

Autism and Nutrition: Are Kids What They Eat?

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Personal Disclosure

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- **Maureen Geraghty, PhD, RD, LD**
 - The Ohio State University LEND Program
- **Clara Lajonchere, PhD**
 - Autism Speaks
- **Patricia Novak, MPH, RD**
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Overview

- Is there a link between diet/nutrition/GI tract/ feeding and autism?
 - History/hypotheses/rationale for dietary approaches
 - Recent *Consensus Statement* on recommendations for diagnosis and treatment of GI disorders in ASD
- Clinical perspectives: how do we support families who want to follow special diets?
 - Characteristics of the “gluten-free/casein-free” diet
 - Nutrition issues/concerns
- Current research
 - STAART protocol (Rochester)
 - Autism Intervention Research – Physical (AIR-P) (Combating Autism Act Initiative)

Autism Spectrum Disorders Diagnostic Criteria

- Qualitative abnormality of social give and take
- Qualitative abnormality of language
- Repetitive behaviors/restricted interests
 - Unusual sensory behaviors (DSM 5 version?)

AND...

- Onset before age three not better explained by another diagnosis

NOTE...

- **Diagnostic criteria for ASD do NOT include GI (or other medical) symptoms.**
- **Clinical practice guidelines for ASD do NOT include routine consideration of GI (or other medical) problems**

Autism and the Gut

- However, multiple reports describe **chronic** GI dysfunctions/symptoms in 9% - 84% of children with ASD
 - Constipation
 - Diarrhea
 - Abdominal bloating, discomfort, irritability
 - GI reflux or vomiting
 - Pathological findings :
 - inflammation of the GI tract
 - abnormalities of the enteric nervous system
 - compromised gut microflora
- Active research currently on-going
 - GI issues
 - Dietary issues
 - Feeding issues

History: Autism and the Gut

- 1961: Asperger suggested a link with celiac disease (gluten intolerance)
- 1992: Gobbi et al reported a connection between the neurological and GI systems in some with celiac disease and epilepsy
- 1990s: Parent groups such as Cure Autism Now (CAN) began organizing to push for more biomedical research
- 2009: Campbell et al:
 - Showed that a variant in the promotor of the gene responsible for an important gut enzyme is associated with ASD
 - **First study to demonstrate a possible genetic cause for the association between autism and GI disease**

Autism and the Gut

- Rationale for looking for “biomedical”, and specifically dietary, approaches to treatment for ASD:

Other disorders suggest a link between brain development and function, behavior and diet

- Seizure disorders
 - Ketogenic diet used in children with intractable seizures
- Metabolic disorders
 - Phenylketonuria (PKU), galactosemia, etc. where lack of a specific enzyme causes significant behavioral and cognitive issues
 - Behavioral/cognitive issues treatable with diet

Dietary Treatments for Symptoms of Autism

- Complementary therapies popular
 - 30% of children with ASD on dietary interventions by the time of diagnosis (Levy et al, 2003)
 - 41% of respondents reported benefits with dietary and nutritional treatments (Hanson et al, 2007)
- Interactive Autism Network (IAN) survey (Hyman, 2009)
 - 54% of respondents using supplements
 - 30% using dietary intervention

Feeding Problems and Autism



Author	N	Prevalence	Discussion
Raiten and Massaro, 1986	40 ASD 34 TD	<u>Food idiosyncracies</u> in 53% v. 18%, <u>won't chew</u> 17.5% v. 6%	No difference in preference for same foods or refusal/dislikes
Schreck et al, 2004	138 ASD 298 TD	<u>Food refusal</u> more common with ASD	Ate fewer foods within each food group
Schreck and Williams, 2006	138 ASD	72% <u>restricted</u> , 57% <u>refusal</u> (touching, presentation, texture, oral motor)	Preferred fewer foods than their families, family greater influence than ASD!
Valicenti-McDermott, 2006	56 ASD 50 DD 50 TD	<u>Selectivity:</u> 60% ASD, v. 36% DD, v. 22% TD	Smelling and not mixing foods more common in ASD

S. Hyman, 2009

Food refusal in ASD may be secondary to:

- Obsessions
- Perseverative interests
- Sensivity to taste and/or smell of food
- Sensitivity to food textures
- Food neophobia (fear of new foods)
- Operant behavior
 - learned aversion
 - punishment e.g. pain



S. Hyman, 2009

Diet “Therapies”: Rationale

GI: Immune/Inflammation /Food Sensitivities/Allergies

- **Gluten-free, casein-free diet (GFCF):** undigested peptides from these proteins cross the intestinal wall (“leaky gut”) and disturb brain neurotransmission causing, or increasing, behavioral symptoms.
 - Increases in urinary peptides seen in some children with ASD.
- **Probiotics:** replace harmful gut flora, possibly resulting from overuse of antibiotics , which may secrete neurological toxins and contribute to the “leaky gut” .
 - Stool samples have shown an excess of “bad” bacteria in some children with ASD
 - Survey of 600 primary care physicians indicated that 19% recommended probiotics for children with ASD; 59% supported families who wanted to use them. (Golnik & Ireland, 2009)

Diet “Therapies”: Rationale

Nutrient Deficiencies

- **Vitamin B-6 (and magnesium):**
 - B-6 plays an important role in neurotransmission
 - Relative B-6 deficiency due to lack of enzyme needed to convert it to its active form.
 - Magnesium given to prevent B-6-induced Mg deficiency
- **Omega -3 fatty acids:** essential fatty acids necessary for brain development
 - Low blood levels in some children with ASD
 - Oral supplementation used by ¼ families (Geraghty, 2009)
 - Reported improvements in behavior following a well designed pilot trial (Amminger et al, 2007)

Diet “Therapies”: Rationale

Metabolic Abnormalities/Oxidative Stress /Inflammation

- **DMG/TMG** (di/trimethylglycine):
 - methyl donors enhance the immune response and neurotransmitter production
- **Vitamin B-12 and folic acid/glutathione**
 - Evidence that methylation pathways may be altered, compromising anti-oxidant/detoxification capacity.
 - Single-nucleotide polymorphisms (small differences in genes) related to these pathways have been identified in children with ASD and their families.

Why do parents choose diets/supplements for their child?

- Frustration with the limitations of current therapies; hope for a cure or improvement in behavior
- Comfort in knowing they have done everything possible for their child; wanting to have some control over the treatment
- Preference for “harmless” treatments vs. drugs
- Dramatic testimonials abound
 - Active promotion at autism conferences attended by parents
 - Websites
- They may give the therapy credit for changes that may have occurred anyway. The greater the efforts, the more biased they may be towards seeing them “pay off”

Defeat Autism Now (DAN!)

www.autism.com/dan/index/htm

- Autism Research Institute (ARI)
 - Founded in 1967 (Bernard Rimland)
 - Supports research and its dissemination on:
 - Triggers of autism
 - Methods of diagnosing and treating autism
- Defeat Autism Now (DAN)
 - Begun in 1995 as a project of the ARI dedicated to educating parents and clinicians
 - “Parents and clinicians who do not regard psychotropic drugs as the best or only means of treating autistic patients will welcome the chance to learn effective strategies for addressing the medical illnesses associated with autism”

Defeat Autism Now (DAN!)

Protocol (www.autism.com/dan/index.htm)

- Eliminate dairy products
- Eliminate cereal grains
- Eliminate foods with refined sugars
- Supplement the diet with vitamins and minerals
 - Vitamins: C, B-6, pantothenic acid
 - Minerals: calcium, magnesium
 - DMG
 - Pycnogenol (“natural” anti-inflammatory)
 - GABA (gamma amino butyric acid) neurotransmitter inhibitor

Autism and the Gut

- **Consensus Report: (Buie et al, *Pediatrics*, Jan., 2010)**
 - Sponsored by the Autism Forum (NW Autism Foundation, **Autism Research Institute**, Autism Society of America, Easter Seals of Oregon)
 - 28 participants representing 10 disciplines, multiple organizations nationwide (also international)
 - 7 working groups, including “nutrition”
 - Publications were identified, graded and evaluated by consensus
- **General findings:**
 - **General absence of high-quality research data preclude evidence-based recommendations at this time**
 - Case reports, epidemiological or poorly controlled studies
 - Consensus Statements (23) developed, refined and accepted

Consensus Statements:

Autism and the Gut (Buie et al, 2010)

- **GI disturbances in ASD, likely highly prevalent, are incompletely understood and may be difficult to evaluate because of problems communicating discomfort/pain**
- Children with ASD and GI symptoms may have more problem behaviors than others with ASD; these may be a sign that a GI evaluation is warranted. Consensus statements (CS) 1-3, 6, 7
- **GI disturbance *specific* to ASD has not been established;** evidence for abnormal GI permeability in ASD is limited and the studies methodologically challenged (CS 4, 5)

Consensus Statements: Autism and the Gut (Buie et al, 2010)

- ASD caregivers and health care providers need to know how to recognize signs and symptoms of GI disorders and other nutritional problems (CS 8, 9)
- **Evaluation by a nutritionist recommended**; anthropometry should be monitored, those with limited diets or taking supplements should be evaluated (CS 9, 10, 16)
- **Additional studies needed** before recommending specific diets for ASD; **data do not support the use of a casein-free or gluten-free diet (or both) as *primary treatment*** (CS 11, 12)

Consensus Statements:

Autism and the Gut (Buie et al, 2010)

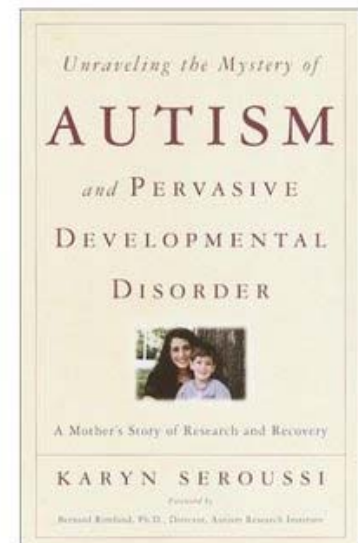
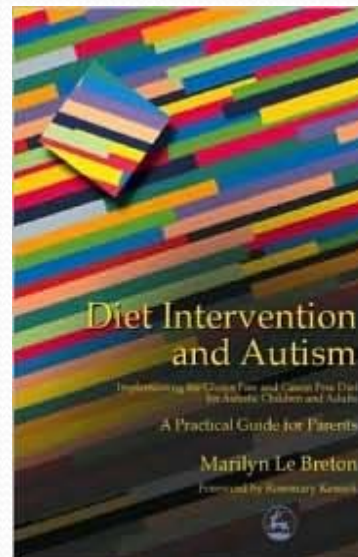
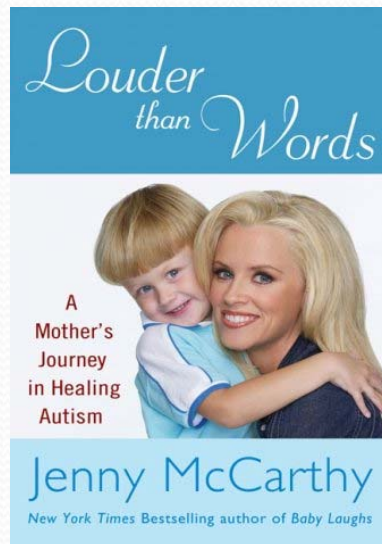
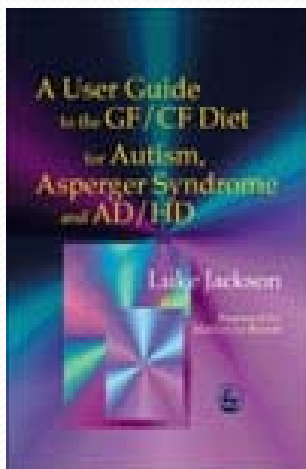
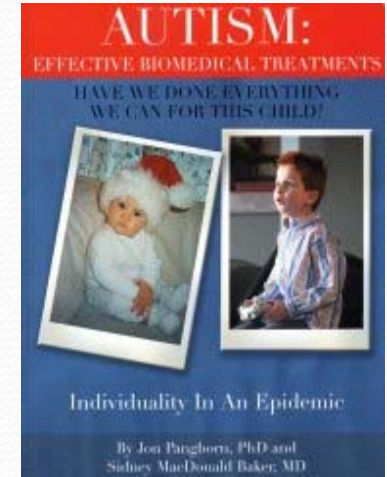
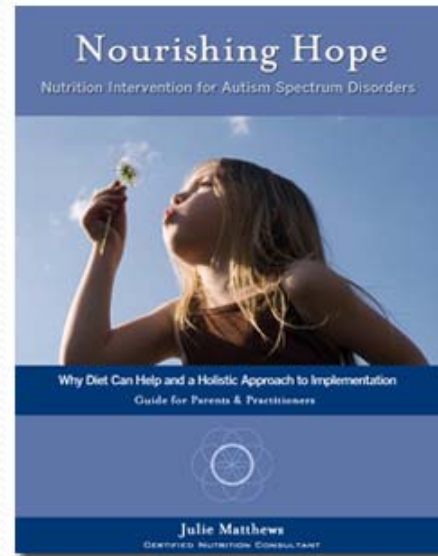
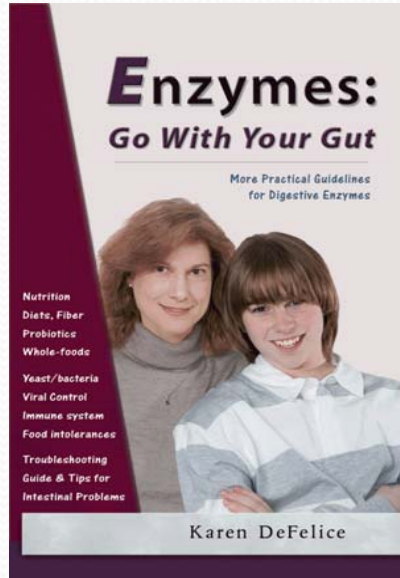
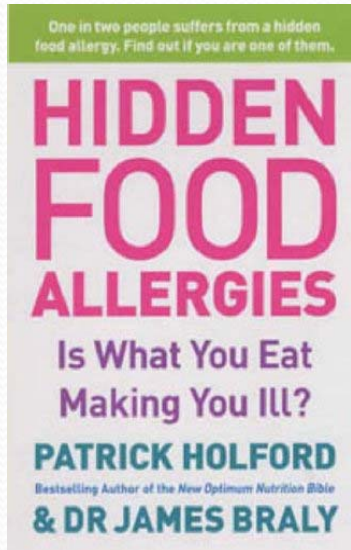
- Detailed history to identify potential associations between GI and/or behavioral symptoms and allergies should be done; **involvement of specialists (GI, nutrition, feeding therapists) can be beneficial** (CS 13-17)
- **Direct relationship between immune dysfunction and ASD not yet proven, but warrants further investigation** (CS 17, 18)
- Well-defined phenotypes and genotypes will enhance further clinical investigations (CS 20 – 23)

Parent Perspective

“I understand the importance of research. However, if I wait for ‘science’ to provide the data, it will be too late. My child will be grown. I have to know something now. I have decisions to make now.”

Quote from a parent attending a conference on complementary and alternative medical therapies in autism: (Elder, 2008)

“Biomedical” Solutions to the Problem?



Where do families get referrals for complementary/alternative therapies?

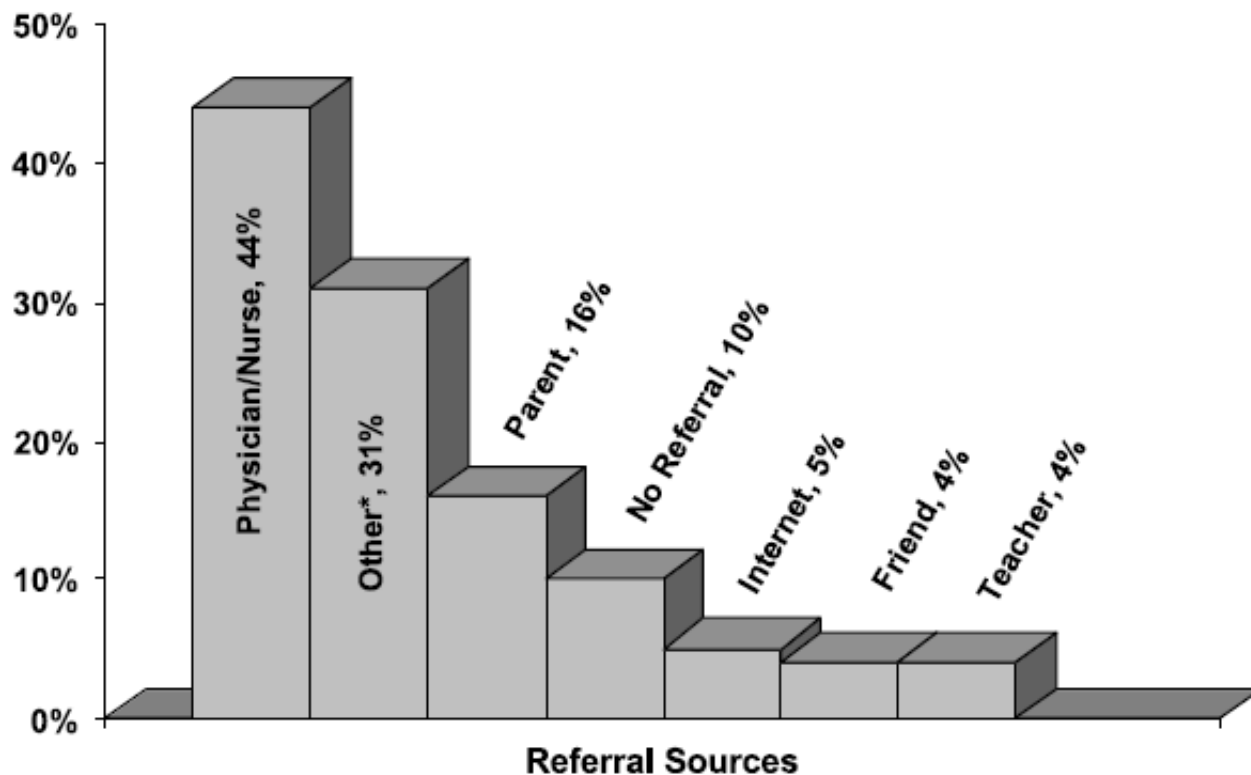


FIGURE 1. Self-reported sources of referrals for complementary and alternative medicine (CAM) therapies. N = 70.

*Other: Nutritionist/chiropractor.

Characteristics of the Gluten-Free/ Casein-Free (GF/CF) Diet

Gluten

Foods to Avoid

- Wheat
 - wheat starch, wheat bran, wheat germ, cracked wheat, hydrolyzed wheat protein
 - einkorn, emmer, spelt, kamut, faro
 - durum, graham, semolina
- Barley
- Rye
- Triticale (cross between wheat & rye)
- Malt, malt flavoring, malt vinegar (generally made from barley, verify the source)

Gluten

Foods to Check (may contain gluten)

- Bouillon cubes
- Brown rice syrup
- Candy
- Chips/flavored potato chips/seasoned tortilla chips
- Cold cuts, hot dogs, salami, sausage
- Communion wafers
- French fries
- Gravy
- Vegetables in sauce
- Breading & coating mixes



- Soy sauce
- Energy bars
- Imitation bacon
- Marinades
- Herbal & nutritional supplements
- Drugs & OTC medication
- Play-Doh ©
- Imitation seafood/ fish
- Matzo
- Rice mixes
- Sauces
- Soups
- Self-basting turkey



Oats

Need to be certified gluten-free

- Oats do not contain gluten, but may be contaminated with wheat during processing
- Celiac.org no longer strictly limits oats



Characteristics of the GF/CF diet

Casein

Foods to Avoid

- Dairy (Milk, yogurt, butter, cheese, cream, cream cheese)
 - casein, caseinate, lactose, whey

Foods to Check (may contain casein)

- Baked goods (bread, pastries, pies)
- Non-dairy creamer (will say “milk” in ingredients)
- Whipped Topping
- Soy Cheese
- Candy
- Sauce (tomato, pesto)
- Salad dressing
- Cereals

Sounds like Dairy/Milk, but does not contain milk, so OK

- Calcium lactate, calcium/sodium stearoyl lactylate, cocoa butter, cream of tartar, lactic acid, sodium lactate



GFCF Nutritional Consequences

Hediger et al. 2007	75 ASD males	Effect of decreased bone cortical thickness in ASD males greater on casein-free diet
Herndon et al. 2008	46 ASD 31 TD (14 GFCF)	More Vit E & less Ca than control
Cornish 2002	37 ASD (8 GFCF)	<u>No differences</u> in nutrient intake on/off diet

Potential nutritional issues with the DAN (CFCF+)Diet

- Potential nutrition problems with the DAN! Protocol
 - Lack of dairy –
 - **vitamin D** at risk as well as **calcium** (bone density issues).
 - often a major source of **protein** for children
 - Lack of grains – **B vitamins, iron**
 - **Lack of refined sugars.... not a problem!**
- Vitamin/mineral supplementation may not be appropriate, sufficient or safe (not regulated)
 - Children's multivitamins lack enough calcium and vitamin D
 - "Gummy" formulations lack iron
- Recommendations for diet may be influenced by profit or ideology (DAN physicians often sell the products as well)

Helping Families Decide: They should know the risks/difficulties

- Discuss with parents
 - Safety of the diet: toxicities; potential deficiencies
 - Efficacy of the diet (based on current evidence)
- Difficult to follow especially when a child eats outside of the house (school, Grandma's)
- Further isolates the child from peers
- Can be more costly than a traditional diet
- If the child is a "picky eater" or has feeding problems, these may be complicating factors when introducing a restrictive diet
- Can lead to nutritional deficiencies ; the more restrictive the diet the greater the risk.

Helping Families Decide: Planning to start the diet

- Do they have the necessary resources?
 - Financial
 - Time and effort
 - Availability of acceptable foods
- Are there plans to ensure dietary compliance (e.g. lists of safe foods?)
 - At home (other family members?)
 - At school
 - At Grandma's
- Are there sources of support to begin/maintain the diet?
 - Clinicians (physicians/nutritionists/dietitians /nurses)
 - Teachers; day caregivers
 - Other parents/parent groups

Improving the GFCF diet

Concern

- Fiber intake
- Calcium, vitamin D intakes
- Iron/zinc intakes

Intervention

- Increase fruits & vegetables
- Increase nuts, flaxseed meal
- Use fortified dairy alternatives
- Increase use of non-dairy calcium sources
- Increase use of meats, beans, fortified foods

Possible Drug-Nutrient Interactions

• ADHD

- Concerta
- Strattera

- ↓ appetite
- ↓ appetite, nausea, vomiting, constipation, diarrhea

• Anticonvulsant

- Depakote
- Keppra

- GI irritation, nausea, vomiting, diarrhea, ↓ serum D and calcium

• Antipsychotic

- Zyprexa
- Risperdal

- Weight gain, ↑ appetite

GFCF Studies

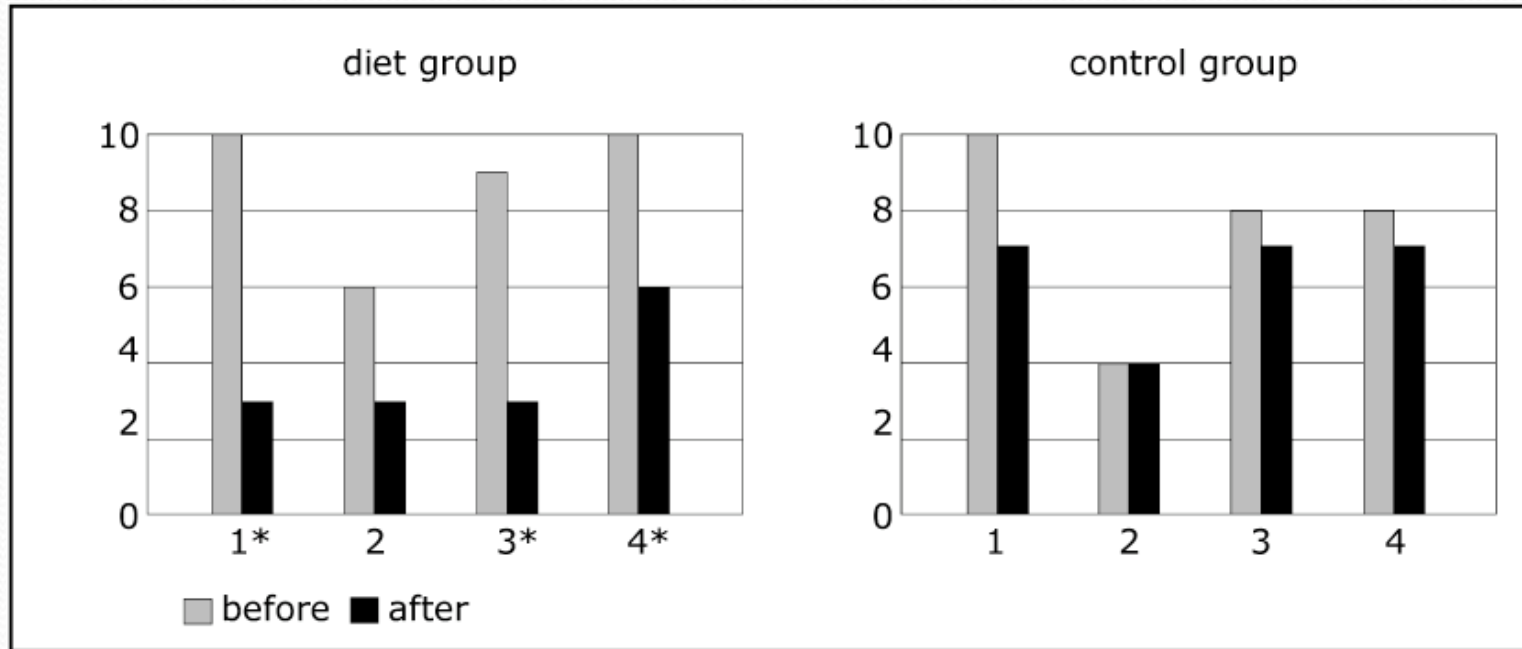
There have been 8 clinical trials, but only 2 were controlled studies

Author	Design	N	Measure	Outcome
Knivsberg 2002	Single blind, Peptide pattern	20	ITPA, DIPAB Over 1 yr	Significant effect in: overall autistic traits, social interaction, and ability to communicate & interact
Elder 2006	Double blind, placebo controlled, crossover	15	CARS, EOC	No change

Methodological difficulties in conducting nutrition/dietary research

- Time-consuming/labor intensive/expensive
- Need to control for concurrent therapies
- Subjectivity hard to overcome
 - Dependence on parental report – accuracy?
 - Adherence to diet – difficult to confirm
 - Controls - hard to disguise what we eat
 - Supplements: difficult to include in analyses of nutrient intake
 - Placebo effect

Improvements noted are hard to measure



1. Aloofness

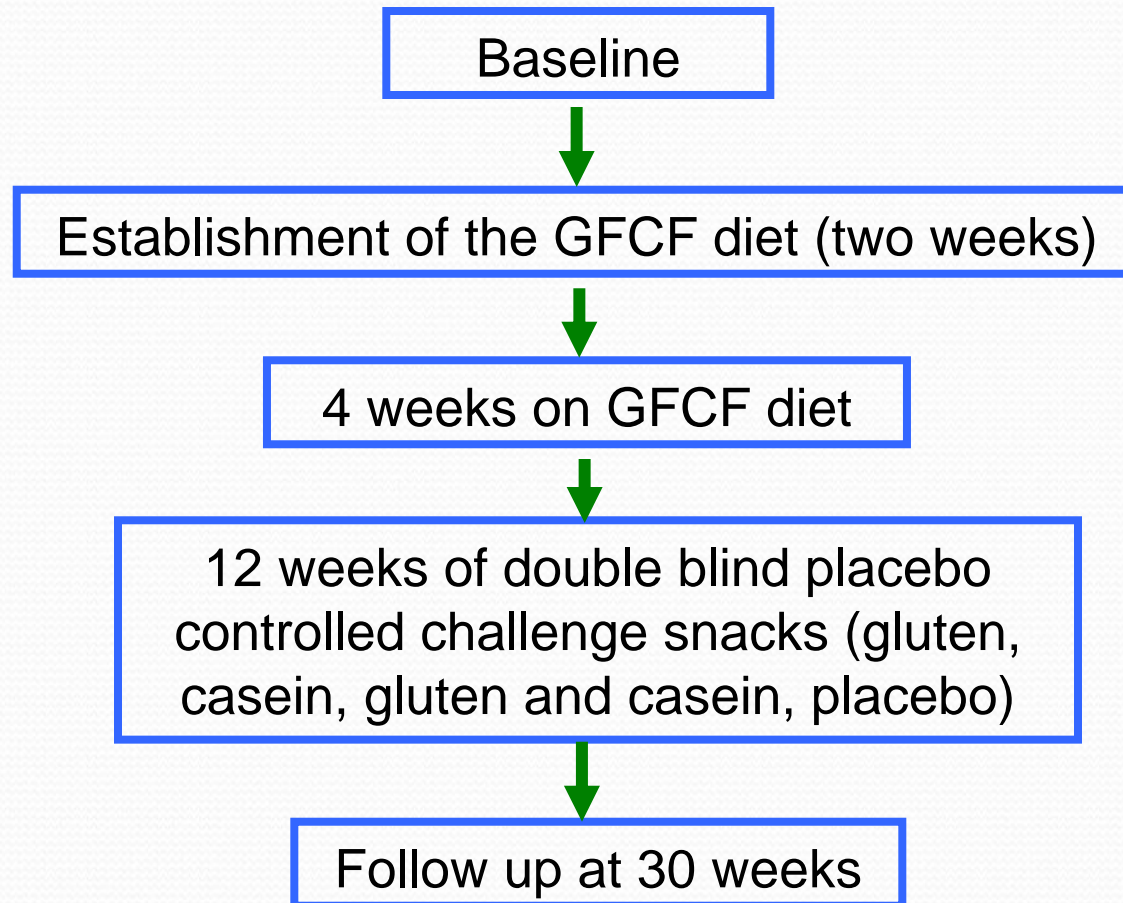
2. Distractibility

3. Routines and rituals

4. Response to teaching

-Knivsberg 2002

Studies to Advance Autism Research and Treatment (STAART) Diet Study Protocol



Autism Treatment Network:



- Established in 2005 as a program of Autism Speaks with the goal of setting best practices for medical management of children with ASD
- 3-fold mission:
 - Establish a network of academic medical centers to model coordinated, interdisciplinary care for children/youth with ASD
 - Develop and disseminate evidence-based standards
 - Implementing a data-registry to track treatments and outcomes for patients at ATN sites
- 17 sites across the US and Canada
- Targeted areas of interest (family-driven):
 - **GI symptoms**
 - Sleep
 - Neurologic/metabolic/genetic evaluations

Combating Autism Act, 2006

- Combating Autism Act Initiative (CAAI) established by, and administered through, the Maternal and Child Health Bureau (MCHB), HRSA, DHHS (nearly \$950 million over 5 years)
- MCHB created, through a competitive granting process in 2008, a 3-pronged effort to “combat autism” (3 year grants)
 - **Training:** expanded funding to MCHB-funded training programs to provide graduate-level clinical training specific to ASD :
 - 39 interdisciplinary *Leadership Education in Neurodevelopmental Disabilities* – LEND Programs) (plus 4 planning grants)
 - 10 Developmental-Behavioral Pediatrics Leadership Training programs
 - **6 state Title V programs** funded to develop/coordinate state-wide service-related activities (early screening, diagnosis, intervention)

MCHB Autism Intervention Research Networks (AIR-P; AIR-B)

- **AIR-P:** focus on physical health; a \$12 million grant went to the ATN (PI: James Perrin, MD, Mass. General Hospital, Boston; co-PI: Clara Lajonchere, PhD, Autism Speaks, USC/CHLA)
 - Sleep disorders
 - GI disorders
- **AIR-B:** focus on behavioral health (also a consortium); grant to UCLA (PI: Connie Kasari, PhD)

AIR-P Objectives

- Conduct research on evidence-based practices for interventions.
- Develop evidence-based guidelines for clinical care
 - Provisional guidelines addressing GI disorders (constipation) are being pilot-tested and will be due out soon
- Disseminate toolkits, research findings and clinical consensus guidelines to pediatricians, other primary care providers, specialty physicians and families.

AIR-P: Diet and Nutrition

- Provide prospective and accurate data to allow for guideline development regarding diet and nutrition for children with ASD
- Obtain accurate data regarding *What Children with Autism Eat in America*, a topic of great interest to parents and clinicians



- Are diets with limited variety providing adequate nutrition?
- Do commonly used supplements have side effects?
- Are low iron stores associated with sleep problems?
- Could diet be related to GI symptoms?

AIR-P Diet and Nutrition Study

- *“Diet and Nutrition in Children with Autism Spectrum Disorders: An Autism Treatment Network Collaborative Study”*
- Co- Investigators:
 - PI Susan L. Hyman, MD (Rochester, NY)
 - 4 other ATN sites with prior research in the area of diet, nutrition and ASD : Arkansas, Cincinnati, Colorado, Pittsburgh
- Subjects: 450 children with ASD enrolled from all ATN sites.
- Objectives:
 - Evaluate nutritional status of children with ASD
 - Examine potential relationships of dietary intake with feeding behavior, food preference and family food preference

Additional AIR-P Diet and Nutrition Studies

- *“Bone Mineral Density in Children with Autism Spectrum Disorder”*
 - Investigate the degree of bone mineral density impairment in children with autism
 - Explore specific risk factors
- *“Markers of Iron Status and Metabolism in Children with Autism Spectrum Disorders”*
 - Evaluate iron intake, iron status and associated sleep disorders in children with ASD

So, are children with ASD what they eat?

Summary

- Children with ASD have an increased incidence of:
 - chronic GI problems
 - selective eating behaviors
- In spite of anecdotal reports suggesting that a subgroup of individuals with ASD responds to dietary intervention, additional data are needed before health professionals can recommend specific modifications.
- Current research (ATN/AIR-P) is focusing on the nutritional status of children with ASD, both on and off restrictive diets. Data will be correlated with other measures of physical health (including sleep issues) as well as behaviors and will shed light on this controversial subject.

So, are children with ASD what they eat?

Summary

- If parents want to try a diet, knowing the difficulties and risks, they should be supported – preferably by a trained nutritionist/RD.
 - Some children may be unable to communicate genuine GI pain and behaviors may be improved
 - Overall diet may be improved – and there is an established link between optimal nutritional status and behavioral health
 - Placebo effect is reportedly very strong
- Cautions:
 - Growth; dietary/supplement adequacy; bone health
 - Potential toxicity of supplements; drug interactions

Resources

- Nutrition and Dietary Supplement Pamphlets
 - Evidence-based; updated regularly
 - References available from Maureen Geraghty PhD, RD, LD Maureen.Geraghty@osumc.edu (ATN site)
 - Available at The LEND Program at the Nisonger Center, the Ohio State University Medical Center www.nisonger.osu.edu
- Titles
 - Probiotics and ASD
 - The Gluten-Free /Casein-Free Diet in ASD
 - Essential Fatty Acids (EFAs) and ASD
 - Vitamin B-6, Magnesium and ASD

Resources: AAP Physician Fact Sheets

(www.aap.org/publiced/autismtoolkit.cfm)

- Complementary and Alternative Medicine Therapies
- How to Decide on Treatments when Parents are Seeking Complementary and Alternative Medicine
- Dietary Treatments used for Behavioral Management
- Eating and Nutrition
- Gastrointestinal Problems

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- **Patricia Novak, MPH, RD**
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