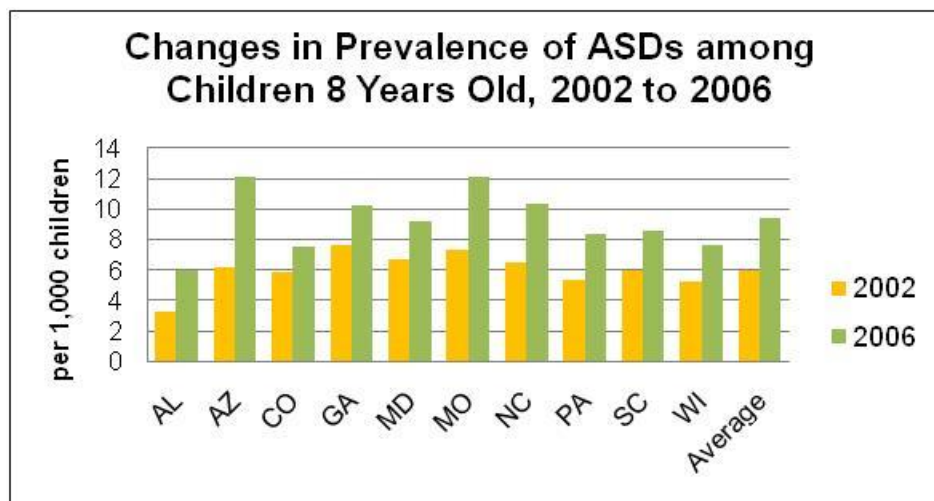


Autism Spectrum Disorders: Non-Pharmaceutical Approaches

In 2006, the CDC approximated that 1% of U.S. children 8 years of age was on the Autism spectrum (approximate range: 1:80--1:240 children [males: 1:70; females: 1:315]). The average prevalence of Autism Spectrum Disorder (ASD)s identified among children aged 8 years increased 57% in 10 of the 11 sites studied from the 2002 to the 2006 surveillance year.¹ Although delays in identification persisted, ASDs were being diagnosed by community professionals at earlier ages in 2006 than in 2002. It appears from this data that a true increase in risk for children to develop ASD symptoms may exist.



These results indicate an increased prevalence of identified ASDs among U.S. children aged 8 years and underscore the need to regard ASDs as an urgent public health concern. Early screening is now occurring in primary care clinics thanks to screening tools such as the Modified Checklist for Autism in Toddlers (M-CHAT), which asks parents 23 questions about their child. (The M-CHAT is copyrighted. Download a free copy and guidelines for use at http://www.firstsigns.org/screening/tools/rec.htm#asd_screens. Modifications to the tool will also be posted on this site.) Research is needed to ascertain the factors that put certain persons at risk, and concerted efforts are essential to provide support for persons with ASDs, their families, and communities to improve long-term outcome.

The Autism Spectrum Disorders (ASDs) form a spectrum of three recognizably different disorders. From least to most severe they are; Asperger's Syndrome, Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), and Autistic Disorder.



Co-existing Disease in ASD (Gut-Immune Link)

The prevalence of gastrointestinal (GI) disease in the autistic population is likely increased over the general population, but the actual level of increase is unclear. Studies indicate that as many as 85% of children with ASDs may suffer one GI illness as compared with 12% of the general population.² The American Academy of Pediatrics (AAP) recommends against routine testing of the GI tract in American patients with ASDs, but evaluation should be considered with recurrent or chronic symptoms.³ The family history, as well as considering the use of biomarkers or testing for allergic disease or food allergies, are paramount to quality of care in patients with ASDs as patients may not verbalize their discomfort.⁴ Some theories of disease presentation in ASDs are related to:

- 1) Increased immune and inflammatory response: This theory is based on increased gut permeability in children with Autism, with opioid-like peptides from casein and gluten being released into the serum and spinal fluid, which can then cross the blood-brain barrier in the central nervous system and limit brain maturation and function.⁵ Evidence that supports this theory is the finding of increased lymphocytes and eosinophils in gut mucosa in children with ASDs.⁴
- 2) Ileal nodular lymphoid hyperplasia and/or chronic colitis occur in higher rates in children with ASDs.³
- 3) The presence of antibodies to gliadin, casein, and gluten are increased in ASD children as compared with the general population.⁶

Disease Presentation in ASDs

Diagnosis of disease in patients with ASDs can be challenging, as decreased communication and interaction are pervasive in ASDs. Background information on common variants of disease presentation in ASDs may aid the clinician in determining the cause of disease and ultimately increase the quality of life for both the patient and the family.

Behavioral outbursts including tantrums, aggression or self injury may be an atypical presentation of abdominal disease including constipation, GERD, gastritis, or intestinal inflammation.⁴ GERD also frequently presents as sleep disturbances, which include difficulty falling asleep or increased awakenings.⁴ Sleep disturbance in children with ASDs may be due to changes in melatonin regulation, and patients may show positive response to melatonin supplementation.³ Sleep apnea should also be considered.³ Behavioral changes that may indicate abdominal concerns are the development of tics, throat clearing, screaming, whining, sighing, moaning, echolalia, and groaning.⁴ Motor behaviors may include grimaces, teeth gritting, pushing on abdomen, oral fixation with constant eating/drinking/or chewing on objects, pica, incessant tapping, change in posturing to include arching and torso rotational distortions.⁴ Increased movement with jumping or pacing, an increase or new onset of aggression, or an increase in repetitive behaviors are other motor disturbances that may reflect abdominal pain.⁴ Irritability and an increase in oppositional behavior are common manifestations of GI disorders as well.⁴ Girls may exhibit behavioral changes with onset of menstruation, and may show response to analgesics or hormonal contraception.³ Since behavioral changes can be a manifestation of any pain, other sources must be considered, such as ear, dental, musculoskeletal, urologic or skin disorders.⁴ Routine



Autism Spectrum Disorders: Non-Pharmaceutical Approaches

situations that the child associates with pain may result in behavioral outbursts with that activity. If the pain is understood, the patient can be taught methods to cope with the pain thereby leading to a decrease in behavioral outburst.

Intensive Behavioral Therapy

Applied behavior analysis (ABA) and Greenspan's floortime intervention for autism in early childhood are first line therapies with proven efficacy through randomized clinical studies. Currently most behavioral treatments use aspects from both approaches:

- **Applied Behavior Analysis (ABA)**. Psychologist Dr. Ivar Lovaas first used ABA with children with autism. This treatment teaches children to change their behavior through rewards and consequences. If children do a task when asked, they are given a small reward that means something to them. If they do not do what is asked, they don't receive the reward. This process is then repeated, ideally many hours a day.

A recent comprehensive meta-analysis suggested that long-term, comprehensive ABA intervention leads to medium to large positive effects in terms of intellectual functioning, language development, acquisition of daily living skills and social functioning in children with autism. "Although favorable effects were apparent across all outcomes, language-related outcomes (IQ, receptive and expressive language, communication) were superior to non-verbal IQ, social functioning and daily living skills, with effect sizes approaching 1.5 for receptive and expressive language and communication skills. Dose-dependent effect sizes were apparent by levels of total treatment hours for language and adaptation composite scores."⁷ Early detection and treatment are critical for optimal outcomes.

- **Greenspan's Floortime Approach**. (Also called DIR for "Developmental, Individual Differences, Relationship-Based Approach). Stanley Greenspan, MD, professor of psychiatry and a leading authority on infants and young children with developmental problems, developed a process that follows an individual child's lead. It encourages the child to initiate play and interaction. The child is immediately rewarded for attempts to interact and play with others. Then without demands being made, the child is gently challenged to master new milestones. The person playing with the child attends to the way a child responds. If the child is overly sensitive, the person may need to be soothing. If the child's response is minimal, the person may need to be more energetic. Floortime focuses on the child's feelings and relationships with caregivers and on how the child deals with sights, sounds, and smells.

Nutritional Problems in ASDs

Individuals with ASD may be resistant to introduction of new foods, and due to food, texture aversions, or hypersensitivities, may lack variability in their diets.⁸ Some children may limit their intake to five or fewer foods.⁹ ASDs may be associated with amino acid deficiencies⁹ or low vitamin D and iron levels.⁴ Autism may also be linked to less dairy and calcium consumption⁸, and concerns have been raised that implementing restrictive diets may lead to more amino acid deficiencies or bone loss.¹⁰ Research has not substantiated these concerns, and has, in fact, disputed them. Exclusion diets did not change the nutrient consumption of 3- to 16-year-old children with ASDs.¹¹ Both children with ASDs and the general population may not be consuming



Autism Spectrum Disorders: Non-Pharmaceutical Approaches

enough fiber, calcium, iron, vitamin E or vitamin B₁₂.⁸ The use of a nutritionist to aid in the development of a healthy and variable diet may be helpful. Growth should be monitored as per regular pediatric care with attention to the potential for malabsorption, maldigestion or poor nutritional quality.⁴ Obesity rates have been found to be increased over the general population in children with ASDs in the 12- to 19-year-old population.⁴

Dietary Modification in ASD

One of the most widely discussed diet modifications for children with ASDs is the Gluten-Free-Casein-free (GFCF) diet. Up to 38% of patients with ASD have used modified diets.¹²

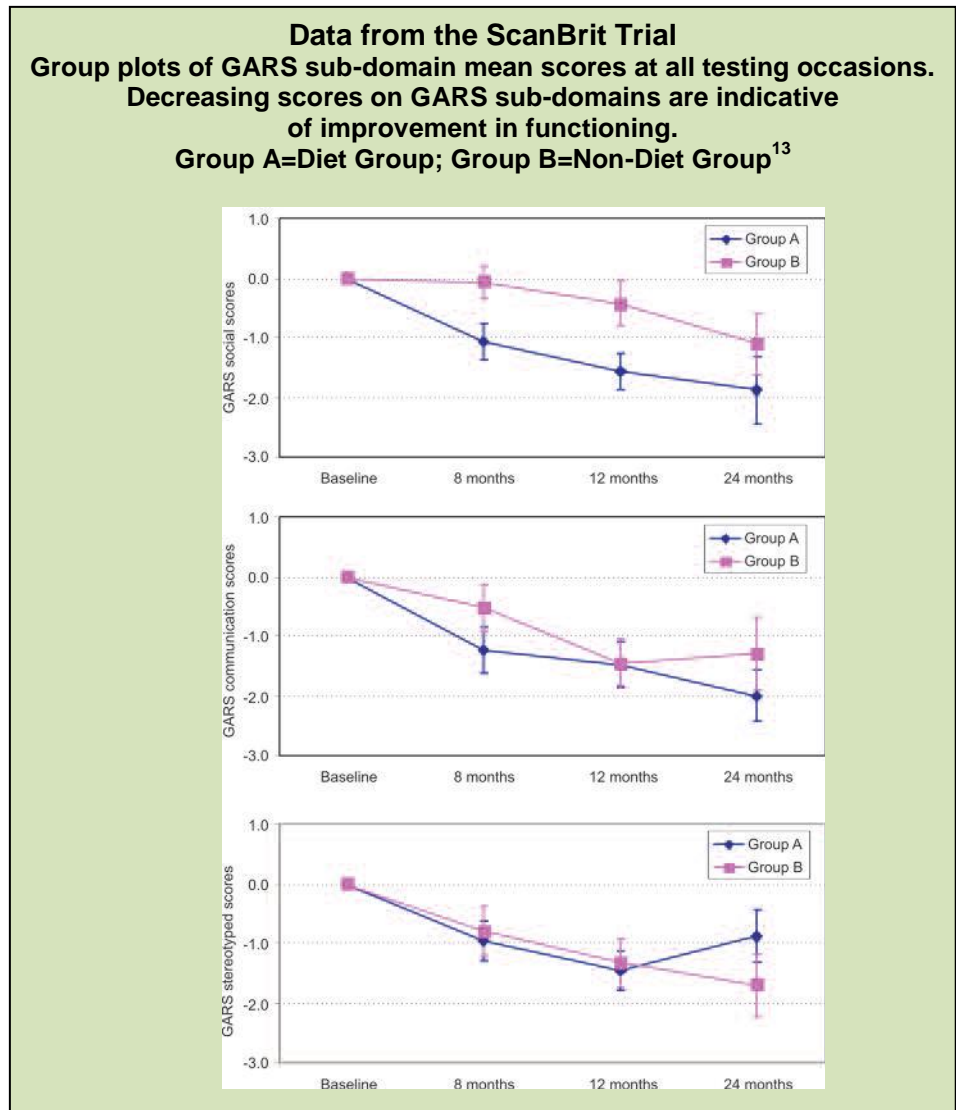
GFCF diet includes the elimination of one of the main wheat proteins, gluten, found in cereals, breads, soups and snacks along with the milk protein, casein, found in dairy products. To access information on the diet, see the *Family Resources* section of the website for Talk about Curing Autism: <http://www.tacanow.org/tag/gfcf/>.

In one study published in 2006, there was no recordable difference on the Child Autism Rating Scale (CARS) or the Autism Diagnostic Interview-Revised (ADI-R) after 12 weeks on the diet. However, 9 out of 15 families who participated in this study opted to keep their children on the GFCF diet.⁶ Parents of 7 of the 15 children reported improvements in language and behavior, including decreased tantrums and hyperactivity.⁶

The ScanBrit trial was a randomized, controlled, single-blind study of the GFCF diet published in 2010 that resulted in significant improvements in Autism Diagnostic Observation Schedule (ADOS) and Gilliam Autism Rating Scale (GARS) scores by the participants on the diet.¹³ Seventy-two Danish children were randomized to the GFCF diet or a control group for 12 months, then extended to 24 months due to the positive outcomes. At 12 months, 26 children were participating in the diet and 29 were on the control diet. Of note in this study, improvement was seen at 8 to 12 months on the diet, stressing the importance for adequate length in these studies, a standard that is not frequently met. Improvements were seen in attention, concentration, social interaction and decreased hyperactivity. Stereotyped and repetitive behaviors also improved with a “sustained trend” after 24 months.¹³

When recommending a GFCF diet, the clinician should look for local support and guidance for families from other parents and professionals. A detailed evaluation of the child’s current health and dietary habits should be obtained before implementing a GFCF diet.² The estimated time for parent education on the GFCF diet is 3 hours.¹⁰ Clinicians should plan to regularly monitor the health and growth of the child.²

In our [patient handout](#), we have provided a nutritious smoothie recipe that you can share with families. A child with ASD may find this appealing. The recipe contains whey protein powder, which promotes glutathione production. (Some children with ASD have too little glutathione in their bodies.) Advise families to look for casein-free options of whey protein powder, although you may want to eliminate whey entirely due to contamination with casein during processing.



Antifungal Therapy

At this time, empiric antibiotic and antifungal therapy is not recommended.⁴ Abnormal cultures from the duodenal aspirate or an abnormal stool culture should be obtained before antimicrobial treatment (which alters the gastrointestinal flora) is initiated.⁴ Anecdotal cases of significant improvement on antifungals and antibiotics do exist, with one child who suffered from chronic constipation and fungal/bacterial infections in addition to ASD exhibiting dramatic improvement when placed on an anti-yeast, and di/polysaccharide free diet.¹⁴ This diet is based on the theory of complex carbohydrates being less readily absorbed leading to gut inflammation and promotion of yeast and gut bacteria that may cause GI symptoms of bloating, constipation and diarrhea.¹⁴ Theories of systemic yeast infections are the basis for treatment with systemic antifungals such as fluconazole.¹⁴



Chelation Therapy

While the FDA has approved the use of metal chelators for acute metal poisoning, chelation in the absence of acute poisoning is an off label use that has resulted in 800,000 physician visits per year.¹⁵ Critics have stated that chelation therapy is risky with little potential efficacy. Further, opponents of chelation therapy argue that even if ASDs were caused by mercury poisoning, the cell damage would be irreversible.¹⁶ Risk of chelators include depletion of essential elements, such as copper, zinc, selenium and calcium.¹⁶ Proponents for use of chelators in ASDs state that autistic children may have an increased susceptibility to toxic chemicals due to lower levels of detoxifying enzymes such as glutathione, cysteine and sulfate.¹⁷

Higher levels of urine porphyrin in patients with ASDs may be linked to higher levels of mercury in children with autism, and the use of chelators has been shown to reduce urine porphyrin levels in three separate studies.¹⁸ ASD children may be genetically susceptible to higher levels of mercury in their body and susceptible to mercury toxicity due to a reduced ability to excrete mercury due to lower glutathione levels.¹⁸ Evidence showing that the use of chelators can improve symptoms in addition to the reduction of porphyrin levels is lacking.¹⁶

Trials funded by the NIH on chelation therapy were halted due to ethical concerns with the informed consent process.¹⁵ Due to the cessation of NIH funded trials, data is not likely to be produced in the foreseeable future.

Methyl B₁₂ and Folate

Methyl B₁₂ supplementation in ASDs is based on the theory that while levels of B₁₂ within the body may be normal, intracellular transport of B₁₂ in ASDs may be impaired.¹⁹ Methyl B₁₂ may be more effective than plain B₁₂ at methylation, which is needed to make glutathione and SAME. Like the GFCF diet, there may be very responsive sub-populations to vitamin B₁₂ injections.¹⁹ This response is assumed to be the result of an overall reduction of oxidative stress.¹⁹ Similar results have been produced with folate supplementation.²⁰ In a case study, one child with normal folate and B₁₂ serum levels had decreased levels of folate in the CSF. Her response to treatment was dramatic.²⁰ At this time it appears that lab testing will not reliably identify which children may or may not respond to Vitamin B supplementation. Until further research results are available, its routine use is not recommended.

Omega 3 Fatty Acid Supplementation

Omega 3 fatty acids are essential components of cell membranes and are quickly incorporated into neural tissue. Changes in dietary lipid content can be reflected in changes in neural lipid composition within days to weeks.²¹ Several studies have indicated abnormally low levels of Omega-3 fatty acid in children with ASDs, while others have reported normal values, indicating that perhaps there is, again, a subset population responsive to therapy.²² Randomized controlled trials of children with ASDs and omega-3 fatty acid supplementation are both limited and underpowered.²² Several studies have shown improvement with omega-3 fatty acid supplementation, but these studies have also been under-powered, unblinded, or without controls.^{21,22} A 2009 pilot study showed improvement in 8 of 9 children with psychiatric testing outcomes at 6 and 12 weeks who were supplemented with 500 mg twice daily, however this study was underpowered and lacked controls.²¹ The lack of research on omega-3 fatty acid supplementation is surprising considering its safety and that it is among the most commonly



implemented complementary alternative medicine (CAM) therapies for ASDs.²² Currently the evidence is insufficient to recommend omega-3 fatty acid supplementation for treatment, but small studies have shown positive trends toward improvement.²² Clearly, further research is needed, especially in the context of what seems to be few adverse effects and a relatively low-cost therapy.²² ([See also our handout on Omega 3 Fats.](#))

Probiotics

Research on the use of probiotics in the treatment of ASDs is limited, and yet it is one of the more frequently used treatments in ASD and one that physicians are more likely to recommend.²³ The use of probiotics is advocated based on the “leaky gut” theory of increased permeability, the theory of bacterial overgrowth, as well as studies indicating candidal excess in the GI tracts of ASD children.^{24,25} Anecdotal cases are prevalent, but evidence based medicine is limited.²³ Unfortunately, no peer-reviewed trials exist at this time.²⁵ Despite probiotics having a “generally recognized as safe” (GRAS) designation, a recommendation for probiotic therapy for ASD cannot be made until further trials are conducted. ([See also our handout on Probiotics.](#))

An Approach to Consider for Children with an ASD

Following is an example of an approach to consider when seeing a child with a diagnosed or suspected ASD:

Presentation

A two-year-old female fails the M-CHAT screening at her 2-year-old Well Child Check (WCC). The patient’s mother is present and has expressed concerns about her daughter’s slow language acquisition, chronic constipation, and eczema.

Intake evaluation

- Convert the WCC visit to a problem-focused visit. Follow guidelines to tease out details of the failed M-CHAT to rule out false positives.
- Perform a targeted physical exam to rule out concomitant disease processes:
 - HEENT (signs of inflammation—chronic rhinitis, OM, tonsil hypertrophy/obstruction)
 - Skin (eczema, Candida dermatitis)
 - Abd exam (tenderness to palpation, cords of stool indicating constipation)
 - Neuro/Musc (eval for hypo/hypertonia)
- Refer appropriately to help obtain a timely diagnosis if justified.
 - (Families can be referred to the website of the National Dissemination Center for Children with Disabilities:
<http://www.nichcy.org/FamiliesAndCommunity/Pages/Default.aspx> . Direct them to click on “State Specific Info” to locate someone in their area who will provide guidance on the process. Or families can call **1-800-695-0285** to learn to whom to speak in their area. They should ask that their child be evaluated under the Individuals with Disabilities Education Act--IDEA).



Key lab tests

As a baseline consider ordering:

- CBC,
- CMP,
- 25-hydroxyvitamin D,
- Carnitine (for hypotonia)
- If there is metabolic acidosis, consider urine for organic acids and refer to genetics if abnormal.

Order other tests as needed if history and/or physical reveal other concerns.

Nutrition

If other disorders are ruled out, a trial of the GFCF diet is warranted in patients newly diagnosed with an ASD. Refer the family to a nutritionist, and for support try to connect them with other families using the GFCF diet. The website www.tacanow.org has excellent information for families. Plan to see the child every 2-3 months for the first year after the diagnosis and dietary change to document growth and response. The results of the SCANBRIT study suggest a trial diet of 6-12 months in duration.

Behavior therapy

Early behavioral intervention is critical for children with ASDs. Refer families to an Early Intervention Program. Each state has a lead contact agency that will provide further guidance to families on the process. Refer families to the website of the National Dissemination Center for Children with Disabilities: <http://www.nichcy.org/FamiliesAndCommunity/Pages/Default.aspx>. Direct them to click on "State Specific Info" to identify their state's lead agency for early intervention services. Or families can call **1-800-695-0285** to learn to whom to speak in their area. Direct parents/caregivers to request that the child be evaluated/treated under the Individuals with Disabilities Education Act (IDEA).

Supplements

At a minimum, recommend a MVI and fish oils. Consider all the following:

- Multiple vitamin
- Vitamin D3, 1000 IU daily
- Probiotics (Florajen4Kids, Primadophilus or Culturelle Jr.)
- Fish oils, 1-2 grams of DHA/EPA daily (Coromega or Barleans Omega Swirl)
- If evidence of hypotonia, consider Levocarnitine, 50 mg/kg/day divided in 2-3 daily doses. Maximum dose = 3 gms daily.

Follow up

A diagnosis of ASD is obviously very powerful and affects the whole family. Plan to see the child back within 3 months of initial diagnosis. The parents may benefit from an individual visit to explore their reactions and answer questions surrounding the diagnosis. There are some very sobering statistics affecting families, such as a divorce rate of 75% in those with autistic children.



Resources

- **M-CHAT**. The M-CHAT is copyrighted. Download a free copy and guidelines for use. Modifications to the tool will also be posted on this site.
http://www.firstsigns.org/screening/tools/rec.htm#asd_screens .
 - **GFCF Diet**. See the *Family Resources* section of the website for Talk about Curing Autism: <http://www.tacanow.org/tag/gfcf/>.
- Referral to Early Intervention Program**. Refer families to the website of the National Dissemination Center for Children with Disabilities:
<http://www.nichcy.org/FamiliesAndCommunity/Pages/Default.aspx> . Direct them to click on “State Specific Info” to identify their state’s lead agency for early intervention services. Or families can call **1-800-695-0285** to learn to whom to speak in their area.
- **Information from the CDC**. To access information for health care providers on ASDs from the CDC, go to <http://www.cdc.gov/ncbddd/autism/hcp.html> .
 - **See the accompanying [patient handout](#) for additional resources for families.**

Books for Clinicians and Families

- ***A Friend Like Henry*** by Nuala Gardner; Sourcebooks, Inc., 2008.
The true story of a boy with autism and the dog who unlocked his world.
- ***The Horse Boy*** by Rupert Isaacson; Little, Brown and Company, 2009.
The story of a family who goes to the ends of the earth to find a way into their son’s life.
- ***Engaging Autism*** by Stanley Greenspan, MD and Serena Wieder, PhD.; First Da Capo Press, 2006.
Describes how to use the floortime approach to help children with ASDs relate, communicate and think.
- ***Changing the Course of Autism*** by Bryan Jepson, MD, with Jane Johnson; First Sentient Publications, 2007.
Describes a scientific approach to autism for parents and physicians.
- ***Autism: Effective Biomedical Treatments*** by Jon Pangborn, PhD and Sidney MacDonald Baker, MD; Autism Research Institute, 2005.
Provides information on testing and treatments.

A corresponding [handout for patients](#) on ASDs is also available.



Autism Spectrum Disorders: Non-Pharmaceutical Approaches

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