Advising Parents of Children with Autism Spectrum Disorders

Evidence on Experimental Therapy and The Role of the Primary Care Provider

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Purpose

• To give you the latest evidence on experimental treatments.

• To explain the roll of the primary care provider (PCP) in the care of the child with ASD.
Overview

- Research Methods and Evidence
- Experimental Therapies
  - Diet
  - Supplements
  - Toxin reduction
  - Neurological agents
  - Immunological agents
  - Gastrointestinal agents
  - Sensory intervention

- Talking to parents about experimental therapies
- The Role of the Primary Care Provider
  - Preventive care
  - Symptom evaluation
  - Medication
  - Associated conditions and coordination of care
How do research studies determine if a type of therapy will be effective?
Research Methods

- Limitations to knowing if a therapy is effective:
  - Too many variables
  - We convince ourselves of results
  - Outcomes vary by individual
Research Methods

- As an example, let’s say a parent removes gluten from a child’s diet for a few weeks and the child’s behavior seems to improve...
Research Methods

- Example: gluten-free diet.
  - Too many variables
Research Methods

- Example: gluten-free diet.
  - Too many variables
  - We convince ourselves of results
Research Methods

- Example: gluten-free diet.
  - Too many variables
  - We convince ourselves of results
  - Outcomes vary by individual
Researchers try to overcome these difficulties in determining effective therapies with several methods...
Research Methods

• Methods to overcome limitations:
  • **Too many variables**
    • Study one variable at a time, compared to placebo *(controlled study)*
    • Subjects divided into groups at random *(randomized study)*
Research Methods

- Methods to overcome limitations:
  - Too many variables
    - Controlled study
    - Randomized study
  - We convince ourselves of outcomes
    - Objective, measurable results (objective outcome)
    - Patients and parents do not know if they are receiving treatment or placebo (blind study)
    - Person measuring results does not know whether subject is receiving treatment or placebo (double-blind study)
    - Try the experimental therapy first on one group, then the other, to see if the results still apply (crossover study)
Methods to overcome limitations:

- Too many variables
  - Controlled study
  - Randomized study
- We convince ourselves of outcomes
  - Objective outcome
  - Blind study
  - Double-blind study
  - Crossover study

Outcomes vary by individual
- Large number of test subjects (large study)
Research Methods

- Ideal study
  - Large
  - Randomized
  - Controlled
  - Double-blind
  - Crossover
  - Objectively measured outcome
- These are hard to come by
Experimental Therapies for ASD

- Diet
- Supplements
- Toxin reduction
- Neurological agents
- Immunological agents
- Gastrointestinal agents
- Sensory intervention
Experimental Therapies for ASD

Diet

- Gluten and/or casein elimination diet
- Specific Carbohydrate Diet™ (SCD)
- Yeast-free diet
Experimental Therapies: Diet

- GLUTEN AND/OR CASEIN ELIMINATION DIET
  - Scientific basis: Digestive proteins are altered
  - Studies
    - Eight poor studies = yes
    - One small good study = no
  - Potential negative effects
    - Malnutrition for child (rare)
    - Inconvenience or guilt for parent
  - Verdict
    - Elimination diet alone cannot be said to help with ASD symptoms
    - Allergy testing may be indicated.
Experimental Therapies: Diet

- **SPECIFIC CARBOHYDRATE DIET™ (SCD)**
  - Scientific basis: Digestive proteins are altered
  - Studies: None
  - Potential negative effects
    - Malnutrition for child (rare)
    - Inconvenience or guilt for parent
  - Verdict: No evidence
**YEAST-FREE DIET**

- Scientific basis: Possible underlying immune abnormalities
- Studies
  - Yeast overgrowth is not seen on endoscopy in children with ASD
  - No studies on effect of low sugar and low yeast diets on symptoms of autism
- Potential negative effects
  - Malnutrition for child (rare)
  - Inconvenience or guilt for parent
- Verdict: No evidence
Experimental Therapies: Diet

**DIET: THE BOTTOM LINE**

- No evidence that alterations in diet will help with symptoms of autism

- Advice: Parents may attempt with guidance, but should not feel bad for not attempting
Experimental Therapies for ASD

Supplements

- Vitamin A
- Vitamin C
- Vitamin B₆ and Magnesium
- Vitamin B₁₂
- Folic Acid
- Omega-3 Fatty Acid
- Dimethylglycine/trimethylglycine
- Carnosine
- Tryptophan
- Tyrosine
**VITAMIN A**

- Scientific basis: Vitamin A is necessary in brain function
- Studies: Anecdotal only
- Potential negative effects: Possible toxic overdose causing irritability, altered mental status, blurred vision, abdominal pain, and insomnia
- Verdict: No evidence, potentially harmful
Experimental Therapies: Supplements

- **VITAMIN C**
  - Scientific basis: Unclear
  - Studies: One small, well-designed study shows improvement in sensory motor symptoms with very high doses
  - Potential negative effects: Unlikely, but high doses may cause stomach upset and diarrhea
  - Verdict: Shows potential, but more study needed
• VITAMIN B₆ AND MAGNESIUM

- Scientific basis: Combination had been described as effective in improving social responsiveness and decreasing aggression

- Studies:
  - One well-designed study shows no effect
  - Other studies show no reliable evidence

- Potential negative effects: None found

- Verdict: No recommendation can be made, likely ineffective
Experimental Therapies: Supplements

- **VITAMIN B₁₂**
  - Scientific basis: Abnormal metabolic lab results normalize with folinic acid, betaine and methylcobalamin (vitamin B₁₂)
  - Studies: Subjective improvement in behaviour noted, but not objectively measured
  - Potential negative effects: None found
  - Verdict: Further study is needed
Experimental Therapies: Supplements

- **FOLIC ACID**
  - Scientific basis: Folic acid may help with catecholamine synthesis and metabolism
  - Studies: No studies in children
  - Potential negative effects: Typically safe, but very high doses of folic acid may induce seizure activity in patients taking anticonvulsant medication
  - Verdict: No recommendation can be made
• **OMEGA-3 FATTY ACIDS**

  - Scientific basis: Omega-3 fatty acids help with neurological function
  - Studies: Small study shows reduced hyperactivity
  - Potential negative effects: increased LDL, gastrointestinal discomfort, vitamin A or D toxicity
  - Verdict: More study needed
• DIMETHYLGLYCINE AND TRIMETHYLGLYCINE

- Scientific basis: helps improve amino acid metabolism and increase glycine levels

- Studies: In small studies, lab findings normalize, but effect on behavior not studied

- Potential negative effects: Unknown

- Verdict: More study needed
Experimental Therapies: Supplements

• CARNOSINE

  ▪ Scientific basis: This protein is presumed to effect GABA receptors
  ▪ Studies: One small uncontrolled study reports improved socialization and receptive vocabulary
  ▪ Potential negative effects: Unknown
  ▪ Verdict: More study needed
• TRYPTOPHAN
  - Scientific basis: Children with ASD have serotonin abnormalities
  - Studies: Depletion of tryptophan causes behavioral deterioration, but no study reports improved behavior with administration of tryptophan
  - Potential negative effects: Unknown
  - Verdict: No recommendation can be made
Experimental Therapies: Supplements

• TYROSINE

  - Scientific basis: Tyrosine is the precursor for dopamine, norepinephrine and epinephrine
  - Studies: None
  - Potential negative effects: Unknown
  - Verdict: No recommendation can be made
Experimental Therapies: Supplements

• SUPPLEMENTS: THE BOTTOM LINE

  ▪ Possibly helpful: Vitamin C and Omega-3 fatty acids; Doses unknown
  ▪ Probably not helpful: Vitamin B₆ with magnesium and dimethylglycine
  ▪ No evidence either way: Vitamin A, Vitamin B₁₂, folic acid, trimethylglycine, carnosine, tryptophan and tyrosine
  ▪ All supplements may be harmful in inappropriate doses

• Advice: Parents should not feel bad for not attempting as there is no evidence to recommend
Experimental Therapies for ASD

**Toxin Reduction**

Chelation of heavy metals
Antifungal medications
CHELATION OF HEAVY METALS

- Scientific basis: Unsupported theory that heavy metal toxicity (from vaccines) causes autism

- Studies: No evidence that heavy metals build up in tissues of children with ASD; no evidence that chelation therapy improves symptoms related to mercury toxicity or to autism disorders

- Potential negative effects: kidney damage, liver damage, hypocalcemia, death

- Verdict: Treatment should be avoided
Experimental Therapies: Toxin Reduction

- **ANTIFUNGAL MEDICATIONS**
  - Scientific basis: Unsupported theory that yeast colonization causes autism
  - Studies: None
  - Potential negative effects: liver damage, skin changes, and diarrhea; chronic use can cause resistant mutations of yeast
  - Verdict: This treatment should be avoided
Experimental Therapies: Toxin Reduction

- **TOXIN REDUCTION: THE BOTTOM LINE**
  - No evidence that chelation or antifungals are effective
- Advice: Parents should be cautioned against
Experimental Therapies for ASD

Neurological Agents
- D-Cycloserine
- Cyproheptadine
- Oxytocin infusion
Experimental Therapies: Neurological Agents

• **D-CYCLOSERINE**
  – Possible improvement in social withdrawal with high dose therapy, but may cause motor tics, increased echolalia

• **CYPROHEPTADINE**
  – Possible improvements in behavior when combined with haloperidol (Haldol) with wide range of potential side effects

• **OXYTOCIN INFUSION**
  – May reduced repetitive behaviors in adults
Experimental Therapies: Neurological Agents

- **NEUROLOGICAL AGENTS:**
  THE BOTTOM LINE

  - Early studies show some promise with D-Cycloserine, cyproheptadine combined with an antipsychotic medication, and possibly, oxytocin, but more studies are needed.

- Advice: Encourage parents to await results of larger, more long-term studies
Experimental Therapies for ASD

Immunological Agents

Intravenous immunoglobulin (IVIG)
Antiviral medications
Experimental Therapies: Immunological Agents

- **INTRAVENTOUS IMMUNOGLOBULIN (IVIG)**
  - One person with ASD reported improvement in symptoms with IVIG, but since IVIG is not easy to come by and can be dangerous, it should be used only in diseases for which it has been shown to be effective

- **ANTIVIRAL MEDICATIONS**
  - There is no scientific basis for the use of antivirals, and no evidence that they are effective, but long-term use can lead to bone marrow suppression, abdominal pain and depression
IMMUNOLOGICAL AGENTS: THE BOTTOM LINE

- No current scientific reason to place a child at risk with IVIG or antiviral medications

- Advise: Cannot be recommended
Experimental Therapies for ASD

Gastrointestinal Agents

- Secretin
- Probiotics and enzymes
- Antibiotic medications
Experimental Therapies: Gastrointestinal Agents

- **SECRETIN**
  - Scientific basis: gastrointestinal abnormalities in ASD
  - Studies: One case study reported three cures; 15 studies show no effect
  - Potential negative effects: Cost
  - Verdict: Not recommended
Experimental Therapies: Gastrointestinal Agents

• **PROBIOTICS AND ENZYMES**

  - Scientific basis: gastrointestinal abnormalities in ASD
  - Studies: One non-blinded, non-controlled study reported that acidophilus plus ENZYMAID improved symptoms
  - Potential negative effects: 40% had behavioral and medical side effects
  - Verdict: Not enough evidence for or against
• **ANTIBIOTIC MEDICATIONS**

  - Scientific basis: Clostridium possible cause of autism
  - Studies: One small study showed short-term improvement in behavior after oral vancomycin
  - Potential negative effects: Nausea, vomiting, rash and skin changes; Long-term therapy with antibiotics breeds resistant strains of bacteria
  - Verdict: Further study needed
Experimental Therapies: Gastrointestinal Agents

**GASTROINTESTINAL AGENTS: THE BOTTOM LINE**

- Possibly helpful: Probiotics, digestive enzymes and treatment for clostridium colitis; Dose and duration not known

- Probably not helpful: Secretin therapy

- Advice: Encourage parents to await results of larger, more long-term studies
Experimental Therapies for ASD

Sensory Interventions

Auditory integration training
Behavioral optometry
Craniosacral manipulation

Facilitated communication
Music therapy
Animal-assisted therapy
Experimental Therapies

Talking to Parents
Talking to parents

- Parents are frustrated, guilty, looking for answers.
- Parents may, understandably, risk side effects, wasted funds, wasted time, and disappointment.
- 50% to 92% have used experimental therapy.
- Parents wish their PCP’s would bring it up.
Talking to parents

- Remain non-judgmental
- Keep communication open
- Empower parents to “do nothing”
- Caution parents to be skeptical
- Reassure parents to wait for results of studies
- Remind parents about effective treatment: behavioral therapy and educational intervention
- Encourage parents to discuss any therapeutic possibilities with child’s PCP
Role of the Primary Care Provider

- Preventive care
- Symptom evaluation
- Medication
- Associated conditions and coordination of care
Role of the PCP

- PREVENTIVE CARE
  - Annual check-up
  - Immunizations
  - Lead testing
Role of the PCP

- **SYMPTOM EVALUATION**
  - Gastrointestinal problems
  - Seizures
  - Sleep disorders
  - Behavioral problems
Role of the PCP

• MEDICATION
  ▪ May be considered, for aggressive, destructive, self-injurious, or anxious behavior
  ▪ Anxiety disorder or major depression may require medical treatment
  ▪ Risks and benefits can be discussed with child’s PCP
Role of the PCP

- ASSOCIATED CONDITIONS AND COORDINATION OF CARE
  - Guidance regarding ASD-associated conditions
    - Fragile X syndrome
    - Tuberous sclerosis
  - Coordinating care with specialist physicians
Advising Parents of Children with Autism Spectrum Disorders

Summary
RESEARCH METHODS AND EVIDENCE

Scientific studies must be well-designed in order to provide reliable results
EXPERIMENTAL THERAPY

- **Diet:** No evidence for or against elimination diet, SCD, or a yeast-free diet

- **Supplements.** Vitamin C and Omega-3 fatty acids may be helpful and need further study. Vitamin B₆ with magnesium and dimethylglycine probably are not helpful. There is no evidence for or against Vitamin A, Vitamin B₁₂, folic acid, trimethylglycine, carnosine, tryptophan and tyrosine

- **Toxin reduction.** There is no evidence for or against chelation and antifungal treatment, but they can be harmful
EXPERIMENTAL THERAPY

- **Neurological agents.** No evidence for or against D-Cycloserine, cyproheptadine or oxytocin therapy
- **Immunological agents.** No evidence for or against IVIG or antiviral medications, but they can be harmful
- **Gastrointestinal agents.** Secretin does not treat symptoms of ASD. No evidence for or against the use of probiotics and digestive enzymes
- **Sensory intervention.** Music therapy and animal-assisted therapy may be helpful and need further study. Auditory integration training and facilitated communication probably are not helpful. No evidence for or against behavioral optometry or craniosacral therapy
TALKING TO PARENTS ABOUT EXPERIMENTAL THERAPY

Respectfully give parents permission to “do nothing”
Summary

ROLE OF PCP

- **Preventive care.** Regular check ups, immunizations, and possibly lead testing
- **Symptom evaluation.** Evaluation of medical causes for gastrointestinal problems, seizures, sleep disorders and behavioral problems
- **Medication.** Discussion of pharmaceuticals agents if medication becomes necessary
- **Associated conditions and coordination of care.** Guidance regarding ASD-associated conditions and coordinating care with specialist physicians when needed
References

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