, whirring fans, or buzzing lights may be distressful and should be reduced if possible. Patients may also be strongly affected by bright lights or scents such as perfumes.

Patients may also have an altered sense of taste, with consequences that go beyond simple "picky eating." Patients should be asked about unusual eating patterns, diets, or food aversions. People with autism spectrum disorders often do not consume adequate vitamin C because of an aversion to fruits and vegetables. Vitamin deficiency may have originated in infancy but may not be identified or treated until adulthood.[28]

The sense of touch may be intensified, causing patients to be extremely ticklish; they may actually prefer to be touched more firmly. When it is necessary to make physical contact with patients, it will make the process easier if the physician determines their comfort level and finds ways to help them endure the experience with the least amount of discomfort.

Some patients with impaired sensory expression may have a high tolerance for extreme temperatures and pain, leading to delay in seeking aid.[29] Patients may downgrade pain levels, masking the severity of an illness or injury.

Transition from pediatric to adult care

Pediatrics is often a warm environment in which children develop a trusting relationship with their care providers. The transition to adult care can be daunting for patients with Asperger syndrome and their families, and many postpone the change for as long as possible.

Although time-consuming, a collaborative effort between the pediatric and adult care teams can dramatically smooth the transition. It can help to have a familiar person from the pediatric team, such as a nurse, be present at the initial interaction with the new adult care team. Both teams should be familiar with the other's clinical practices and be aware of the patient's stressors and ways to ameliorate them.[30]

THE SEARCH FOR A CAUSE CONTINUES

Numerous studies are attempting to understand the anatomic and physiologic causes of autism spectrum disorders, and to find effective treatments and improve the quality of life.

Prenatal factors implicated

Several recent studies have focused on environmental factors during pregnancy as risk factors for autism spectrum disorder. Selective serotonin reuptake inhibitors were found to increase the risk,[31] but the severity of the mother's depressive illness must be considered before counseling against using these drugs. Older maternal or paternal age was also found to increase the risk of an autism spectrum disorder.[32] Recent research indicates that older fathers are in particular more likely to have children with disorders such as autism because of an increase in random mutations associated with advanced age.[33]

In the *DSM-V*, Asperger syndrome will be subsumed under 'autism spectrum disorder'

Maternal illness during pregnancy is also associated. Preliminary studies found an increased risk of autism if the mother had had a prenatal viral infection.[34] A more recent study found that untreated fever during pregnancy rather than a specific viral infection is more strongly linked.[35]

Maternal antibodies have been implicated as well. One review found that psoriasis is the only maternal autoimmune condition signifi-

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cantly associated with the development of an autism spectrum disorder.[36] Elevated levels of antibodies against the fetal brain have been found in mothers with autistic children.[37] One study found that autistic children and their siblings have elevated antibrain antibodies in distinct brain regions, including the caudate nucleus, putamen, prefrontal cortex, cerebellum, and cingulate gyrus (why the siblings are spared from having the disorder is unclear).[38] Some have questioned whether a child's own immune system might even be involved.[39]

Functional magnetic resonance imaging reveals multiple differences

Functional magnetic resonance imaging (fMRI) has been used to investigate impaired social interaction, specific deficits of facial perception and recognition, sensory processing, working memory, and "theory of mind." Hypoactivation, hyperactivation, and decreased functional connectivity have been observed depending on the mental processes evaluated.[40]

When undergoing facial perception tasks, subjects with autism spectrum disorders exhibit hypoactivation in the lateral aspect of the middle region of the fusiform gyrus, responsible for face identification. But they have significant activation of the limbic system, specifically the amygdala, during facial recognition. Hypoactivity in the fusiform gyrus is observed when trying to identify faces or read facial expressions.[41,42] This cluster of findings helps explain misinterpretations, misidentification, and heightened affect.

A specific diagnostic tool for adults is the Adult Asperger Assessment

A hallmark characteristic of autism is the difficulty patients have in determining intentions and interpreting others' behavior, thoughts, or emotions. Studies of people with autism spectrum disorders show that areas often responsible for "sensitivity to others" are hypoactive.[43] There is also diminished activation in the medial cingulate cortex, normally activated when these people are asked to think about themselves and who they are.[44]

The resting state in the brains of people with autism spectrum disorders is abnormally activated.[45] They are often particularly good at attention to detail but challenged in integrating information needed for general executive functioning. Impaired sensory processing makes it difficult for them to simultaneously interpret multiple sources of sensory input.[46]

Perhaps some of the most exciting fMRI news comes from infant studies. Radical and axial diffusivity and fractional anisotropy techniques demonstrate differences in the brains of infants 6 to 24 months old, before symptoms of autism spectrum disorders are observed. It is hoped that early intervention could come into play before the syndrome develops fully.[47]

The synthesis of input of social and emotional cues is sometimes referred to in the literature as "theory of mind." It is impaired in Asperger syndrome,[48] as manifested by a lack of empathy and by challenges in perceiving others' thoughts and feelings. The basis of impairment may be related to abnormalities in the amygdala.[49] Normal awareness involves the integration of multiple neural networks in the anterior paracingulate cortex, the superior temporal sulci, and the temporal poles bilaterally, but different regions appear to be used in patients with Asperger syndrome.[50] A small series of five case studies using positron emission tomography indicated that the left prefrontal cortex was the primary location for theory of mind in Asperger syndrome.[51]

Epilepsy, gastrointestinal problems, and sleep disturbances are associated

About 25% of people with autism spectrum disorders have epilepsy vs 2% to 3% in the general population. Asperger syndrome is associated with a much lower but still elevated risk of 4% to 6%.[47,52]

Gastrointestinal complaints, most often constipation or chronic diarrhea, are much more common in children with autism spectrum disorders than in the general population. Preliminary data showed that children with an autism spectrum disorder have a 42% rate of gastrointestinal problems vs 12% in unaffected siblings. There is also a correlation between the severity of gastrointestinal problems and severity of autistic symptoms.[53]

Research is ongoing to determine the prevalence of insomnia or interrupted sleep in those with autism spectrum disorders.[54–56] Changes in sleep architecture can explain nighttime activity.

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NONTRADITIONAL CONSIDERATIONS

Dietary treatment: Mixed findings

A popular hypothesis is that adherence to a gluten-free or casein-free diet can reduce symptoms of autism spectrum disorders. Preliminary reports identified several cases of children showing improvement.[57] However, this has not been replicated, and more studies refute benefits of these diets.[58]

Essential nutritional needs should be met with any diet, whether it is designed to reduce symptoms or not. Patients with autism spectrum disorders may have strong food aversions, and dietary supplements of vitamins and minerals may be required.

Vaccines do not cause autism

Despite popular concern, recent research indicates that vaccines do not cause autism. Thimerosal, a mercury-based preservative used in childhood vaccines, was at one time implicated as a risk factor for autism spectrum disorders. The US Centers for Disease Control and Prevention (CDC) issued a precaution against using thimerosal-containing vaccines while testing was done to determine the effects on neuropsychological development.[59] The CDC study as well as newer studies did not demonstrate that exposure to mercury causes these neuropsychological concerns, but researchers have continued to study the subject.[60–62] The original study implicating thimerosal was disproven as scientifically unsound and fraught with conflict of interest and legal concerns. It has since been retracted, and its findings have been completely discredited.[63]

Other areas of research

Current research is exploring the higher prevalence of autism spectrum disorders in particular families.[64–66] Autism and autism spectrum disorders may be caused by hundreds of simultaneous gene alterations or may develop as a result of reduced gene expression in two areas of the cerebral cortex where higher-order processing occurs, in the frontal and temporal lobes.[67]

Although genetic theories of autism predominate, a 2011 project suggests that environment is also important. A study of twins found that genetics accounted for 40% or less of cases of autism spectrum disorder, with at least 55% of cases being attributable to environmental factors.[68]

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