

## Autism 200 Series Biomedical Therapies A Practical Approach

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## What are Biomedical Therapies?

- Can be defined as any agent or therapy that directly influences the body's internal environment
- Includes diet/nutrition, nutraceuticals, pharmaceuticals, etc.
- Traditionally excludes "hands-on" therapies (ABA, speech, OT, vision, AIT, CST, neurofeedback, etc.)

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## Case Study

- 3 ½ yo male
- Normal pregnancy and delivery
- Normal motor milestones
- "Picture perfect" baby
- At 16 months, says first word
- Enjoys physical play, investigates environment
- Likes to play by himself

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### Case Study (cont.)

- At 18 months, no more words and not responding to his name
- Told probably just “late talker”
- 24 months, hearing test normal
- 30 months, hand flapping when excited
- Speech therapy started; referred for evaluation to r/o autism

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### Case Study (cont.)

- 36 months, diagnosed with autism
- Enrolled in developmental preschool, ABA therapy, OT, speech therapy
- Now echoes some words
- Eye contact improved
- Loose stools, poor attention, poor sleep

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### Questions

- What caused this (“if I could just figure it out”)?
- He’s improving, but is it fast enough?
- Am I doing everything I can?
- Do I believe the stories and try unproven (and potentially risky) treatments?
- What do I do first?

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## Fast Forward...

- Age 7, 1<sup>st</sup> grade with 1:1 aide
- Struggling with social skills
- Impulsive behaviors difficult to control, can be violent
- Severe anxiety over “trivial” events
- Unable to stay on complex tasks
- Teachers suggesting medication trial

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## Fast Forward (again)

- Age 16, ritualistic behavior interfering with daily activities
- Explosive behaviors which were gone have recurred
- Becoming more isolated
- Now what?

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## Biomedical Therapies in Autism

10 Rules to Get You Started

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### Rule #1

*Psychoeducational therapy is the foundation of treatment.*

- Biomedicals should never *replace* behavioral approaches.
- Highly unlikely that any biomedical will have maximal effect without an appropriate psychoeducational program.

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### Rule #2

*No biomedical therapy has proven to be effective in treating “core features” of autism.*

- Minimal “class 1” evidence exists for biomedical therapies in ASD.

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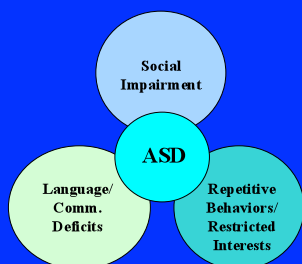
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### ASD – Core Features



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### Rule #3

*Autism treatment is symptom-based.  
Stratify treatment options based on risk.*

- Classic decision making for symptom-based diagnosis.
- Because treatments generally have little or no efficacy data, risk plays heavy role in decision-making.

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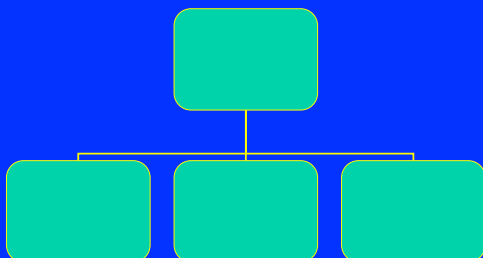
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**PDD (DSM-IV) = ASD**  
**“symptom/behaviorally based”**



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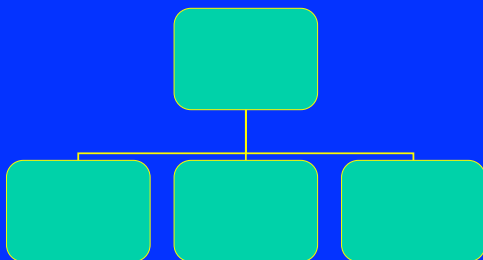
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**ASD**  
**“causally based”**



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### Causes of ASD

- 85% idiopathic, more common HFA, 4:1 m/f
- Symptomatic/cryptogenic more commonly associated with MR, 1:1 m/f ratio
  - Genetic (tuberous sclerosis, fragile X, Angelman's, Down's)
  - Structural (migration defects, Moebius)
  - Perinatal (anoxia, infectious)
  - Epileptic (infantile spasms, Landau-Kleffner)

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### Common Co-morbid Symptom Clusters in ASD - Behavioral

- Anxiety/OCD (rigidity, sensory sensitivity, transition difficulties, "desire for sameness")
- Attention deficit (focus, impulsivity, planning, organization)
- Mood instability (rapid cycling, extreme behaviors, poor impulse control)

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### Common Co-morbid Symptom Clusters in ASD - Medical

- Sleep (initiating, night-time awakening)
- GI (IBS, food sensitivities, inflammatory)
  - Esophagitis responsible for severe aberrant behaviors
- Seizures
  - 30-40% classic autism with seizures by teens
  - Epileptiform discharges associated with poor progress? (causal vs. epiphenomenon)

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### Rule #4

*Maximizing health goes a long way.*

- Don't always assume aberrant behaviors are purely due to autism.
- Follows similar rule as other CNS conditions.
- Physical exercise, sleep very important.

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### Rule #5

*Don't go out on a limb if making good progress.*

- The opposite is also true – a lack of expected progress through conventional treatments warrants consideration of biomedical therapies.

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### Measuring Progress in ASD

- Clinical Global Impression – Parent Rating
  - Accurate, although often won't know why
- Clinical Global Impression – Clinician Rating
- Objective Measures
  - Difficult to obtain in clinical setting

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**Biomedical Therapies –  
Barriers to Clinical Research**

- Poorly understood mechanisms/etiology
- Probable multiple causes
- Lack of biomarkers
- Pediatric population
- Poor funding
- Minimal pharmaceutical industry support

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**Rule #6**

*Implement new treatment in  
“controlled” setting if possible.*

- Avoid starting or changing therapies simultaneously, including hands-on therapies and changes in schedule or routine.

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**Rule #7**

*Define your endpoints.*

- Likelihood of successful treatment will increase if goals of treatment are clearly defined.
- Define duration of treatment and objective (target symptom).

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### Rule #8

*Use “on-off” protocol if benefit not clear.*

- Difficult to see subtle benefit when improving anyway.
- Trial of discontinuation to observe regression – suggest “on” phase of 1-3 months.

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### Rule #9

*Combinations usually work better than pushing the dose of a single agent.*

- Pervasive nature of the disorder often requires addressing multiple neurotransmitter systems.
- The population is sensitive. Start low and go slow.
- Remember to identify your target.

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### Rule #10

*A treatment that gives benefit today is not necessarily beneficial tomorrow.*

- Some treatments may be age-specific.
- The reverse may also be true regarding treatment tolerability.

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**Biomedical Therapies**

- Dietary Modification
- Supplements
- Pharmacological – Medical
- Pharmacological – Behavioral
- Experimental

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**Biomedical Therapies –  
Dietary Modification**

- Gluten and casein free most common
- Possible improvements in hyperactivity, sleep, GI, and core feature
- Improve health vs. core feature?
- Additional behavioral benefit
- [www.gfcfdiet.com](http://www.gfcfdiet.com)

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**Biomedical Therapies –  
Dietary Modification (cont.)**

- Theories
  - “Opioid excess theory” related to undigested proteins interfering with brain function
  - “Autoimmunity theory” related to immune response (IgG Abs) to specific undigested proteins
  - Both theories imply “leaky gut”
  - Improvement over time expected (healing vs. development)

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## Biomedical Therapies – Supplements

- “Nutritional”
  - Zinc/iron (common deficiencies)
  - Others (individually based on diet)
- “Therapeutic”
  - Omega-3 EFAs (Amminger, Biol Psychiatry, 2007). Improved hyperactivity, ?anxiety.
  - High dose B6/magnesium (Mausain-Bosc, Magnes Res, 2006). Improved attention.
  - Dimethylglycine (Kern, J Child Neurol, 2001)

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## Biomedical Therapies – Supplements (cont.)

- Methylcobalamin/folinic acid
  - Cofactors in methylation/sulfation enzyme pathways
  - Important for integrity of CNS, immune, GI (Moretti, Neurology, 2005)
  - Improved biomarkers in 20 autistic children (James, J. DAN! Meeting, Portland, 2003)
  - Clinically unproven

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## Biomedical Therapies – Antifungal/bacterial/viral

- Antifungal based on “gut dysbiosis” theory
  - ? Antiinflammatory effect
- 2 small group studies of antibacterial therapy showing unsustained benefit
- Antiviral based on “stealth virus” theory or latent GI viral infection (Wakefield, Lancet, 1998 – data later shown to be falsified)

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**Biomedical Therapies –  
Sleep Disorder**

- Most effective for sleep initiation
  - Melatonin
  - Clonidine
  - Trazadone
  - Tricyclics
  - Gabapentin
  - Neuroleptics
- Consider sleep study

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**Biomedical Therapies –  
GI Dysfunction**

- IBS symptoms common
- 24% of autistics with GI symptoms (Molloy, Autism, 2003)
- Consider GI study for unexplained severe behaviors
  - Prevacid trial (possible esophagitis)

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**Biomedical Therapies –  
Pharmacological**

- Serotonin Transporter Inhibitors (SSRIs)
- Stimulants/non-stimulant ADD meds
- Neuroleptics
- Anticonvulsants
- Sympatholytics
- Others

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## Biomedical Therapies – Pharmacological (cont.)

- **SSRIs**
  - Supported by studies implicating 5-HT (PET, blood)
  - Supported by open label studies (fluoxetine, sertraline, citalopram) and blinded study (fluvoxamine)
  - Targets anxiety, ritualistic/compulsive/repetitive behaviors, maladaptive behavior, aggression

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## Biomedical Therapies – Pharmacological (cont.)

- **Stimulant/non-stimulant ADD meds**
  - Targets ADHD symptoms (attention, hyperactivity)
  - Frequent paradoxical worsening
  - Good safety data
  - Stimulants (methylphenidate, lisdexamfetamine)
  - alpha-adrenergic agonists (guanfacine, clonidine)
  - Newer non-stimulants (atomoxetine, modafinil)
  - Consider amantadine as alternative

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## Biomedical Therapies – Pharmacological (cont.)

- **Neuroleptics**
  - Targets irritability, aggression, impulsivity, ritualistic behavior
  - Good class 1 evidence (risperidone, aripiprazole)
  - Higher risk profile (weight gain, ? Diabetes, movement disorders)

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## Biomedical Therapies – Pharmacological (cont.)

- **Anti-convulsants**
  - ? Association with regression
  - Up to 46% with EEG epileptiform findings
  - Target mood stabilization, irritability, compulsions, aggressiveness
  - ? Language improvement (Stobbe, AES Meeting, 2006)
  - Better safety with newer agents (oxcarbazapine, lamotrigine)

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## Biomedical Therapies – Experimental

- Goal to find treatments of “core” features (language, social) not just symptom management
- No good supportive data currently

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## Biomedical Therapies – Experimental (cont.)

- **Chelation therapy**
  - Based on mercury/toxic metal theory
  - Oral DMSA approved for acute mercury and lead toxicity
  - ? risk
  - Newborn hair study (Holmes, 2003)
  - Urine DMSA challenge study (Bradstreet, 2003)
  - Urinary porphyrin study discredits theory (Woods JS, 2010)

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## Biomedical Therapies – Experimental (cont.)

- **Acetylcholinesterase Inhibitors**
  - FDA approved for Alzheimer’s
  - Targets system important for language/memory
  - Acetylcholine neurons diminished in path. Studies
  - Several positive open-label studies
  - Good safety data in adults

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## Biomedical Therapies – Experimental (cont.)

- **Immunomodulatory therapy**
  - Supported by studies of immune system irregularities
  - Increased 1<sup>st</sup>-degree relatives with auto-immune disorders
  - Regressive pattern
  - Small studies with prednisone, IVIg

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## Biomedical Therapies – Experimental (cont.)

- Hyperbaric Oxygen Therapy (HBOT)
  - Based on oxidative stress theory
  - Two studies presented, conflicting data
  - Needs more research
- Stem cell research (Duke University)
- Oxytocin (Hollander E, 2008)
- Transmagnetic Stimulation (TMS)
- Neurofeedback Therapy
- Naltrexone
- Secretin
- Center for Neurological Health (Bastyr U.)

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**Thanks!**

Contact Us  
Seattle Children's Autism Center  
206-987-8080  
[www.seattlechildrens.org](http://www.seattlechildrens.org)

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