JPPT | Case Series

Pediatric Scurvy: How an Old Disease Is Becoming a New Problem

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Ascorbic acid (vitamin C) functions as a cofactor and antioxidant within the human body that enables tissue growth and repair, but vitamin C is not intrinsically produced. Scurvy, or ascorbic acid deficiency, has traditionally been viewed as a historical disease. With the incidence of autism spectrum disorder and food restriction on the rise, children's hospitals may see increasing cases of scurvy. This is a single-center, retrospective case series including patients aged 7 to 14 years who were admitted to the Kentucky Children's Hospital with scurvy in the 2018–2019 period. Although selective or restricted eating is not an uncommon behavior among children, especially toddlers, parents of autistic children frequently report their children to be exceedingly selective eaters. However, there currently are conflicting findings on whether this leads to nutritional inadequacy. Although no guidelines exist for the treatment of scurvy, the mainstay of therapy is reintroduction of vitamin C. Oral therapy is generally preferred, but vitamin C can be given parenterally when necessary. In conclusion, oral aversion is a symptom commonly seen in patients with autism spectrum disorder and other developmental delays, potentially leading to increased cases of scurvy. Treatment of scurvy includes reintroduction of vitamin C into the diet. However, oral supplementation may pose unique challenges in this patient population.

ABBREVIATIONS ASD, autism spectrum disorder; CDC, Centers for Disease Control and Prevention; CT, computerized tomography; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; G-tube, gastronomy tube; IM, intramuscular; IV, intravenous; KCH, Kentucky Children's Hospital; MRI, magnetic resonance imaging; NG, nasogastric; SQ, subcutaneous

KEYWORDS ascorbic acid; ascorbic acid deficiency; case series; dosage forms; pediatrics; scurvy

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Introduction

Ascorbic acid (vitamin C) functions as a cofactor and antioxidant in several metabolic and oxidative reactions that enable tissue growth and repair within the human body. Despite its critical role, vitamin C cannot be intrinsically produced within the human body and therefore must be obtained via dietary sources. Patients who have chronically restricted vitamin C intake are at risk for impaired bone formation and vascular damage, which ultimately manifests as clinical scurvy, a series of non-specific presentations including bone pain, extremity swelling, petechiae, and gingival bleeding.[1]

Because of fortification of food and abundance of nutritional supplements in developed countries, scurvy, or vitamin C deficiency, has traditionally been viewed as a historical disease or a disease of third-world countries. Incidence of scurvy varies across the world, with rates reaching as high as 73.9% in India.[2] Scurvy has been reported in the United States, with a prevalence of clinical scurvy at 7.1%.[2] The vast majority of patients diagnosed with scurvy in the United States have concomitant disease states that increase the risk of nutritional deficiency, such as substance abuse, eating disorders, dietary restrictions, or iron overload.[3]

According to the Centers for Disease Control and Prevention (CDC), the prevalence of autism spectrum disorder (ASD) is on the rise, with an incidence of 1 in 59 children in 2016, which is a 3-fold increase from the 1 in 150 children with ASD in 2000.[4] In 1943, Kanner[5] published his findings of 11 children who exhibited 3 pattern behaviors: extreme autistic loneliness, delayed echolalia, and resistance to change. Although diagnostic criteria for autism have changed since that article was published, the primary principles defined by Kanner have remained the same. In the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV)[6] published by the American Psychiatric Association in 1994, diagnosis of autism continued to be based on symptomatology in 3 key areas: social reciprocity, communicative intent, and restricted and repetitive behaviors. Changes made to the 5th edition, DSM-V,[7] published in 2003, included converging of subtype diagnoses of autistic disorder, Asperger syndrome, pervasive developmental disorder not otherwise specified, and disintegrative disorder into an umbrella diagnosis of "autistic spectrum disorder." Diagnosis now relies heavily on symptomatology seen in 2 major categories: social communication/interac-

tion and restricted and repetitive behaviors. Because of the convergence of multiple disease states and the changes in diagnostic criteria in 2003, it is possible that the drastic rise in the incidence of ASD from 2000 to 2016 may be skewed; however, the health care–related ramifications of increased diagnosis remain a concern.

Despite scurvy being a well-defined clinical condition, first identified as early as the 14th century, diagnosis is often delayed in pediatric patients because of the disease's generic presentation. Although diagnoses of scurvy are considered rare in developed nations, the increased prevalence of ASD, dietary restrictions (often times self-imposed), and oral aversion seem to be bringing scurvy back to the forefront of pediatric patient populations.[8] The purpose of this article is to review scurvy cases seen at Kentucky Children's Hospital (KCH), as well as to review the current literature regarding scurvy diagnosis and treatment in the United States.

Case Series

Patient 1. Patient 1 was a 7-year-old male (25 kg) with ASD who presented to the hospital with a reported history of difficulty ambulating over the previous 3 weeks. His parents had been managing the pain prior to admission using ibuprofen and hydrocodone/acetaminophen suppositories. On the day of presentation, the patient's parents complained of a new-onset subjective fever. The child was non-verbal at baseline and had limited ability to communicate pain. At home, his diet was extremely limited and consisted only of water, nacho cheese–flavored chips, cheddar-flavored crackers, and apples.

On exam, the patient actively kicked both legs, and his hips could be passively rotated without signs of discomfort. He showed no discomfort during palpation of spine and extremities. Over the course of the hospital stay, he developed worsening bruising on both lower extremities. On hospital day 3, gingival bleeding and a petechial rash were noted by the team as well. However, the parents reported the presence of the petechial rash as chronic.

A sedated MRI scan was completed on hospital day 4 and showed enhancement of the margins of the sacrum and ilium at the sacroiliac joint, the posterior iliac bones, and the apophyses of the pelvis. Based on this, the exam was read by the radiology team as concerning for scurvy. A plasma vitamin C concentration was obtained at this time. However, at our institution, plasma vitamin C is a "send-out" lab that often takes days to result.

This patient presented challenges with medication delivery. He had an extreme oral aversion to both the tablet and liquid vitamin C, despite extensive work with child life specialists. After the MRI, ascorbic acid 300 mg (12 mg/kg) was added to 250 mL of normal saline to be given intravenously for presumed scurvy. This was later changed to an IV multivitamin containing vitamin C as well as vitamin A, vitamin D3, thiamine, pyridoxine, niacinamide, dexpanthenol, vitamin E, vitamin K, folic acid, biotin, and vitamin B12. Additionally, because of his extremely limited diet and significant nutritional deficiencies, the possibility of gastronomy tube (G-tube) placement was discussed with the family. The family ultimately refused placement during admission but planned to continue discussions pending speech therapy and nutrition interventions on an outpatient basis. In preparation for discharge, the team pharmacist consulted with a local compounding pharmacy that prepared ascorbic acid 100 mg (4 mg/kg) rectal suppositories for outpatient use.

The patient's plasma vitamin C concentration returned after discharge as <0.1 mg/dL (reference range: 0.4–2.0 mg/dL). Concurrently, he also was found to have a low vitamin D concentration of 11 ng/mL (reference range: >19 ng/mL) and a low vitamin B12 concentration of 183 pg/mL (reference range: 210–1033 pg/mL).

Overall, on discharge, bleeding and bruising, as well as the pain and range of motion in extremities, had improved, although the patient was not back to his normal activity level per the parents. Family could not be reached for follow-up phone call when it was attempted postdischarge.

Patient 2. Patient 2 was a 10-year-old male (32 kg) with a history of ASD who presented to the hospital with a chief complaint of bilateral leg weakness. His parents reported a decline in patient mobility over the past month. They also reported a change in mental status, with overall decreased playfulness. Additionally, they had noticed bilateral ankle swelling and mild bruising along the calves. Home medications only included a liquid iron supplement, which had been recently started by the patient's pediatrician.

The patient was mostly non-verbal and had very specific dietary habits. He ate primarily fast-food quesadillas, cheeseburgers and French fries, macaroni and cheese, peanut butter and jelly sandwiches, pizza, and plain submarine sandwiches. Of note, there were minimal to no vegetables or fruits present in his diet.

On physical exam, he had a significant petechial rash covering his calves, which parents stated had recently worsened. He also had oozing gums above several teeth. In addition to significant edema in his lower extremities, his calves were tender to the touch, and he resisted passive movement of his legs.

At the time of presentation, the differential was broad, including Guillain-Barré syndrome, hematologic malignancy, viral infection, and myositis. His workup included a CT of the chest and abdomen as well as X-rays of the lower extremities, which were grossly normal, aside from demineralization. Labwork included iron studies, thyroid studies, vitamin D concentration, urine study, plasma vitamin C, cytomegalovirus and parvovirus, peripheral smear, serum Epstein-Barr polymerase chain reaction, and serum lead. Similar to the case listed above, many of these were send-out

tests, the results for which were not available until after hospital discharge.

The patient was empirically started on a liquid multivitamin and an ascorbic acid 250 mg (8 mg/kg) tablet once daily on day 2 of his hospitalization. The ascorbic acid tablet was crushed and placed in soda to ease delivery. On day 3 of his hospitalization, a cholecalciferol 2000 international units tablet (60 international units/kg) and calcium carbonate suspension 750 mg (23 mg/kg) 3 times daily were started in addition to his home iron supplementation. He also received 5 mL/kg of packed red blood cells on day 2 of hospitalization because of a hemoglobin value of 4.8 g/dL, for which hematology was consulted.

During hospital days 1 through 3, the patient's pain was controlled with ketorolac injections and warm compresses applied to the calves. This was transitioned to liquid naproxen on days 4 and 5. On hospital day 4, both the patient's parents and the medical team noted that pain was beginning to improve. On hospital day 5, patient 2 was still unable to walk on his own but was able to be assisted to the toilet with fewer signs of pain. He was discharged home with outpatient physical and occupational therapy appointments as well as an autism specialist follow-up appointment. Discharge medications included multivitamin, iron supplement, ascorbic acid, cholecalciferol, and calcium carbonate. After Patient 2 was discharged, his plasma vitamin C concentration returned as <0.1 mg/dL (reference range: 0.4–2.0 mg/dL). Additional lab results included a plasma vitamin D concentration of 19.7 ng/mL (reference range: >19 ng/mL), a vitamin B12 concentration of 699 pg/mL (reference range: 210–1033 pg/mL), and an iron concentration of 15 mcg/dL (reference range: 50–120 mcg/dL). The patient's parents were unable to be reached for follow-up.

Patient 3. Patient 3 was a 10-year-old male (38 kg) with ASD who presented with painful mouth lesions on the soft palate. His parents reported that about a month prior to presentation, he had dental caries and baby teeth that fell out, followed by development of oral sores that were now making eating painful. His primary care provider and dentist were concerned for a mouth abscess and had prescribed 14 days of amoxicillin/clavulanate with little improvement. They also reported recent fevers as high as 102°F (38.9°C) and frequent nosebleeds lasting 10 to 15 minutes apiece. Additionally, they described joint pain in his knees for the past 2 months as well as intermittent pain in his back and all 4 extremities.

The patient was verbal but had limited ability to communicate pain. His parents reported his diet consisted almost entirely of chicken nuggets and chocolate milk. His home medications included sertraline (50 mg daily), polyethylene glycol (8.5 g once daily), guanfacine extended-release (2 mg daily), and mirtazapine (15 mg daily at bedtime).

On exam, he was found to have a petechial rash and redness around the hair follicles on his legs, as well as mandibular gum swelling. The initial differential included dental abscess, malignancy, and/or nutritional deficiency. A vitamin C concentration was drawn as well as an iron concentration. The iron resulted as 11 mcg/dL (reference range: 50–120 mcg/dL). Hemoglobin on admission was 7.9 g/dL (reference range: 10.6–13.4 g/dL). No lower extremity imaging was obtained during the patient's stay.

On hospital day 2, an ascorbic acid 125 mg (3.3 mg/kg) tablet was started twice daily by mouth. On hospital day 4, elemental iron 65 mg (1.7 mg/kg elemental iron) twice a day was started, and on hospital day 5, a multivitamin was started in addition to the ascorbic acid. The patient's pain was controlled throughout his stay with an acetaminophen 325 mg (9 mg/kg) tablet every 4 hours as needed. He had no problems with medication delivery and could swallow tablets without issue. During his hospital stay, he worked with a hospital nutritionist and successfully was able to incorporate new foods into his diet, including broccoli cheddar soup, protein shake supplements, potatoes, hamburgers, pancakes with syrup, strawberry cheesecake, and pasta. Overall, his oral intake was greatly improved upon discharge. Follow-up appointments were made for outpatient physical therapy and pediatric dentistry as well as with the patient's primary care provider. After discharge, the patient's plasma vitamin C concentration resulted as <0.1 mg/dL (reference range: 0.4–2.0 mg/dL). His mother was reached via telephone 2 days after discharge and reported that he was eating well, sitting up more, and drinking nutritional shakes.

Patient 4. Patient 4 was a 6-year-old male (25 kg) with a past medical history significant for ASD, cerebral palsy, and asthma, who presented for evaluation of fevers, weight loss, and dental abscesses following decreased oral intake at home. Of note, parents had noticed a slightly abnormal gait and resistance to ambulation. Prior to admission, his pediatrician had noted a dental abscess that had started bleeding as well as a microcytic anemia on laboratory findings. Parents reported a limited diet, consisting mostly of peanut butter candies, fast-food cheeseburgers, grilled cheese sandwiches, chips, and sodas. Home medications included fluticasone (110 mcg/inhalation 2 puffs twice daily) and montelukast (5 mg once daily).

On admission, the patient was started on clindamycin IV 244.8 mg (10 mg/kg) every 6 hours, which was changed to ampicillin/sulbactam IV 1200 mg (50 mg/kg of ampicillin) every 6 hours for the dental abscess. Additional labs were drawn for evaluation of the microcytic anemia, including a plasma vitamin C, vitamin D, and vitamin B12. On day 1 of hospitalization, the vitamin D concentration resulted at 14.3 ng/mL (reference range: >19 ng/mL), and vitamin B12 resulted at 913 pg/mL (reference range: 210–1033 pg/mL). Following this, the patient was started on ergocalciferol 50,000 international units (2000 international units/kg) every

7 days. Oral and Maxillofacial Surgery and Speech Language Pathology were consulted. On evaluation, Speech Language Pathology noted increased stress when the patient was asked to hold typically preferred foods. In addition, X-rays of the knees and hips resulted without abnormality.

On day 3 of hospitalization, a nasogastric (NG) tube was placed to provide the patient with nutritional support. The following day pediatric surgery was consulted for consideration of G-tube placement and the patient underwent a CT scan for evaluation of the dental abscess. In addition, the patient was started on an ascorbic acid 250 mg (10 mg/kg) tablet daily for presumed scurvy as well as 24 mg of elemental iron (1 mg/kg elemental) 3 times daily and a multivitamin (0.5 mL) twice daily. On day 5, the patient's vitamin C concentration resulted at <0.1 mg/dL (reference range: 0.4–2.0 mg/dL). In addition, the ampicillin/sulbactam was discontinued because of a CT scan showing no evidence of oral abscess, and the patient was noted to have improvement of leg pain and gum bleeding. Patient was discharged home on hospital day 7 with plans to continue ascorbic acid, ergocalciferol, and ferrous sulfate. G-tube placement was scheduled as an outpatient procedure 1 week after discharge. The family was unable to be reached for visit follow-up.

Patient 5. Patient 5 was a 14-year-old male (31.5 kg) with a prior medical history significant for ASD, attention deficit hyperactivity disorder, and gastroesophageal reflux who presented with increased weakness and lower extremity pain. His presentation was accompanied by decreased oral intake, multiple falls, dehydration, and a weight loss of 10 pounds. On physical exam he was noted to have a petechial rash. A lower extremity X-ray from the emergency department was significant only for diffuse osteopenia. Initial differential was broad and included autoimmune disease, polyarticular arthritis, neoplasm, electrolyte disturbances, rhabdomyolysis, and nutritional deficiency. However, initial laboratory values resulted within expected ranges. His home diet consisted primarily of fast-food French fries, lemon-lime soda, and chocolate bars. Because of the concern for malnutrition, the patient was started on IV nutritional supplementation ("rally pack") containing thiamine 100 mg/L, adult multivitamin 10 mL, and magnesium sulfate 2 g/L once daily for 3 days, and multiple plasma vitamin concentrations were drawn. His vitamin B12 resulted at 222 pg/mL (reference range: 210–1033 pg/mL), and folate resulted at 3.9 ng/mL (reference range: >4.8 ng/mL). Home medications included mirtazapine (15 mg once daily at bedtime), ranitidine (150 mg twice daily), and loratadine (5 mg once daily).

On day 2 of admission, ophthalmology saw the patient for photophobia and noted no evidence of corneal disease. In addition, the patient agreed to attempt meal supplementation with nutritional shakes, which he unfortunately did not tolerate. The patient's vitamin D resulted at 7.2 ng/mL (reference range: >19 ng/mL). His pain was managed with scheduled acetaminophen 480 mg (15 mg/kg) every 6 hours and ketorolac IV 15 mg (0.5 mg/kg) every 6 hours. On day 3, the patient was noted to have lower extremity bruising. The following day, the patient received an NG-tube and was started on ergocalciferol 50,000 international units (1500 units/kg) weekly. Additionally, he was started on omeprazole orally 20 mg (0.6 mg/kg) daily because of continued emesis and symptoms of reflux. His retinol binding protein resulted at 1.4 mg/dL (reference range: 3–6 mg/dL), which is indicative of a vitamin A deficiency. Additionally, he was started on liquid multivitamin with zinc at a dose of 1 mL once daily. On day 5, the patient was noted to have improvement in lower extremity pain but continued to have emesis that parents believed was related to discomfort from the NG-tube. His vitamin B6 resulted at 12.4 nmol/L (reference range: 20–125 nmol/L). At this time, he was started on propranolol 10 mg (0.3 mg/kg) twice daily for anxiety per a recommendation from the adolescent clinic physician. In addition, he was started on vitamin C intravenous 200 mg (6 mg/kg) diluted in 250 mL dextrose 5% in water (D5W) every 24 hours as well as transitioned from ergocalciferol to cholecalciferol 2000 international units (64 international units/kg) daily. On the following day, the patient's vitamin C concentration resulted at 0.15 mg/dL (reference range: 0.4–2.0 mg/dL), confirming a diagnosis of scurvy. At this time, he was transitioned to an ascorbic acid 250 mg (8 mg/kg) tablet once daily. On day 7, the pediatric surgery team was consulted for evaluation of long-term feeding access and recommended continuation of NG-tube followed by outpatient scheduling of G-tube placement. His vitamin B1 resulted at 38 nmol/L (reference range: 70–180 nmol/L). Despite improvement in movement and overall lower extremity pain, the patient was still noted to be non-ambulatory.

The patient was discharged home on hospital day 8 with planned continuation of ascorbic acid, cholecalciferol, multivitamin, omeprazole, and propranolol. Of note, the patient's previous home mirtazapine was discontinued. In addition, he was discharged with a wheelchair, rolling walker, and bedside commode as well as an outpatient referral for physical therapy/occupational therapy because of continued difficulty ambulating. The patient had a planned follow-up visit scheduled with the adolescent clinic as well as pediatric surgery. Family was contacted 2 days after discharge and reported that the patient was still having a difficult time standing unassisted.

A summary of each patient case can be found in Table 1.

Discussion

To diagnose ASD, 2 of the following 4 criteria must be met within the category of restrictive and repetitive behaviors: 1) repetitive speech, motor movements, or

Table 1. Summary of Patient Cases

Case	Sex	Age (yr)	Wt (kg)	PMH	Vitamin C Serum Concentration at Diagnosis (mg/dL)	Treatment
1	M	7	25	ASD	<0.1	Ascorbic acid 300 mg (12 mg/kg) in 250 mL normal saline → IV MVI daily → ascorbic acid 100 mg (4 mg/kg) rectal suppository daily
2	M	10	32	ASD	<0.1	Ascorbic acid 250 mg (8 mg/kg) tablet once daily + liquid MVI
3	M	10	38	ASD	<0.1	Ascorbic acid 125 mg (3.3 mg/kg) tablet twice daily + MVI tablet
4	M	6	25	ASD, CP, asthma	<0.1	Ascorbic acid 250 mg (10 mg/kg) tablet daily + MVI liquid
5	M	14	31.5	ASD, ADHD, GERD	0.15	IV nutritional supplementation ("rally pack") → ascorbic acid 250 mg (8 mg/kg) tablet once daily + MVI liquid with zinc

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; CP, cerebral palsy; GERD, gastroesophageal reflux disease; MVI, multivitamin; PMH, past medical history

use of objects; 2) excessive adherence to routines, ritualized patterns of behavior, or excessive resistance to change; 3) highly restricted interests that are abnormal in intensity or focus; and/or 4) hyperreactivity or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment.

Although selective or restricted eating is not an uncommon behavior among children, especially toddlers, parents of autistic children frequently report their children to be exceedingly selective eaters. When considering the diagnostic criteria of "resistance to change" and "extreme focuses on sensory aspects of the environment," it is not surprising that children with ASD may have a more restricted diet. A survey[9] distributed to 100 parents of autistic children found that the majority of parents (67%) reported that their child was a "picky eater," regardless of appetite. More than 45% of parents reported that their child was reluctant to try new foods, ate too few foods, and/or displayed rituals around eating. Another survey[10] found that over 80% of parents of ASD children reported that their child ate a restricted diet. When compared with neurotypical children, parents of children with ASD aged 7 to 9.5 years reported[11] that their child refused statistically more foods. In addition, males with ASD ate a statistically smaller variety of food over a 3-day period when compared with controls.[12]

It is well documented that children with ASD eat more restricted diets than do typically developing children. However, there currently are conflicting findings on whether this diet difference leads to nutritional inadequacy. Although some studies[12–14] have found that children with ASD have sufficient nutrient intakes despite restricted diets, one study[15] reported that children with ASD were more likely to have an inadequate intake of iron, vitamin D, vitamin C, niacin, riboflavin, and zinc. Although the study was small, the author reported that 9 out of 17 children (53%) were found to be deficient in one or more nutrients. Because of a paucity of literature, especially comparative studies, surrounding this topic, it remains unknown whether a diagnosis of ASD increases the risk or even correlates with diagnosis of nutritional deficiencies.

A chart review[3] was conducted to identify patients with insufficient ascorbic acid concentrations at Texas Children's Hospital over a 5-year period. Of the 151 patients who were identified, 32 had an ascorbic acid concentration reported at <23 µmOl/L (0.4 mg/dL) and therefore were considered "low" per their hospital laboratory standards. Of the 32 identified, 4 patients were reported to have a neurological condition, 3 of whom were diagnosed with ASD and one who was developmentally delayed. All 4 children with neurological conditions were noted to have a lack of diet diversity.[3] Other case series[8,16–18] have found similar results, with a large percentage of those diagnosed with scurvy having a concurrent diagnosis of a neurological condition, predominantly ASD. In fact, a recent literature review[16] identified 77 cases of scurvy published between 2000 and 2018. Of those, 41% had ASD and 31% had intellectual disabilities.

Although no guidelines exist for the treatment of scurvy, the mainstay of therapy is reintroduction of vitamin C. Previous studies[19–21] have suggested a vitamin C dose of 100 to 300 mg daily in children with scurvy. The American Academy of Pediatrics recommends treating with 100 mg 3 times daily for at least 1 week, followed by 100 mg daily until symptoms have resolved.[22] As scurvy tends to occur most predominantly in those with oral aversion and/or restricted diets, treatment of this population can pose unique problems. Incorporation of vitamin C–containing foods, such as citrus fruits, should always be attempted. Families should work closely

Table 2. Pros and Cons of Vitamin C Dosage Forms

Dosage Route	Pros	Cons	Cost
Oral	• Many types of dosage forms • Easily assessable • Cheap • Easy to transport • Painless	• Requires patient cooperation • May be difficult in patients with oral aversion	$0.04–$0.10 (per mL/each)
IV/IM/SQ	• Does not require patient cooperation • Bypasses oral route in those with aversions	• Painful • Expensive • Requires special training to administer	$2.04–$2.64 (per mL)
Rectal	• Bypasses oral route in those with aversions • Does not require special training to administer	• Requires specialty compounding • Can be difficult to administer	Variable

with a nutritionist to identify foods and liquids that are tolerated by each patient.

Vitamin C can be found in a variety of oral dosage forms, including, but not limited to, capsules, chewable tablets, and powders. Oral vitamin C replacement is the preferred route of administration. In instances of severely restricted diets, it is not unusual for patients to have other concurrent vitamin deficiencies.[23–27] Because of these deficiencies, the use of a multivitamin as a standalone therapy or in addition to ascorbic acid supplementation may be necessary. Oral supplementation offers many benefits. First, ascorbic acid is found in a wide variety of dosage forms and can, therefore, be more easily customized to account for palatability and texture concerns that may accompany ASD. Second, oral dosage forms are easy to attain, routinely being stocked at local grocery stores and pharmacies. Third, oral ascorbic acid can be given without regard to meals; and, finally, the cost of many oral dosage forms is routinely inexpensive, usually costing less than $0.10 per dose.

In instances of extreme oral aversion, ascorbic acid can be administered via the IM, IV, or SQ route. Of these options, the IM route is preferred, depending on manufacturer.[28,29] Ascorbic acid is available in a 500 mg/mL (50 mL) single-use vial and can be diluted in dextrose 5% in water, sterile water for injection, or other suitable solutions. Administration via the IV route can result in infusion reactions, specifically dizziness, nausea, flushing, and/or headache.[28,29] Ascorbic acid solution for injection can be expensive, with a cost of approximately $2/mL. The cost for a 50-mL vial to our institution was $178.89. In addition to the up-front cost of the medication, the product is supplied as a single-use vial, meaning the unused portion expires 4 hours after initial puncture, thus leading to a significant amount of waste when preparing doses required for pediatric administration.[28,29] When compared with an equivalent dose of oral vitamin C, an intravenous dose is 2000% more expensive. As mentioned in our first patient case, by utilizing IV multivitamin, which cost our institution $12.03 per dose, we were able to provide a more cost-effective regimen as well as provide the patient with other needed nutrients. In addition, the feasibility of maintaining a home regimen of IM or SQ ascorbic acid requires additional equipment and training.

Finally, in cases in which neither oral nor parenteral formulations are an option, ascorbic acid can be compounded into a rectal suppository. This, however, requires specialty compounding and may therefore be a more expensive option as well. Because of our experience with multiple types of dosage forms at KCH, if patients are unable to tolerate oral ascorbic acid tablets, which can be crushed and given through an enteric tube, or liquid formulation, our recommendation is to use an IV multivitamin solution, ensuring that dosing of each component is appropriate. A list of dosage form pros and cons can be found in Table 2.

Our study had a few limitations. First, this was a retrospective chart review of patients admitted to KCH and therefore may not be generalizable to other institutions. Patients were identified via pharmacist review of charts and were not pulled from a database. Because of this method, it is reasonable that other patients may have been seen at KCH who were not included in the review. Although some patients could be reached for admission follow-up, these calls typically took place within a few days after discharge. Therefore, the authors were unable to confirm long-term outcomes and/or adherence. Additionally, some patients could not be reached for initial follow-up screening. Some patients included were found to have multiple vitamin deficiencies, which could cloud the clinical presentation. Finally, this chart review only evaluated patients who were deficient in vitamin C and, therefore, could not make any comparison to patients with ASD who were not nutritionally deficient.

Conclusions

In conclusion, oral aversion is a symptom commonly seen in the general pediatric population, and even more

so in those patients with ASD and other developmental delays. Although scurvy has traditionally been viewed as a historical disease, it is being seen more often. Treatment of scurvy centers on reintroduction of vitamin C into the diet, either via behavioral modification or supplementation. Oral supplementation may pose unique challenges in this patient population.

ARTICLE INFORMATION

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Ethical Approval and Informed Consent Given the nature of this study, the project was exempt from institution review board/ethics committee review, and informed consent or patient assent was not obtained.

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