Care of the patient with an autism spectrum disorder by the general physician

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ABSTRACT

Autism spectrum disorders (ASD), comprising classic autism, Asperger syndrome, Rett syndrome, childhood disintegrative disorder and pervasive development disorder-not otherwise specified, represent complex neurodevelopmental conditions characterised by impaired social interactions, difficulties with communication and repetitive, stereotyped behaviours. It is estimated that up to 1% of the general population may be affected by an ASD. Whether due to improved diagnostic techniques or a true rise in incidence, the prevalence of patients with ASD is rising, and these individuals are increasingly encountered in a variety of healthcare settings. Care givers of patients with an ASD report frequently that lack of awareness of the complications of these disorders and the method of appropriately assessing these individuals impair the effective delivery of healthcare to this patient population. It is now clear that patients with an ASD, in addition to the defining characteristics of these disorders, can present to the outpatient, emergency department and inpatient settings with a variety of psychiatric, neurological, gastrointestinal, nutritional/metabolic, dental, ophthalmological, cardiovascular, gynaecological, traumatic and musculoskeletal conditions that can require acute intervention. In addition, the common treatments given to patients with an ASD may result in side effects and complications that may require acute intervention. For physicians who encounter patients with an ASD, the combination of impaired social interactions, difficulties with communication and stereotyped behaviours creates an additional barrier to diagnosis and treatment of these individuals. Careful preparation of the examination environment, direct engagement of care givers and the patient and the use of communication techniques and pharmacological adjuncts can aid physicians in treating the patient with an ASD in the outpatient, emergency department and inpatient settings.

INTRODUCTION

Autism spectrum disorders (ASD), comprising classic autism, Asperger syndrome, Rett syndrome, childhood disintegrative disorder and pervasive development disorder-not otherwise specified (PDD-NOS), represent complex neurodevelopmental conditions characterised by impaired social interactions, communication difficulties and repetitive, stereotyped behaviours.[1] Typically, patients with an ASD show signs and symptoms in childhood that include poor or regressed language skills, impaired ability to respond to common social cues and behavioural patterns that focus on one object or situation to the large-scale exclusion of others.[1]

Whether due to improved diagnostic techniques or a true rise in incidence, the prevalence of patients with ASD is rising, and these individuals are increasingly encountered in a variety of healthcare settings. The Centers for Disease Control and Prevention estimate that the prevalence of ASD in the USA is one in 110 births with a male to female ratio of 4:1.[2] Up to 1.5 million Americans carry a diagnosis of ASD with an estimated annual healthcare services cost of $90 billion.[3] In the next decade, with the ageing of the ASD patient population, that cost is expected to rise to $200 billion.[4] Globally, the estimated prevalence of ASD is 0.6%–1% of the population.[5]

Increased understanding of ASD has also led to studies on the nature of healthcare utilisation by this patient population. Among children with ASD, utilisation of preventive, outpatient and inpatient care is higher than among patients without ASD. Parents of children with autism reported a higher mean number of preventive care (3.89 (95% CI 3.57 to 4.21) vs 2.51 (95% CI 2.49 to 2.53)), emergency department (0.18 (95% CI 0.12 to 0.23) vs 0.10 (95% CI 0.09 to 0.10)) and non-emergency (2.80 (95% CI 2.44 to 3.16) vs 1.56 (95% CI 1.54 to 1.58)) visits per year in comparison with children without autism.[6] Families of patients with an ASD report significant financial burdens that accompany the treatment of this disorder, unmet medical and social support needs and difficulties with referral within the healthcare system. These factors all likely contribute to presentation to physicians who are not specialists in the care of this patient population.[7] Little data exist on the nature of healthcare resource utilisation by adults with ASD, likely due to the relatively recent focus of the medical community on the treatment of these patients. However, it is foreseeable that with the ageing of the ASD population, presentation of this patient population in a variety of healthcare settings will increase.

Despite the above factors that will likely cause patients with an ASD to present more commonly to the non-specialist physician, there is a paucity of literature for general physicians on how to approach the clinical assessment of the patient with an ASD or the common presentations of acute illness that may result in the need for care in either the outpatient, emergency department or inpatient setting.[8–11] This article reviews the existing literature on how general physicians may approach the management of the adult and paediatric patients with an ASD and the common disease processes that can result in their need for acute care.

CHARACTERISTICS OF ASDS

The common thread of ASD is impairment in socialisation and communication and repetitive or stereotyped behaviours. However, the five conditions that comprise ASD differ significantly in the degree to which each of these underlying categories present clinically. Classic autism manifests at a younger age, shows evidence of a genetic aetiology and commonly causes regression in communication and socialisation. It is associated with intellectual disability and seizures and has a poor prognosis of recovery of function despite intensive therapy. In contrast, Asperger syndrome manifests at a later age and is not commonly associated with intellectual disability or seizures. Outcomes with therapy are much better when compared with classic autism. Childhood disintegrative disorder is an extremely rare condition, almost exclusively seen in male subjects, where the patient shows a dramatic loss of communication and socialisation often with associated seizures and intellectual disability. Rett syndrome affects female subjects almost exclusively with the impairments in communication and socialisation and repetitive behaviours also associated with loss of muscle tone and inability to perform normal motor activities. PDD-NOS is a catch-all diagnosis for individuals manifesting a preponderance of ASD symptoms without a clear ability to classify into one of the above four conditions due to one or more missing characteristics required for that diagnosis. Table 1 describes in detail the clinical and epidemiological aspects of the five diagnoses that comprise ASD.[12–19]

OUTPATIENT PHARMACOLOGICAL AND ALTERNATIVE TREATMENT MANAGEMENT OF ASD

Medications prescribed to patients with ASD focus on the management of aggressive, repetitive and self-injurious behaviours, irritability and impairments in socialisation. Risperidone is the most studied medication in this population and shows the best evidence of providing benefit to these patients. In a randomised controlled trial comparing risperidone to placebo in children of age 5–17, the risperidone cohort showed a 69% improvement in behavioural measurements, including irritability, social withdrawal and communication impairments, compared with 12% in the placebo cohort.[20–22] Methylphenidate shows modest evidence for improvement in irritability in patients with ASD.[22–24] Valproate also shows modest evidence for benefiting patients with an ASD in reducing repetitive behaviours.[23 24] Despite common use, there is little evidence to support that selective serotonin reuptake inhibitors aid in the management of core symptoms or self-injurious behaviour in the paediatric ASD population. Melatonin may aid with insomnia as aetiology of the exacerbation of core symptoms of ASD.[23 25 26] Selective serotonin reuptake inhibitors may be more beneficial in adults with ASD in the management of obsessive-compulsive symptoms, aggression and anxiety.[25] Other treatments seen commonly in this patient population include secretin, gluten-free and casein-free diets, probiotics, chelation and vitamin therapy. None have shown clear benefit in the clinical trials in which they have been assessed.[22 23 27] Table 2 describes the pharmacological and alternative therapies commonly utilised in the ASD patient population and the recognised adverse effects that may cause acute presentation.[20–28]

MEDICAL CONDITIONS ASSOCIATED WITH ASD

In discussing the medical conditions associated with ASD, it is apparent that only recently have investigators begun to explore the related ailments that can manifest in this patient population. Much of the literature on ASD associated acute medical conditions consists of case series and retrospective analyses. As such, the evidence for which acute conditions may be associated with ASD and cause patients with an ASD to present clinically to the general physician is limited. However, the studies that do exist are of relevance to general physicians who now are and in the future will be faced with managing these patients even in the context of incomplete evidence.

Psychiatric conditions associated with ASD

Up to 85% of patients with an ASD manifest a psychiatric disorder requiring acute management. The most common psychiatric condition associated with ASD is anxiety, seen in 43%–84% of this patient population, followed by depression, obsessive-compulsive disorder and oppositional defiant disorder/other behavioural problems.[12] Psychotic disorders, ranging from

Table 1 Epidemiological and clinical characteristics of autism spectrum disorders

	Classic autism	Asperger syndrome	Childhood disintegrative disorder	Rett syndrome	Pervasive developmental disorder-NOS
Age of onset	0–3 years old	>3 years old	3–4 years old—sudden onset	>3 years old though regression may manifest sooner (6–18 months)	Variable
Sex ratio	2:1 male to female	4:1 male to female	Male predominance (rare diagnosis)	Female predominance (rare diagnosis)	Variable
Communication impairment	Delayed to non-verbal	Not delayed, but impaired in quality	Delayed to non-verbal	Loss of speech	Variable
Socialisation impairment	Poor interactions or reciprocity	Poor interactions or reciprocity	Abrupt loss of social skills	Loss of speech and motor function extending to gaze and ability to grasp social cues	Variable
Behavioural impairment	Classic preoccupation with parts of items and stereotyped mannerisms	Variable—may only show limited interests	Abrupt behavioural change and loss of normal behaviours for age	Compulsive movements with loss of muscle tone	Variable
Association with intellectual disability	>60%	Mild to no association	Severe disability	Common association—moderate to severe	Mild to severe disability
Clinical functional outcome with current interventions	Poor to fair	Fair to good	Poor—by age 10 similar to severe autism	Unknown given rarity of disease—middle age life expectancy	Fair to good

NOS, not otherwise specified.

Table 2 Outpatient pharmacological and alternative management of autism spectrum disorders

Medication	Symptom targeted	Side effects
Risperidone	Irritability, social and communications impairment	Weight gain, xerostomia, elevated prolactin level, somnolence, extrapyramidal symptoms (tremor, gait abnormality)
Methylphenidate	Hyperactivity	Decreased appetite, insomnia, irritability, abdominal discomfort, xerostomia
Valproate	Mood stabilisation	Paradoxical aggression, hyperammonaemia, liver enzyme elevation, sedation, xerostomia
Selective serotonin reuptake inhibitors	Obsessive-compulsive symptoms, stereotyped behaviours, self-injurious behaviour	Agitation, suicidal ideation, buccoglossal syndrome (tardive dyskinesia), xerostomia
Secretin	Social, behavioural and communications impairment—poor evidence of efficacy	Minor irritability, hyperactivity, vomiting
Gluten-free and casein-free diets	Social, behavioural and communications impairment—limited evidence of efficacy	Expensive, potential for nutritional deficiencies, constipation
Probiotics	Social, behavioural and communications impairment—no evidence of efficacy	None reported—anecdotal interaction with antibiotics
Chelation therapy	Social, behavioural and communications impairment—no evidence of efficacy	Hypocalcaemia (edentate disodium), Stevens–Johnson syndrome (2,3-dimercapto-1-propanesulfonic acid sodium)
Vitamin therapy	Social, behavioural and communications impairment—no evidence of efficacy	Vitamin toxicity in elevated doses
Melatonin	Insomnia	None reported
Clonidine	Tic disorders, irritability	Hypotension, sedation

brief psychotic episodes to schizophrenia, are more prevalent in the ASD population. In a 2006 English study of autistic children and young adults with intellectual impairment, 30% showed evidence of schizophrenia on DASH-II testing, utilised to assess for emotional and behavioural disturbances in patients with severe handicaps, in comparison with 8% of controls.[29] A 2008 Danish study reported a 6.6% rate of schizophrenia or other delusional or psychotic disorders in adults diagnosed with autism in infancy compared with 0.9% of controls ($p<0.08$).[30] In a Danish study of patients with atypical autism, the percentage of adults with schizophrenia spectrum disorders was 34.8% in comparison with 3.1% of controls.[31]

Adults with ASD may also more commonly manifest substance abuse disorders. A 2009 European study of adults with normal intelligence and ASD reported a 16% prevalence of substance abuse, most commonly involving alcohol and the subset of PDD-NOS patients. In contrast, Asperger syndrome patients were less likely to show evidence of substance abuse when compared with the PDD-NOS patient population.[32] However, Asperger syndrome patients have been identified as being at particular risk for anxiety disorders and are also at risk for suicidal tendencies. A 2010 Turkish study found that 42% of adolescents with Asperger syndrome showed evidence of suicidal behaviour, commonly associated with a combination of anxiety and major depression.[33]

Therapy for concomitant psychiatric conditions in the ASD population consists of a combination of counselling and pharmacotherapy, including risperidone and selective serotonin reuptake inhibitors.[21–25] For general physicians, the key issue is to recognise the high incidence of psychiatric conditions in the ASD population and that such ailments can place patients at risk for suicidal tendencies or other acute psychological impairments. Appropriate management will be based on the ability to arrange subspecialty follow-up and the degree of psychiatric impairment manifested in the patient with an ASD.

GI conditions associated with ASD

Considerable controversy exists as to whether ASD is associated with an increased prevalence of gastrointestinal (GI) diseases. Survey studies of parents of children with an ASD and retrospective observational cohort studies from centres that specialise in the management of patients with an ASD report a prevalence of 24%–42% of GI symptoms in this patient population, with chronic diarrhoea and constipation being most common.[34–36] However, prospective observational studies have not confirmed that the prevalence of GI symptoms in patients with an ASD is higher than the general population.[37] One possible explanation for this discrepancy is that it is typical in the ASD population for stereotyped behaviours to include a focus on eating only particular foods to the exclusion of a broader diet which may lead to GI symptoms.[38] In addition, it is well recognised that there is a relationship between ASD behavioural and GI symptoms. Patients with ASD who are experiencing abdominal pain may show evidence of unusual behaviour, including frequent clearing of the throat, screaming or moaning, wincing or facial grimacing, sleep disturbances or self-injurious actions. Conversely, worsening of ASD core symptoms may result in changed GI habits, including constipation, diarrhoea or changes in oral intake, in this patient population. This may also lead to presentation in the acute setting.[39 40]

This relationship between ASD core behaviours and GI symptoms creates a serious diagnostic dilemma for the acute evaluation of these patients. The absence of weight loss, decreased growth, GI tract blood loss (occult or otherwise), significant vomiting or diarrhoea, fever or reproducible right sided abdominal pain suggest a greater likelihood of functional abdominal pain in the paediatric ASD population and may allow the foregoing of more indepth imaging evaluation of such patients.[40] As typical GI conditions can present in the ASD population as in the general population, the general physician must carefully utilise all sources for an accurate patient history, largely relying on care givers given the communication impairments in patients with an ASD.[39 40] Once emergent causes of abdominal pain have been ruled out, it may be appropriate to attempt a trial of polyethylene glycol for constipation symptoms. Alternatively, a trial of a proton-pump inhibitor may be appropriate where behavioural symptoms (sleep disturbance, self-injurious actions or evidence of abdominal discomfort related to meals) suggest the presence of gastro-oesophageal reflux disease and other aetiologies have been ruled out.[40]

Nutritional and metabolic conditions associated with ASD

As noted above, the stereotyped behaviours of patients with an ASD often extend to patterns of only eating certain foods or

only eating at particular times. As a result, patients with an ASD are at risk for nutritional deficiencies. Case reports and small case series have reported patients with an ASD afflicted by scurvy and hypomagnesaemia.[41 42] The use of alternative gluten-free and casein-free diets can also place the patient with an ASD at risk for vitamin and nutritional deficiency, including vitamins A, B_{12} and thiamine.[23 43 44] One of the classic symptoms of Rett syndrome is weight loss, and decrease in muscle mass with cachexia is a cause of death in this patient population.[45] For non-specialist physicians, it is necessary to be aware that nutritional deficiencies in the ASD population may cause these patients to present with unusual conditions not typically seen in the general population.

ASD can be associated with a number of metabolic disorders. Some, such as phenylketonuria, are commonly diagnosed in infancy and treated immediately. Others, such as mitochondrial disorders, may only present in the setting of physiological stress, manifesting through laboratory abnormalities such as increased ammonia or lactate levels.[46] While the diagnosis of such conditions is not common, it is important for general physicians to recognise that patients with an ASD may have underlying concomitant metabolic disorders that can cause derangements such as lactic acidosis and hyperammonaemia.

Neurological conditions associated with ASD

The most common acute neurological conditions associated with ASD are epilepsy and seizure disorders. The estimated prevalence from observational studies ranges from 22% to 30%, with a greater association in classic autistic patients who also show evidence of intellectual disability. No particular pattern of seizure or specific anti-seizure medication has been shown to be more prevalent or effective in managing this condition, respectively, in patients with an ASD.[47–49] For general physicians, the evaluation and management of a patient with an ASD presenting with a seizure or multiple seizures is similar to the non-ASD population.

Motor impairments are also commonly seen in the ASD population. Deficits and delays in fine and gross motor function, purposeful motor movement (praxis) and gait abnormalities fall under this area of disability. Hypotonia may manifest in patients with an ASD at a young age, with a prevalence of 51% in one study, but appears to improve as patients reach adulthood.[50] Tic disorders, with a prevalence of 8%–10% in patients with an ASD, are treated clinically with clonidine or guanfacine most commonly.[12] Evaluation of patients with an ASD with these impairments is similar as that in the non-ASD population.

Catatonia

Catatonia has been increasingly recognised as a syndrome that affects autistic individuals. There have been two large studies that show that catatonia may occur in up to 12%–17% of autistic adolescents and young adults.[51 52] Symptoms of catatonia in the autistic patient tend to be described as decreased speech or mobility, freezing during actions, posturing, staring, negativism and echophenomena. Fink and Taylor in 2003 reported two sets of criteria for diagnosing catatonia in the autistic patient population. The first set consists of immobility, drastically decreased speech or stupor of at least 1 day duration, associated with at least one of the following: catalepsy, automonic obedience or posturing. The second set includes, in the absence of immobility, drastically decreased speech or stupor and a marked increase from baseline, for at least a week, of at least two of the following: slowness of movement or speech unless prompted, freezing during actions, difficulty crossing lines, inability to cease actions, stereotypy, echophenomena, catalepsy, automatic obedience, posturing, negativism or ambitendency.[53]

The duration of symptoms, detailed descriptions of behaviour and the patient's baseline psychomotor state are all important in the history. Physical examination should elicit the baseline mental status, responsiveness to stimuli, posture and tone of the patient, as well as any signs of dehydration, infections or trauma.[54]

The differential diagnosis of catatonia is broad and may include infectious, endocrinological, neurological and autoimmune causes. Medication induced conditions may include serotonin syndrome, neuroleptic malignant syndrome, acute dystonia and withdrawal from benzodiazepines or dopaminergic drugs. Recreational drugs such as PCP, mescaline, cocaine, ecstasy and opiates have been reported to cause the emergence of catatonia. Other causes may include hypocalcaemia, tetanus, rabies, status epilepticus, parkinsonism, stroke and acute delirium.[54]

When catatonia is diagnosed in the autistic patient, the initial treatment is lorazepam. The lorazepam challenge test consists of giving 1 mg of intravenous lorazepam and assessing for changes (ie, increased movement, speech or responsiveness). If there is no response, another 1 mg bolus is given. If there is improvement, the patient will need to be admitted for several days of escalating lorazepam doses until resolution. Doses of lorazepam as high as 24 mg per day are recommended to achieve therapeutic benefit. If the lorazepam challenge test fails, bilateral electroconvulsive therapy is highly effective, and psychiatry consultation is urgently needed upon hospital admission.[54 55]

Sleep disorders associated with ASD

Sleep disorders occur in 44%–83% of school-aged children with ASD. The specific complaints are most commonly insomnia, including restless sleep, difficulty falling asleep and maintaining sleep, bedtime resistance, cosleeping and early awakening. Sleep dysfunction in the patient with an ASD is thought to be multifactorial. Abnormal dopaminergic activity in the prefrontal cortex, elevated levels of catecholamines and abnormally low levels of melatonin with elevated levels in the daytime have all been reported as possible aetiologies.[56]

Patients with an ASD may present with worsening of their underlying behavioural symptoms, insomnia or parasomnias (sleepwalking, bruxism or nightmares).[56 57] New or worsening violent behaviour should prompt an urgent sleep assessment referral. Given that epilepsy is common among patients with ASD, thrashing movements, confusion or agitation during sleep times should be carefully differentiated from seizure activity based on history from care givers or the patient if possible. Insomnia can be treated with improved sleep hygiene (bedtime routines and avoiding parental/care giver reinforcement of bad sleep practices) and possibly melatonin.[26 56] It is appropriate for the general physician to refer a patient with an ASD with evidence of a sleep disturbance to a sleep specialist for long-term management.

Dental conditions associated with ASD

Dental ailments in patients with an ASD are often due to a combination of stereotyped behaviours in this patient population and prescribed medications for their ASD. Self-injurious behaviour, destructive chewing habits and bruxism can cause dental damage. Due to the communication abnormalities that commonly affect patients with an ASD, the pain caused by dental damage may manifest as changes in behaviour or poor oral intake.[58 59] However, studies in the dental literature suggest

that, in comparison with the general patient population, the rate of dental caries is lower in the ASD population.[60 61]

Prescribed psychotropic and antiseizure medications can cause a variety of oral and dental complications that can cause ED presentation. Xerostomia (dry mouth) is the most common oral/dental side effect of these medications in the ASD patient population and has been associated with all of the commonly prescribed medications in the ASD population discussed above. Other specific side effects seen in the ASD population are parotid gland swelling and pain associated with clonidine use, oral candidiasis and periodontal abscess with olanzapine use and buccoglossal syndrome (tardive dyskinesia) with fluoxetine use. Antiepileptic medications can cause gingival hyperplasia.[58]

Due to the impairments in communication, patients with an ASD with dental conditions may present with behavioural changes, self-injurious actions or poor oral intake.[58 59] As such, the general physician must consider dental ailments in the differential of what may be causing such non-specific complaints and attempt to perform a careful oral examination in the ASD patient population. Therapy for the above diagnoses is similar as that in the non-ASD population. However, in the paediatric ASD population, parents may have objections to therapies, such as antibiotics or dental materials, which contain fluoride, gluten or casein, believing that they may interact with alternative therapies.[59] Close discussion with the parents and the outpatient dentist can aid in resolving such impasses.

Ophthalmological conditions associated with ASD

Restricted dietary intake among patients with an ASD can place them at risk for vitamin deficiencies and resultant ocular complications. Case reports and short case series have reported visual loss in autistic patients due to vitamin A deficiency and optic neuropathy due to vitamin B_{12} deficiency.[43 44] Case series have also reported that the rising use of therapy swings in the ASD population as part of occupational and physical therapy programmes that include vestibular stimulation may place these patients at risk for metallic corneal foreign bodies. Direct trauma during therapeutic use of the swing that is not reported by the patient is the likely cause of such foreign bodies. Patients will present with changes of behaviour suggestive of pain with physicians needing to consider that a corneal foreign body is the cause. Given the sensitivity of patients with an ASD to close invasive physical examination, removal of such foreign bodies after diagnosis may require general anaesthesia in an operating room setting.[62]

Orthopaedic conditions associated with ASD

In comparison with the general population, adults with classic autism may be at a lower risk for fractures. A 2011 Danish retrospective analysis of a longitudinal observational cohort over a 30-year period of time found that 11.9% of classic autism patients experienced a fracture in comparison with 24.7% of controls. The most prevalent types of fracture in the autistic cohort were those of the forearm (5.9%) and skull and facial bones (3.4%). Diagnosis and therapy are similar to the general population.[63]

In Rett syndrome patients, it has been reported that scoliosis and hip displacement are the primary orthopaedic complications of this condition. A 2009 Australian study reported a prevalence of 48% (95% CI 30% to 67%) for hip displacement greater than 30% of the joint surface area and a prevalence of 87% (95% CI 70% to 96%) for scoliosis.[64] Such orthopaedic ailments can present with increased pain and behavioural changes, gait abnormalities and extremity contractures necessitating surgery.[64 65] For the general physician, the key issue is clinical suspicion for these diagnoses with evaluation and follow-up with orthopaedics on an urgent basis when diagnosed.

Self-injurious behaviour in patients with an ASD

A common difficulty in patients with an ASD is self-injurious behaviour. A 2008 study from South Carolina comparing patients with an ASD with those without disability found that the RR of any injury treatment in the emergency department or hospital setting was 1.20 (95% CI 1.04 to 1.39) in the ASD cohort in comparison with the general population. Patients with an ASD were more likely to present with injuries to the head, face and neck (RR: 1.47 (95% CI 1.13 to 1.90)) and less likely to experience fractures (RR: 0.54 (95% CI 0.32 to 0.91)).[66] A 2006 Italian study found that the most common forms of self-injurious behaviour in patients with an ASD were head hitting and hand biting with mild improvement over a 6-month period of time with risperidone therapy.[67] For general physicians, therapy of self-injurious behaviour is similar to that seen in same-type injuries in the non-ASD population. However, awareness of the common injury pattern in these patients can aid in determining whether a change or increase in such behaviour may be due to an underlying pathology as described above.

Cardiovascular conditions associated with ASD

A number of pathologies associated with ASD may be due to autonomic dysfunction. GI (chronic constipation and diarrhoea) and urological (urinary retention or enuresis) symptoms, sleep pattern abnormalities and syncope/orthostasis in patients with an ASD may be related to abnormalities in autonomic regulation. A 2005 study that compared paediatric patients with an ASD with the above autonomic symptoms with those without autonomic symptoms and non-autistic controls found that symptomatic patients with an ASD in comparison with controls had significantly less cardiac vagal tone and parasympathetic activity. As a result, symptomatic patients with an ASD had a significantly higher baseline heart rate (102 vs 85), diastolic blood pressure (82 vs 62) and mean arterial pressure (96 vs 77) in comparison with non-ASD controls.[68] While this single centre study is limited, for physicians clearly focused on vital sign abnormalities, a careful history elucidating chronic autonomic symptoms may provide an explanation for elevated vital signs without need for further invasive investigations.

Gynaecological conditions associated with ASD

As with other associated conditions, patients with an ASD may present with behavioural changes that relate to gynaecological development and disorders. A 2010 retrospective study found a pattern of mood and behavioural abnormalities as perceived by care givers associated with menarche and occurring cyclically with menstruation. Similar behavioural changes were also seen with metrorrhagia and menorrhagia. Patients showed improvement with the use of oral contraceptive medications.[69] For treating physicians, a careful menstrual history can aid in determining the underlying diagnosis causing behavioural changes in the patient with an ASD who cannot communicate clearly their discomfort with these gynaecological conditions. For patients with an ASD experiencing pain from gynaecological conditions, non-steroidal anti-inflammatory medications are considered preferred therapy.[69]

Infectious disease in patients with an ASD

Due to the communication impairment associated with ASD, these patients may not express the classic symptoms associated

with infectious disease, such as verbalised shortness of breath or pain. However, it does not appear that patients with an ASD are at a higher risk for infectious disease in early childhood in comparison with the general paediatric population. A 2007 case control study comparing 403 patients with an ASD to 2100 controls found that the overall rate of infection was similar (95% in patients with an ASD compared with 97.5% of control patients). There was a slightly decreased odds of upper respiratory infections (OR: 0.65 (95% CI 0.48 to 0.88), possibly due to decreased reporting of symptoms such as ear pain in the ASD cohort, and a slightly higher odds of genitourinary symptoms (OR: 2.2 (95% CI 1.2 to 4.0), primarily urinary tract infections, though commonly associated clinical factors such as circumcision were not controlled for.[70] For physicians caring for paediatric patients, these data suggest that paediatric patients with an ASD can be viewed similarly as the general paediatric population with regard to risk of infections.

Oncological conditions associated with ASD

To our knowledge, no long-term study has evaluated the association of oncological disease with ASD. However, a single retrospective study from North Carolina published in 2010 found no increased prevalence of paediatric malignancies among patients with an ASD in comparison with the general paediatric population between 1997 and 2007.[71]

APPROACH TO THE EVALUATION OF THE PATIENT WITH AN ASD

Location of encounter

Box 1 summarises essential strategies for obtaining the history, physical examination and laboratory/diagnostic imaging evaluation and completing therapeutic interventions for the adult or paediatric patient with an ASD. The initial step in caring for patients with an ASD is identifying a location most conducive to patient evaluation and limiting overstimulation of the patient. Common distraction techniques used by care givers,

Box 1 Strategies for obtaining the history, physical examination and diagnostic evaluation and completing therapeutic interventions for the patient with an autism spectrum disorder (ASD)

On arrival

1. Prepare a quiet examination room without loud equipment or clutter. Avoid rooms with bright or fluorescent lighting if possible.
2. Unless the patient requires immediate intervention, discuss with the care giver the best way to approach the patient, focussing on techniques to touch the patient and words, textures or smells that should be avoided.
3. Disseminate this information to the entire treatment team (nurses and support staff).

History

1. Obtain the history from both the patient and the care giver. Use vocabulary or techniques for questioning suggested by the care giver.
2. Directly address the patient and reorient the conversation to the patient. For example, rather than ask the care giver, 'How does 'Charlie' talk?', state, ''Charlie', I'm now going to ask your 'Mom' how we can talk together.' Once the care giver answers, repeat that answer back to the patient using his/her name to reinforce the direct relationship with the patient.
3. Utilise distraction techniques suggested by care giver, such as television, music, movies or toys, as age appropriate.
4. Establish how the patient communicates 'yes' and 'no' either by asking directly or showing how he/she can do this.
5. Keep questions short, direct and simple. Avoid multi-step questions. Example: Use 'Does your head hurt?' rather than 'Point where it hurts.' The same applies to requests to follow particular directions.
6. Specific historical facts that should be obtained include:
   a. Baseline behaviour, communication ability and degree of social impairment
   b. Baseline dietary habits, including type and timing of oral intake
   c. Baseline pharmacological therapy, including alternative agents and diets
   d. Vaccination and menstrual history
   e. Baseline sleep pattern

Physical examination and diagnostic evaluation

1. Look for repeated movement such as swaying, tics or repeated phrases. These behaviours can be comforting if the patient is in an agitated state. If the behaviour becomes rapid and intense in its repetition, it can also be an indicator that the person is about to become overwhelmed and explosive. Allow the patient personal space if this occurs, and do not force the patient to stand still.
2. Do not force eye contact. Instead, ask the patient to look at your tie, a pocket or necklace.
3. Consider using pain scales or pain assessment techniques that include the care giver.
4. Use step-by-step explicit communication to the patient of what will happen next in the examination.
5. In consultation with the care giver, show the steps in the examination on the care giver or stuffed animal, as age appropriate, prior to performing on the patient.
6. Reward completion of tasks in the physical examination and diagnostic evaluation.
7. If sedation is required, consider use of benzodiazepines for anxiolysis and/or ketamine for sedation.

Therapeutic interventions

1. Consider medication taste in prescribing pharmacological therapy, possibly including paediatric formulations for adult patients.
2. Show the patient the materials that will be used for splinting or bandaging if applicable. Allow patient to feel these materials prior to use.
3. Model the intervention on the care giver and cover the splint or bandage with non-threatening images for paediatric or adolescent patients with an ASD.

such as the use of television, movies or toys, should be embraced. Advanced preparation to remove unnecessary clutter and loud equipment from the examination room prior to evaluation can help reduce sensory overload for the patient with an ASD.[9–11 72] Asking care givers if the patient dislikes being touched in a certain manner or dislikes certain textures or smells can help the general physician avoid noxious triggers to the patient. Physicians caring for patients with an ASD in the acute care setting may also get information regarding behaviours, preferences and activities of their patient from the outpatient provider.[9–11 73] Communication of these preferences to the entire staff caring for the patient will also help maintain consistency throughout the visit to give the highest chance of successful evaluation.[9–11 72]

History

Given the limited communication capability in most patients with an ASD, care givers need to be empowered to be part of the medical team so that a complete history is obtained. Care givers of patients with an ASD may feel very passionate about their use of alternative therapies and may resent any questioning of these interventions. Approaching care givers in a non-judgemental fashion is therefore essential.[74] Among the many alternative therapies tried on patients with an ASD, the more common include dietary supplements (vitamins, proteins/amino acids, fatty acids, digestive enzymes, minerals), hormones (melatonin, secretin) and modified diets (primarily gluten-free and casein-free diets.[22 27] Other alternative therapies used on patients with ASD include chiropractic, acupuncture, chelation, neuro-feedback and hyperbaric oxygen.[22 27] Understanding which alternative therapies are being used can direct the general physician to look for potential side effects from these therapies (table 2).

Patients with an ASD receive non-traditional therapies and may not have received standard vaccinations in childhood.[75] This may increase the risk of particular infectious diseases (tetanus, mumps, measles, rubella, etc) not commonly seen in the general population for which general physicians should have heightened awareness when seeing a patient with an ASD.

Physical examination, diagnostic evaluation and invasive therapies

The physical examination requirements for a patient with ASD are no different than for other patients. However, limitations in communication may not allow the general physician to get an accurate localisation and description of symptoms, especially pain. Working with care givers to use words familiar to the patient with an ASD and as 'interpreters' of the patient's verbal and physical responses to the exam is essential. Extra attention must also be given to the use of sign language and other communication techniques employed by patients with an ASD with verbal impairments.[73] Traditional pain scales that rely on self-reporting of pain may be less effective with patients with an ASD.[76] Scales that incorporate care giver-identified child-specific pain behaviours may be more effective in paediatric patients with an ASD.[73 76] Nader *et al* reported that autistic children display similar responses to pain as non-autistic children. They noted increased facial expression of pain when compared with a matched control population.[77] Therefore, assessing for pain using non-traditional methods may be required. Techniques used to help patients with an ASD tolerate the invasive parts of the physical exam include extensive and honest communication regarding what you are doing. This may be best done with step-by-step explanation or accomplished after demonstrating the exam or procedure on a care giver or stuffed animal, as age appropriate. When discussing painful procedures, such as lab draws, sample collection or imaging studies, it is best to describe each step of the procedure prior to starting and allow the patient to touch and feel all the equipment that will be used.[9–11 72] It is also useful to reward good behaviour or cooperation with the procedure. Simple rewards, such as stickers or books for paediatric or adolescent patients with an ASD, respectively, can be helpful when trying to obtain buy-in from a patient with an ASD.[72]

When distraction techniques prove to be insufficient, sedation may be employed. In our experience with the ASD population, the most commonly used drug class for anxiolysis is benzodiazepines (oral midazolam or intramuscular/intravenous lorazepam at standard weight based dosing). Procedural sedation can be effected most easily with intramuscular or even oral ketamine given the low side effect profile and lack of need for intravenous access. It is controversial as to whether premedication with midazolam is needed to avoid emergency reactions from ketamine sedation, but the possibility should be discussed with the patient and care giver where appropriate.[78 79]

When administering treatments to patients with an ASD, extra time and attention need to be spent to ensure that barriers such as oral and textural aversions are managed. Parents anecdotally report difficulty getting patients with an ASD to take medications, and physicians often forget to take into account taste when treating patients with an ASD. Compliance with other forms of treatments, such as splints, casts, sutures and bandages, may be challenging in patients with an ASD who frequently have tactile sensitivities. Techniques that may prove useful focus on identifying and reducing exposure to tactile stimulations that bother the patient as well as spending extra time to allow exposure to the supplies being used.[9–11 72] Covering splints or bandages with less threatening stickers or drawings in paediatric patients with an ASD can also be useful. Engaging the care giver with similar splints or casts may also reduce the threat in the eyes of the patient with an ASD.

CONCLUSION

Patients with an ASD are becoming more prevalent in a variety of healthcare settings. For general physicians who do not

Main messages

- Patients with autism spectrum disorders (ASD) are rising in prevalence and increasingly encountered in a variety of healthcare settings by general physicians. Care givers of patients with an ASD report that the current healthcare system poorly provides for this challenging population.
- Existing data suggest that a variety of acute conditions can cause patients with ASDs to present to general physicians in the outpatient, emergency department and inpatient setting. Such acute conditions make clear that ASDs are not simply confined to the neurodevelopmental realm but extend to a variety of areas of medical practice.
- The approach to the assessment and treatment of the patient with an ASD requires special preparation and a sensitive approach to the patient and their care giver. Without such preparation and sensitivity, the diagnostic assessment and treatment of patients with an ASD are likely to be ineffective and potentially endanger these individuals when most in need.

Current research questions

- The nature of health resource utilisation by adults with ASDs is still unclear and requires ongoing evaluation. As the population of patients with an ASD rises in prevalence, it is likely that health resource utilisation will increase. Without research into the nature of that utilisation, healthcare resources for this population will be allocated inappropriately.
- High quality research trials on the management of ASDs are required to formulate a more evidence-based approach to the care of these patients. Currently, there is little evidence to support the commonly used pharmacological agents used in patients with an ASD.
- Educational initiatives that make general physicians aware of the complexities of diagnosis and management of patients with an ASD are needed. These initiatives should be evaluated for effectiveness as the prevalence of this patient population rises. The rising prevalence of patients with an ASD makes it imperative that the general healthcare community becomes aware of the multidimensional nature of the ASD spectrum of illness.

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regularly see patients with an ASD, understanding the spectrum of disease in this patient population and approaching the evaluation of these individuals with sensitivity and the inclusion of the expertise of care givers will aid in the care of this challenging and emerging patient population.

MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F): ANSWERS AFTER THE REFERENCES)

1. Which statement is true regarding autism spectrum disorders?

A. There is a female predominance.
B. The approximate prevalence is 1%.
C. There is no evidence of a genetic aetiology to these conditions.
D. Age of onset is typically in adolescence.

2. Which statement is true regarding the pharmacological and alternative treatment management of patients with an autism spectrum disorder?

A. The pharmacological agent with the most evidence to support effectiveness is risperidone.
B. Dietary modification has been shown to be effective in the treatment of autism spectrum disorders.
C. Selective serotonin reuptake inhibitors are rarely used in the management of autism spectrum disorders.
D. There is no evidence to support the use of melatonin in patients with an autism spectrum disorder manifesting sleep impairments.

3. Which statement is true regarding catatonia in the patient with an autism spectrum disorder?

A. Catatonia primarily affects the patient with an autism spectrum disorder in early childhood.
B. Preferred treatment consists of electroconvulsive therapy.
C. The lorazepam challenge test consists of up to two rounds of providing 1 mg of lorazepam to the catatonic patient with an autism spectrum disorder.
D. Most patients with an autism spectrum disorder with catatonia can be discharged with outpatient therapy.

4. Which statement is true regarding gastrointestinal conditions in the patient with an autism spectrum disorder?

A. There is no correlation between behavioural changes in the patient with an autism spectrum disorder and gastrointestinal symptoms.
B. In paediatric patients with an autism spectrum disorder, the lack of fever or right sided abdominal pain may suggest a functional cause to gastrointestinal symptoms.
C. Behavioural changes in the patient with an autism spectrum disorder are usually a manifestation of acute gastrointestinal pathologies.
D. Polyethylene glycol should not be used to treat constipation in the patient with an autism spectrum disorder.

5. Which statement is true regarding the obtaining of history, physical examination and diagnostic evaluation and the management of the patient with an autism spectrum disorder?

A. A standard clinic or hospital room is appropriate for the evaluation of the patient with an autism spectrum disorder.
B. Care giver attitudes towards alternative therapies do not hinder the use of standard medical treatment in patients with autism spectrum disorders.
C. Given the communication difficulties that can affect patients with an autism spectrum disorder, all verbal attempts at addressing the patient should instead be directed at the care giver, where available.
D. Oral ketamine is safe and effective for procedural sedation of the patient with an autism spectrum disorder.

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ANSWERS

1. (A) F; (B) T; (C) F; (D) F
2. (A) T; (B) F; (C) T; (D) F
3. (A) F; (B) F; (C) T; (D) F
4. (A) F; (B) T; (C) F; (D) F
5. (A) F; (B) F; (C) T; (D) T

Care of the patient with an autism spectrum disorder by the general physician

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