Autism Spectrum Disorder: Update On Screening and Management

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Faculty Disclosure Information

• In the past 12 months, I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

• I do intend to discuss an unapproved/investigative use of a commercial product/device in my presentation, which will be disclosed at the time of discussion.
Learning Objectives

• Describe early social & communication “red flags” for autism spectrum disorder.
• Interpret ASD surveillance and screening tools.
• Recommend evidence-based, effective interventions for ASD.
Social Communication Deficits

Autism Spectrum Disorder

Restricted, Repetitive Behaviors

Laura Carpenter, PhD 2013
# Autism Spectrum Disorder

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*Need 3/3*  
*Need 2/4*
Emma is a 24 month old girl who presents for her 24 month WCC.

**HPI:** Emma’s last WCC was at 18 months of age. At that time the hx and PE were normal, but she had no words. A recommendation of ‘watchful waiting’ was made by her previous PCP. She appears to hear normally and follows simple commands. She is extremely active and is ‘in constant motion.’ She has temper tantrums several times a day which last anywhere from 2-10 minutes. She is not aggressive.
Past Medical History:

- Birth history: 3.5 kg, born at term, uncomplicated SVD, no prenatal exposures or perinatal exposures. She passed her newborn screen.
- 6 episodes of otitis media
- GER diagnosed at 6 months, now resolved
Diagnostic Lag in ASD

- Average age of first parental concern: 1 year, 7 months
- Average age of first evaluation (SC): 3 years, 10 months
- Average age of first ASD diagnosis: 4 years, 5 months
Emma

• Developmental History
  – Gross/fine motor
    • GM: sat alone 8m, first steps 13 m, runs with toddler gait, ascends stairs holding a rail
    • FM: pincer grasp
  – Speech-language/Communication: mama, dada, sometimes points to things she wants
  – Cognitive: looks for hidden toys
  – Personal/social: gives mom kisses
  – Adaptive/ADLs: drinks from a cup, uses a spoon, but spills

• Behavioral History: as in HPI
Emma: Family/Social History

- Mother 30 y/o, good general health, h/o depression and anxiety, has associates degree, RN
- Father 28 y/o, struggled in school, HS degree, backhoe operator
- Sister 4 y/o, ‘shy’ but doing well in preschool
- Brother 4 months old, no concerns
- Maternal uncle-slow in school, killed in MVA
- Maternal aunt-healthy, married, HS degree
- Maternal GF-HTN, HS degree
- Maternal GM-DM, HS degree
Emma: Physical Examination

- Weight 20%; Height 30%, OFC 95%
- No dysmorphic features
- Looks like her mother
- Bilateral serous OM
- Skin findings normal
- Neurological exam: hyperextensibility of wrists, elbows

NEXT STEPS?
Developmental Testing

• Ages and Stages Questionnaire-3
  – Fails Communication, Communication, Problem solving, Personal-social
  – “Monitor” for Fine Motor, Gross Motor

What other measures should you get?
M-CHAT-R

- Measures social reciprocity, language, some motor
- 2-stage screener 16-30 months
- 6th grade reading level
- now 20 questions
  - Now recommending use only total score cutoff 3-6 items → complete f/u interview*
  - fail ≥ 7 → refer directly for evaluation*
- High false positive rate (PPV 0.06) without the follow-up interview

M-CHAT-R

- M-CHAT-revision: designed to reduce # of cases who initially screen + and need the F/U interview
- 16,000 low-risk toddlers (18 and 24 months)
- Dropped 3 items (peek-a-boo, playing with toys, wandering without purpose)
- Reorganized remaining 20 items, simplified language
- Added examples to provide clarity
- Lowered the age of dx by 2 years compared with current dx
M-CHAT-R-F Scoring

- For all items except 2,5,12, the response ‘NO’ indicates ASD risk; for items 2,5, 12, “YES” indicates ASD risk.
- Low Risk: total score 0-2; if <24 months, screen again after 2\textsuperscript{nd} birthday
- Medium-Risk: total score is 3-7; administer F/U interview to clarify at-risk responses. If M-CHAT-R/F remains at 2+, child has screened positive and refer for diagnostic evaluation and EI.
- High-Risk: Total score is 8-20, acceptable bypass F/U and refer for diagnostic evaluation and EI.
Please answer these questions about your child. Keep in mind how your child usually behaves. If you have seen your child do the behavior a few times, but he or she does not usually do it, then please answer no. Please circle yes or no for every question. Thank you for every question.

1. If you point at something across the room, does your child look at it?  (FOR EXAMPLE, if you point at a toy or an animal, does your child look at the toy or animal?)
   - Yes
   - No

2. Have you ever wondered if your child might be deaf?
   - Yes
   - No

3. Does your child play pretend or make-believe? (FOR EXAMPLE, pretend to drink from an empty cup, pretend to talk on a phone, or pretend to feed a doll or stuffed animal?)
   - Yes
   - No

4. Does your child like climbing on things? (FOR EXAMPLE, furniture, playground equipment, or stairs)
   - Yes
   - No

5. Does your child make unusual finger movements near his or her eyes? (FOR EXAMPLE, does your child wiggle his or her fingers close to his or her eyes?)
   - Yes
   - No

6. Does your child point with one finger to ask for something or to get help? (FOR EXAMPLE, pointing to a snack or toy that is out of reach)
   - Yes
   - No

7. Does your child point with one finger to show you something interesting? (FOR EXAMPLE, pointing to an airplane in the sky or a big truck in the road)
   - Yes
   - No

8. Is your child interested in other children? (FOR EXAMPLE, does your child watch other children, or does he or she cry to them?)
   - Yes
   - No

9. Does your child show you things by bringing them to you or holding them up for you to see—not to get help, but just to share? (FOR EXAMPLE, showing you a flower, a stuffed animal, or a toy truck)
   - Yes
   - No

10. Does your child respond when you call his or her name? (FOR EXAMPLE, does he or she look up, talk or babble, or stop what he or she is doing when you call his or her name?)
    - Yes
    - No

11. When you smile at your child, does he or she smile back at you?
    - Yes
    - No

12. Does your child get upset by everyday noises? (FOR EXAMPLE, does your child scream, cry, or make a funny noise such as a vacuum cleaner or loud music?)
    - Yes
    - No

13. Does your child walk?
    - Yes
    - No

14. Does your child look in the eye when you are talking to him or her, playing with him or her, or dressing him or her?
    - Yes
    - No

15. Does your child try to copy what you do? (FOR EXAMPLE, wave bye-bye, clap, or make a funny noise when you do)
    - Yes
    - No

16. If you turn your head to look at something, does your child look around to see what you are looking at?
    - Yes
    - No

17. Does your child try to get you to watch him or her? (FOR EXAMPLE, does your child look at you for praise, or say “look” or “watch me”)
    - Yes
    - No

18. Does your child understand when you tell him or her to do something? (FOR EXAMPLE, if you don’t point, can your child understand “put the book on the chair” or “bring me the blanket”)
    - Yes
    - No

19. If something new happens, does your child look at your face to see how you feel about it? (FOR EXAMPLE, if he or she hears a strange or funny noise, or sees a new toy, does he or she look at your face?)
    - Yes
    - No

20. Does your child like movement activities? (FOR EXAMPLE, being swung or bounced on your knee)
    - Yes
    - No

**For all items except 2, 5, 12, the response ‘NO’ indicates ASD risk; for items 2, 5, 12, “YES” indicates ASD risk.**

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# M-CHAT-R-F: Scoring and Actions

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Total Score</th>
<th>Action</th>
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<tbody>
<tr>
<td>Low-Risk</td>
<td>0-2</td>
<td>Passed-no action required If &lt;24 months, rescreen after 2\textsuperscript{nd} birthday</td>
</tr>
</tbody>
</table>
| Medium-Risk     | 3-7         | Administer F/U interview (failed items)  
|                 |             | **Score = 6**                                                          |
| High-Risk       | 8-20        | Can bypass follow-up interview  
|                 |             | Refer for diagnostic evaluation and to EI                             |

For all items except 2, 5, 12, the response ‘NO’ indicates ASD risk; for items 2, 5, 12, “YES” indicates ASD risk.
1. If you point at something across the room, does __________ look at it?

**Yes**

Please give me an example of how he/she will respond if you point at something (If parent does not give a PASS example below, ask each individually.)

**PASS** examples
- Looks at object
- Points to object
- Looks and comments on object
- Looks if parent points and says "look!"

**FAIL** examples
- Ignores parent
- Looks around room randomly
- Looks at parent’s finger

**Yes only to PASS example(s)**

PASS

**Yes only to FAIL example(s)**

FAIL

Which one does he/she do most often?

Most often is **PASS** example

PASS

Most often is **FAIL** example

FAIL
You review the results of the screening tests with the mother.

“Based on our conversation, as well as the results of the screening test(s), I have some concerns about Emma’s development”

*Use language that encourages follow-up*

*Avoid negative and meaningless words*

*Be sensitive to cultural meanings of words*
Children who screen positive on ASD screening tests should be referred for services immediately!!

• Do not wait for a formal evaluation to be completed
• Refer all children with language delays to audiology
• Most will need speech-language therapy; some will need occupational therapy; all will need Applied Behavior Analysis (ABA)- type therapy
Barriers to Timely Referral/Diagnosis

- Concerns about screening instruments
  - Fear of causing families unnecessary alarm (false positives)
  - Lack of consensus regarding screening
- Concerns about office visit limitations
  - Time limitations
  - Reimbursement
  - Parent report vs. physician observation
- Concerns about evaluation process
  - Where to refer/long wait lists
  - Diagnostic stability
- Concerns about efficacy of therapy
• Emma’s parents are referred to Early Intervention.

• Formal autism evaluation using the ADOS results in a diagnosis of autism.

• Further developmental assessment results in a diagnosis of global developmental delay.
What about the siblings?

Emma’s parents ask about their 4-month-old son and risk of autism. You reply that his risk of ASD is:

A. Same as the general population.
B. Higher than the general population b/c of male gender.
C. Higher than the general population b/c of having a sibling with ASD.
D. B & C
When to Screen for Autism

- **Routine Developmental Surveillance at all well-child visits with autism screening at 18, 24 months**
  - Open ended questions about concerns re: child’s development and behavior
  - Ascertainment of social and language milestones
  - Child observation

- **Parental Concerns**
  - Language is typically the first reported concern
  - First concerns arise around 15-18 months and are reported to PC several months later

- **Siblings of Children with Autism**
  - US: Recurrence risk of 18-25% (20x greater than general population); European study: 5-10%
  - Siblings also at greater risk for other difficulties
How Early is Too Early?
Challenges to Early Screening

• Standard criteria, gold standard diagnostic tools, and best judgment of experienced clinicians rarely applied <18 months

• Differences may not be observable in the first year of life
  – Lack of reliable, sensitive and specific tools for early screening

• Some diagnostic criteria for autism are typical behaviors for infants/toddlers
  – Echolalia (until MA 18-24 months)
  – Repetitive movements (until MA 6-9 months)
  – Insistence on sameness (MA 3 years)
  – Lack of pretend play (until MA 14-18 months)
  – Jargoning (until MA 18 months)
Signs of Autism in the First Years

• ↓ attention to face, eyes
• Limited response to name
• Minimal showing, sharing of attention
  – Delayed pointing
• Limited shared affect

How early are these signs?
Sibling Studies: Declining Trajectories

↓ after 6 months

↓ after 9 months

Flat instead of typical ↑

Ozonoff et al, 2011
Deficits are more significant than excesses
Red Flags before 6 months

• Failure to...
  – Look at faces
  – Smile at others
  – Coo/vocalize with pleasure

Zwaigenbaum et al, 2005; Ozonoff et al, 2011
Red Flags 6-12 months

- Failure to...
  - Respond to name
  - Babble
  - Play social games
  - Display bright affect

Zwaigenbaum et al, 2005; Ozonoff et al, 2011
Red Flags at 12-18 months

• Failure to...
  – Follow a point
  – Point to request
  – Point to indicate interest
  – Use gestures
  – Imitate
  – Show interest in peers

Zwaigenbaum et al, 2005; Ozonoff et al, 2011
Regression

- DOES appear to be a real phenomenon
- 25-30% regress during the second year of life, depending on definition used and sample
- Ozonoff et al (2010): regression may be the norm and not the exception
  - High risk sib study: ↓ in rates of early social communication behaviors around 1st birthday vs. controls
  - No difference b/w groups at 6 months
- Always refer for evaluation
Screening Tools for Young Children

- Modified Checklist for Autism in Toddlers – R/F
- Communication & Symbolic Behavior Scales-Developmental Profile: Infant-Toddler Checklist
- Screening Tool for Autism in Two Year Olds
- Social Communication Questionnaire
Communication and Symbolic Behavior Scale – DP Infant Toddler Checklist (CSBS-ITC)

• Designed to screen communication delays 6-24 months
• 24 questions, 5-10 minutes
• Separates speech, social, and symbolic communication
• For autism: sensitivity and specificity .89
• Repeated screening: Identified >90% of those with ASD
CSBS DP Infant-Toddler Checklist

Child's name: __________________________ Date of birth: __________ Date filled out: __________

Was birth premature? [ ] Yes [ ] No If yes, how many weeks premature? __________

Fused out by: __________________________ Relationship to child: __________

Instructions for caregivers: This Checklist is designed to identify different aspects of development in infants and toddlers. Many behaviors that develop before children talk may indicate whether or not a child will have difficulty learning to talk. This Checklist should be completed by a caregiver when the child is between 6 and 24 months of age to determine whether an evaluation is needed. The caregiver may be either a parent or another person who nurtures the child daily. Please check all the choices that best describe your child's behavior. If you are not sure, please choose the closest response based on your experience. Children at your child's age are not necessarily expected to use all the behaviors listed.

Emotions and Eye gaze

1. Do you know when your child is happy and when you child is upset? [ ] Not Yet [ ] Sometimes [ ] Often
2. When your child plays, does he/she look at you to see if you are watching? [ ] Not Yet [ ] Sometimes [ ] Often
3. Does your child smile or laugh while looking at you? [ ] Not Yet [ ] Sometimes [ ] Often
4. When you look at a toy and point to a toy across the room, does your child look at the toy? [ ] Not Yet [ ] Sometimes [ ] Often

Communication

5. Does your child let you know that he/she needs help or wants an object out of reach? [ ] Not Yet [ ] Sometimes [ ] Often
6. Does your child show interest in or pay attention to you, do you hear your child trying to get your attention? [ ] Not Yet [ ] Sometimes [ ] Often
7. Does your child do things just to get you to laugh? [ ] Not Yet [ ] Sometimes [ ] Often
8. Does your child try to get you to notice interesting objects—just to get you to look at the objects, not to get you to do anything with them? [ ] Not Yet [ ] Sometimes [ ] Often

Gestures

9. Does your child pick up objects and give them to you? [ ] Not Yet [ ] Sometimes [ ] Often
10. Does your child show objects to you without giving you the object? [ ] Not Yet [ ] Sometimes [ ] Often
11. Does your child wave to greet people? [ ] Not Yet [ ] Sometimes [ ] Often
12. Does your child point to objects? [ ] Not Yet [ ] Sometimes [ ] Often
13. Does your child nod his/her head to indicate yes? [ ] Not Yet [ ] Sometimes [ ] Often

Sounds

14. Does your child use sounds or words to get attention or help? [ ] Not Yet [ ] Sometimes [ ] Often
15. Do your child string sounds together, such as oh, oh, ma ma, gaga, bye bye, baba? [ ] Not Yet [ ] Sometimes [ ] Often
16. About how many of the following consonant sounds does your child use: na, ne, be, da, ga, wa, la, ya, sa, sha? [ ] None [ ] 1-2 [ ] 3-4 [ ] 5-6 [ ] over 8

Words

17. About how many different words does your child use meaningfully? [ ] None [ ] 1-3 [ ] 4-10 [ ] 11-30 [ ] Over 30
18. Does your child put two words together (for example, more cookie, bye bye Daddy)? [ ] Not Yet [ ] Sometimes [ ] Often

Understanding

19. When you call your child's name, does he/she respond by looking or turning toward you? [ ] Not Yet [ ] Sometimes [ ] Often
20. About how many different words or phrases does your child understand (for example, 'where's your tummy,' 'where's Daddy,' 'give me the ball,' 'come here,' without showing or pointing, your child will respond appropriately)? [ ] None [ ] 1-3 [ ] 4-10 [ ] 11-30 [ ] Over 20

Object Use

21. Does your child show interest in playing with a variety of objects? [ ] Not Yet [ ] Sometimes [ ] Often
22. About how many of the following objects does your child use appropriately: cup, bottle, bowl, spoon, comb or brush, toothbrush, wastebasket, vehicles, toy telephone? [ ] None [ ] 1-2 [ ] 3-4 [ ] 5-6 [ ] over 8
23. About how many blocks (or rings) does your child stack? [ ] None [ ] 1-2 [ ] 3-4 [ ] 5-6 [ ] over 8
24. Does your child pretend to play with toys (for example, feed a stuffed animal, put a doll to sleep, put an animal figure in a vehicle)? [ ] Not Yet [ ] Sometimes [ ] Often

Do you have any concerns about your child's development? [ ] Yes [ ] No If yes, please describe on back.
Social Communication Questionnaire

- ≥ 4 years, mental age > 2 years
- Can use in 3 year old with modified scoring (12 vs 15 fail)
- 40 items, 5-10 minutes
- English and Spanish
- Current and lifetime forms
- Sensitivity 85-96%, Specificity 67-80% for an ASD
- >90% high scorers have neurodevelopmental disorder
- $32.95/20 forms
Social Communication Questionnaire

• Lifetime Form
  – focuses on the child’s entire developmental history
  – provides total score that identifies individuals who should be referred for a more complete evaluation

• Current Form
  – inspects the child’s behavior over the most recent 3-month period
  – aids in treatment planning, educational intervention, and measurement of change over time
Screening Tool for Autism in Two Year Olds (STAT)

- Second level screening tool for autism
- 20 minute play-based interactive session
- 10 scored items include play (2), imitation (4), directing attention (4)
- Does not require language comprehension
- Validation sample used DSM-IV criteria and the Childhood Autism Rating Scale as gold standard
  - Sensitivity .83; Specificity 0.86
- Study of high-risk infants 12-23 months: Sens 95%, Spec 73%
On the horizon...

- ‘RITA-T’: Rapid Interactive Screening Test for Autism in Toddlers*
  - Administered in scored in 10 min
  - High Sens/Spec for ASD in high-risk group
- ‘SORF’: Systematic Observation for Red Flags
  - Requires videotaping

Approaches to Treatment

• Educational/Behavioral Interventions
• Family support and training
• Medical management
  – Routine well-child care
  – Co-occurring conditions
• Complementary and alternative therapies
Treatment Objectives

Decide what you are treating!

- Core ASD Symptoms?
  - Social Reciprocity
  - Repetitive and restrictive behaviors (“RRB”)
- Coexisting Conditions?
  - Challenging/disruptive behaviors
  - Affective Disorders
  - Sleep disturbances
  - Seizure disorders
  - Others (GI, feeding problems)
Educational/Behavioral Interventions

• ASD specific symptoms
  – Communication, social relatedness, RRB

• Coexisting developmental/learning problems
  – Cognitive/adaptive, academic

• Behavioral Challenges
Educational Interventions

Characteristics:
• Early, intensive, individualized
• Teach adaptive skills
• Work on generalizing and maintaining skills
• Address behavioral treatment
• Provide inclusion with supports
• Provide objective monitoring
Approaches to Treatment

- Educational/Behavioral Interventions
  - Early Intervention programs
  - Intensive Behavioral Approaches: ABA, DTT, EIBI
  - Developmental models: DIR, Floortime, Denver
  - Integrated models: TEACCH, Denver, SCERTS
  - Speech and language therapy
  - Occupational therapy
  - Social skills instruction
Behavioral Interventions

• Applied Behavioral Analysis (ABA)
• Discrete Trials Training (DTT)
• Early Intensive Behavioral Intervention (EIBI)

• Teaches new skills by breaking down into elements and reinforcing
  – Differential reinforcement of other behavior
  – Differential reinforcement of communication
  – Token economy
• Emma’s parents agree she needs all recommended traditional therapies.

• They would like to know about alternative treatments, as parents in the local autism support group expressed great results with their children with such therapies.

• Your response ??
Complementary & Alternative Therapies

• CAM is defined by the National Center for Complementary and Alternative Medicine as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.”
Complementary & Alternative Therapies

• CAM use is common in children with ASD
  – 50-75% of children with ASD being treated with CAM (Wong et al, 2006, Hanson et al, 2007)
  – Almost 1/3 referred for ASD evaluation treated with dietary therapies (Levy et al, 2003)
  – Parents may be reluctant to share information regarding CAM use with their child’s doctor (Wong et al, 2006)
    • Concern about physician disapproval
    • No need for disclosure
    • Physician did not ask
    • Physician not knowledgeable about CAM
Complementary & Alternative Therapies

**Biological Treatments**
- Dietary modifications
- Vitamins/supplements
- Chelation therapy
- Melatonin
- Antibiotics/Antifungals
- Immunoglobulins
- Hyperbaric oxygen

**Non-Biological Treatments**
- Auditory integration therapy
- Behavioral optometry
- Craniosacral manipulation
- Music therapy
- Yoga
Gluten/Casein Free Diet

- **Cochrane review, 2009:** Insufficient evidence at this time to support the use of gluten/casein free diets.
  - Further study needed with well-designed trials.
  - Further information needed regarding potential risks.
- **Recent studies:**
  - **Whiteley et al, 2010, Nutritional Neuroscience**
    - 72 children, diet vs. no diet, improvements in tx group
  - **Hymen, et al, NIMH trial**
    - Small increase in social interaction after eating food containing gluten or casein (NS).
    - Small increase in social language after the gluten challenge (NS).
Gluten/Casein Free Diet

- **Clinical Considerations**
  - Feasibility of implementing diet
    - Child’s current eating habits
    - Added time, effort and expense
    - Plans to ensure compliance in and out of home
  - Nutritional considerations
    - Monitor weight gain
    - Maintaining adequate intake of protein, calcium, vitamin D
    - Consultation with nutritionist
  - Plan for evaluating response to intervention
• **Vitamin B6 and Magnesium**
  – Cochrane review of 3 small controlled studies, insufficient evidence to support use
  – Generally safe, but toxicity may occur at elevated doses
    • Tolerable upper limits in children:
      – Vitamin B6 (30-80 mg/day)
      – Magnesium (65-350 mg/day)
Vitamins and Supplements

- **Omega 3 Fatty Acids**
  - Polyunsaturated fatty acids
    - ALA from nuts, seeds; EPA and DHA from fatty fish
    - High concentrations of DHA in neural tissues
    - Some studies show decreased levels of omega 3 in ASD children
  - 1 placebo controlled trial in 13 children (Amminger et al, 2007)
    - Hyperactivity and stereotypy scales on ABC trended towards significance
    - 1 child withdrew due to GI complaints & lack of benefit
  - Remaining studies uncontrolled, some showing benefit
  - Main side effects related to GI upset
Complementary & Alternative Therapies

- Ask families about use of CAM therapies
- Encourage families to educate themselves about evidence
- Advise parents to be wary of treatments that:
  - Are based on overly simplified scientific theories
  - Promise dramatic improvements or cure
  - Have shown efficacy only in case reports/anecdotal data
  - Are said to have no adverse side effects
- Develop plan to evaluate efficacy, side effects
Challenging Behavioral Symptoms

- ADHD sx
  - Hyperactivity
  - Impulsivity
  - Inattention
- Irritability:
  - Aggressive outbursts
  - Mood lability
  - Self-injurious behavior
- Anxiety
- Depression
- Repetitive behaviors:
  - Stereotypic movements
  - Repetitive play
  - Inflexible routines
  - Perseverative speech
- Sleep disturbances
Managing Disruptive Behaviors in Youth with ASD

• ‘Associated Symptoms’
  – Symptoms that interfere with ‘living and learning’
  – Symptoms that disrupt school, home activities and public outings
• ‘Diagnostic overshadowing’: attributing disruptive sx to the ASD dx
• Meds can facilitate response to therapy and learning
• Can improve overall functioning by ↓ issues from associative behaviors
Take a good ROS!

- Changes in environment
- Transition? Move to new school?
- Puberty?
- Reduced ability to communicate?
- Learned behaviors?
  - Unintentional reinforcement of negative behaviors? Rewarded for behavior by negative attention, getting out of undesired task
- Parent/family stress?
Medical Evaluation

- General ROS to rule out any source of discomfort
- Stay on top of chronic issues such as allergies, constipation, GERD, etc
- Routine dental care
- Adolescent girls and dysmenorrhea
  - Consider OCP, Depo-Provera
- Sleep issues
Comorbid psychiatric dx/Dual Dx

• Comorbid disorders in ASD
  – 71% with at least one disorder, 41% with 2+
  – Social anxiety 29%
  – ADHD 29%
  – ODD 3%

• Risk Factors
  – Seizure disorder
  – Age, IQ, severity of ASD sx, adaptive functioning
Clinical Approach to Challenging Behaviors

- Careful assessment of target behaviors
  - Timing, intensity, triggers, response to interventions
  - Use of behavioral scales
  - Obtain input from multiple sources (home, school)

- Assess existing and available supports
  - Behavioral services
  - Educational program
  - Family supports
Why Do Behaviors Occur?

- To communicate wants and needs
- To get attention
- To escape boring or aversive demands
- To provide stimulation or sensory regulation

Also occur:
- Due to skill deficits (don’t understand expectations)
- Due to performance deficits (has skills but won’t comply with requests)
- Neurologic or psychiatric symptoms
Psychopharmacology in ASD

• Goal is to reduce challenging behaviors and improve response to behavioral and educational interventions

• Psychotropic medication use in ASD is common
  – Frequency: studies range from 35-64%
  – Consistent findings: ↑ use with older age, presence of intellectual disability or psychiatric co-morbidity, Southern US
  – **Stimulants, alpha₂ agonists, anti-psychotics, and SSRIs most common (depends on age)**
Principles of psychopharmacological treatment

- Avoid frequent dose or drug changes unless good reason (side effects or not effective)
- Risk/benefits must be clear
- Start low and go slow
- Include discussion of adverse effects
- Monitor effectiveness with teacher/parent behavior checklists - baseline and with titration
Autism Spectrum Pharmacotherapy

- No medications approved for core symptoms
- Medications often used to treat related sx, such as depression, anxiety, and aggression
- Stimulants, long acting alpha$_2$ agonists approved for ADHD
- Risperidone and aripiprazole are FDA approved for irritability
- Individuals with autism are often very sensitive to adverse effects (as are children with other disabilities), even at low doses

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<tr>
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<th>FDA approved</th>
<th>Age</th>
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<tbody>
<tr>
<td>Anxiety</td>
<td>duloxetine</td>
<td>≥7</td>
</tr>
<tr>
<td>OCD</td>
<td>fluoxetine</td>
<td>≥7</td>
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<tr>
<td></td>
<td>fluvoxetine</td>
<td>≥8</td>
</tr>
<tr>
<td></td>
<td>sertraline</td>
<td>≥6</td>
</tr>
<tr>
<td></td>
<td>clomipramine</td>
<td>≥10</td>
</tr>
<tr>
<td>Depression</td>
<td>fluoxetine</td>
<td>≥8</td>
</tr>
<tr>
<td></td>
<td>escitalopram</td>
<td>≥12</td>
</tr>
</tbody>
</table>
Autism Spectrum Pharmacotherapy

- Insistence on Sameness/repetitive behavior: relative lack of evidence to support due to consistently high placebo response in RCT
- RCT of low-dose (2.5 mg) buspirone showed improvement in ADOS restricted and repetitive behavior score*
  - No change with placebo and 5 mg dose
- Anxiety: often use SSRIs, at low doses

*Chugani et al. J Pediatr 2015
Targeting inattention, hyperactivity, impulse control

- **Stimulants**: less effective than in typical ADHD, but still effective.
  - ‘ADHD’ not exactly the same. Internal distractibility, psychomotor agitation
  - RUPP Study- 50% responders, 18% discontinued 2° side effects
  - Preschool study: 50% improvement, 50% with side effects
ADHD and Non-Stimulants in DD: What’s the Evidence?

• **Alpha$_2$ Agonists**
  – 2 positive small DBPC trials
  – clonidine $\rightarrow$ ↓ hyperarousal
  – guanfacine $\rightarrow$ ↓ hyperactivity

• **Atomoxetine**
  – Noradrenergic reuptake inhibitor
  – 2 positive RCT
    • ↓ hyperactivity
    • No change in stereotypic behavior, irritability
Anxiety, OC and perseverative behavior

- Overlap with perseverative, obsessive behaviors
- Treat with SSRIs, but few RCT support
- May have some effect on core sx of ASDs (socialization, communication, stereotypical behaviors)
- Watch for activation as side effect
  - Start with very low dose, titrate slowly
- Cost:Benefit: Usually worth trial for target sx of anxiety and perseveration
Disruptive behaviors

- Tantrums, meltdowns
- Aggression, property destruction
- Self-injurious behaviors
- Elopement (running away)
Aggression: medication

- With ADHD-maximize stimulant medication
- Alpha agonists
  - Clonidine: up to .4 mg/day
  - Guanfacine: up to 4 mg/day
- Atypical Antipsychotics
  - Target agitation and aggression
  - Aripiprazaole (Abilify) and risperidone (Risperdal) approved for ‘irritability’ associated with autism spectrum disorders
  - Side effects: weight gain, risk of metabolic syndrome
  - Monitor with lipid profile, fasting glucose, prolactin
  - Hgb A1c
  - Monitor for movement disorders (use DISCUS or AIMS)
Atypical Antipsychotics: MOA

- Block D₂ receptors
- Used to control symptoms of agitation, aggression, and SIB
- Try meds with fewer SE first
- All similar in efficacy, differ in potency & side effects
- Atypical antipsychotics: more specific dopamine antagonists, less SE
Aggression: medication

Antiepileptic Drugs
• Few studies show efficacy in ASD for mood stabilization
• ~30% will have at least one seizure
• Can use as ‘add-on’ to neuroleptic for additional mood stabilization
• Medications
  – Valproic acid
  – Carbamazepine
  – Oxcarbamazepine
  – Levetiracetam (Keppra)
  – Lamotrigine (Lamictal)
If medication does not work

- Ensure adequate dose
- Evaluate adherence to medication regimen
- Re-evaluate targeted symptoms
- Optimize behavioral interventions and visual supports
- Assess for side effects
- Ensure adequate trial
  - Atypical Antipsychotic: 3-8 weeks
  - SSRI: 6-8 weeks
  - Use longer trial if partial response
Inadequate/partial response

• If no response, taper med and try another in same family
• If partial response, add adjunctive medication
  – If alpha agonist for impulse control issues (with aggression, destructive behaviors) add an atypical antipsychotic.
  – If atypical antipsychotic for agitation and aggression, add a mood stabilizer.
  – If SSRI for anxious/agitation/perseverative-OC behavior, add an atypical antipsychotic.
Monitor Response

- Determine outcome parameters and time course of trial prior to treatment
- Ongoing collaboration among physicians, parents, schools, and child
  - Teacher and parent report important
  - Aberrant Behavior Checklist, Clinical Global Index, Child Attention Problems Scale
- Direct observation
- Scheduled appointments to monitor course and effects
Psychopharmacology: Monitoring

- Careful follow-up for efficacy and side effects
  - Atypical antipsychotics: extrapyramidal sx, tardive dyskinesia (AIMS, DISCUS)
  - Teacher and parent report important: Aberrant Behavior Checklist, Clinical Global Index, Child Attention Problems Scale
- Use drugs only as long as there is clear evidence that benefits outweigh SE
- Except for stimulants, dose reduction and discontinuation should be gradual
  - Especially anti-psychotics (behavioral rebound, withdrawal dyskinesia)
- No standard taper, generally 25% per week
Selected References

- Robins DL, et al. Validation of the modified checklist for autism in toddlers, revised with follow-up (M-CHAT-R/F).*Pediatrics* 2014;133; 37.
Helpful Websites

- www.cdc.gov/actearly
- www.cdc.gov/autism
- www.firstsigns.org
- www.autismspeaks.org/
- http://www2.gsu.edu/~psydlr/M-CHAT/Official_M-CHAT_Website.html
- www.autism-society.org/site/PageServer
- AAP Clinical Report http://aappolicy.aappublications.org/
- AAP Developmental-Behavioral Pediatrics www.dbpeds.org
- AAP Council on Children with Disabilities/Medical Home http://www.medicalhomeinfo.org/about/CSOCWD.html
Additional Slides Not Covered in Lecture
Prevalence of Autism Spectrum Disorders

- 11 ADDM sites, age 8 yrs
- Prevalence **14.7 per 1,000** (1:68 children)
  - Range: 5.7 to 21.9/1,000
  - 1 in 42 boys
  - 1 in 189 girls
  - Male:Female 3.6-5.1
- Increase of 29% from 2008, 64% from 2006; 123% from 2002
- ~ half with average-above avg IQ

United States, 2010 (MMWR 2014)
DSM-5: Autism Spectrum Disorder

Must meet criteria A, B, C, and D

A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays, and manifest by 3 of 3 symptoms

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least 2 of 4 symptoms

C. Symptoms must be present in early childhood (but may not become fully manifest until social demands exceed limited capacities).

D. Symptoms together limit and impair everyday functioning.
<table>
<thead>
<tr>
<th>Severity Level for ASD</th>
<th>Social Communication</th>
<th>Restricted interests &amp; repetitive behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level 3</strong></td>
<td><strong>‘Requiring very substantial support’</strong></td>
<td>Preoccupations, fixated rituals and/or repetitive behaviors markedly interfere with functioning in all spheres; Marked distress when rituals or routines are interrupted; very difficult to redirect from fixated interest or returns to it quickly.</td>
</tr>
<tr>
<td></td>
<td>Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning; very limited initiation of social interactions and minimal response to social overtures from others.</td>
<td></td>
</tr>
<tr>
<td><strong>Level 2</strong></td>
<td><strong>‘Requiring substantial support’</strong></td>
<td>RRBs and/or preoccupations or fixated interests appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress or frustration is apparent when RRB’s are interrupted; difficult to redirect from fixated interest.</td>
</tr>
<tr>
<td></td>
<td>Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions and reduced or abnormal response to social overtures from others.</td>
<td></td>
</tr>
<tr>
<td><strong>Level 1</strong></td>
<td><strong>‘Requiring support’</strong></td>
<td>Rituals and repetitive behaviors (RRB’s) cause significant interference with functioning in one or more contexts. Resists attempts by others to interrupt RRB’s or to be redirected from fixated interest.</td>
</tr>
<tr>
<td></td>
<td>Without supports in place, deficits in social communication cause noticeable impairments. Has difficulty initiating social interactions and demonstrates clear examples of atypical or unsuccessful responses to social overtures of others. May appear to have decreased interest in social interactions.</td>
<td></td>
</tr>
</tbody>
</table>
A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays (must meet all 3 criteria)

1. Deficits in social-emotional reciprocity
2. Deficits in nonverbal communicative behaviors used for social interaction
3. Deficits in developing and maintaining relationships, appropriate to developmental level
B. Restricted, repetitive patterns of behavior, interests, or activities (must meet 2/4 criteria)

1. Stereotyped or repetitive speech, motor movements, use of objects
2. Excessive adherence to routines, ritualized behavior, or excessive resistance to change
3. Restricted, fixated interests abnormal in intensity or focus
4. Hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment
Functional Behavioral Assessment

- Gathers information about when the behaviors are likely to occur
- Develops and tests hypotheses about function of the behavior
  - **Setting events**: ↑ likelihood a behavior may occur
  - **Antecedents**: events occurring prior to a behavior
  - **Consequences**: events following a behavior
Prevention

• Academic Modifications
  – Visual schedules
  – Clarify instruction and expectations

• Predictability
  – “priming”, overlearned routines
  – Mnemonics, self-cuing

• Safe Places/Safe People

• Control Stimulation/Calming Strategies
Visual Supports

- Most effective and powerful tool used to reduce disruptive behaviors and increase appropriate behaviors
- More powerful than medication!
- Effective for all cognitive levels and ASD severity
- A visual is a guide to show what to do, what not to do, what to expect in the future, when and why things are done
- Visuals help to generalize social rules, so that one rule can apply to several situations
Types of Visual Supports

- **Visual schedules**
  - Identifies activities during the day
  - Especially good if any change in routine
  - Can include child’s preferred choices for activities
  - Less favorable activities can be shown followed by preferred activities
Types of Visual Supports

- Social Stories
  - Presents information in a concrete visual manner
  - Explains new and unfamiliar situations in an understandable way
  - Goal: to understand the event/task, to increase comfort with event/task, suggest appropriate responses to new event
School Requirements

• When a child’s behavior is interfering with learning the school is required by IDEA to:

• Complete a **Functional Behavioral Assessment (FBA)**

• Create a **Positive Behavior Intervention Plan (PBIS)**
Making Appropriate Referrals IDEA: 0-36 months

Part C: Early Intervention

- Provides services to children (ages 0-3) who have, or are at risk for, developmental disabilities
- Offered through a state agency - state to state variability and variations
- Individual Family Service Plan (IFSP) developed
- Primary care provider can refer patients directly to the state agency
- Agency evaluates to determine whether he/she qualifies for services
Making Appropriate Referrals
IDEA: 3-5 years

Section 619 of Part B: Preschool Special Education Program

- Provides services to children ages 3-5
- State to state variations
- Offered through the school system
- Primary care physicians cannot refer directly in some states
- Encourage parents to request an Individualized Education Program (IEP) evaluation from the local school
- IEP/services may include: special instruction, ST, OT, PT, assistive technology, counseling, audiology, etc.
Developmental Screening: Coding & Billing

- 96110: Developmental screening
  - Includes interpretation and report
  - Expectation is screening tool completed by a non-physician staff member and reviewed by the practitioner
  - No physician/practitioner work is included in the RVU
  - Reported in addition to E/M services provided on same date, with modifier (-25)
  - Report for each screen administered

- 96111: Developmental testing
  - Used for extended developmental testing typically provided by the provider (i.e. direct testing)
  - Includes the interpretation and report
  - Based on 1 hr of physician work (2.67 RVUs)
  - Reported in addition to E/M services provided on same date, with modifier (-25)
  - Single unit code

SC CMS payment $8.70  SC CMS payment $130
• Sleep problems are highly prevalent in ASD (44-83%)
  – Evidence of abnormal melatonin regulation in ASD
• Sleep hygiene, behavioral management 1st line
• Limited data to support diphenhydramine, clonidine
• Melatonin
  – Clinical studies have shown some benefit
    • Small RCTs showed increased sleep duration and reduced sleep latency (Wirojanan, 2009, Garstang, 2006)
    • Retrospective study of 107 children showed only 3 with side effects of daytime sleepiness and enuresis (Andersen, 2008)
  – Recommendations of 1-6 mg 1 hr before bedtime
## SSRI Treatment Choices

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Forms</th>
<th>Start Dose</th>
<th>+/- by</th>
<th>Max Dose Dep/OCD/Anx</th>
<th>+RCT Evidence Dep/anx/OCD</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>Capsule 20,30,60</td>
<td>30 mg</td>
<td>30 mg</td>
<td>120 mg</td>
<td>N/Y</td>
<td>8+ (anx)</td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>Tab, liquid</td>
<td>10mg</td>
<td>10mg</td>
<td>40mg</td>
<td>Y/N</td>
<td>N</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>Tab, liquid</td>
<td>5mg</td>
<td>5mg</td>
<td>20mg</td>
<td>Y/N</td>
<td>12+ (Dep)</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>Tab, capsule, liquid</td>
<td>10 mg Dep 5 mg OCD</td>
<td>5-10mg</td>
<td>40/60 mg</td>
<td>Y/N</td>
<td>7+ (OCD) 8+ (Dep)</td>
</tr>
<tr>
<td>Fluvoxamine (Luvox)</td>
<td>Tab, liquid</td>
<td>25mg BID</td>
<td>25mg</td>
<td>300mg</td>
<td>N/N</td>
<td>8+ (OCD)</td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>Tab, liquid</td>
<td>10mg</td>
<td>10mg</td>
<td>60mg</td>
<td>N/N</td>
<td>N</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>Tab, liquid</td>
<td>25mg</td>
<td>12.5-25mg</td>
<td>200/150mg</td>
<td>Y/N</td>
<td>6+ (OCD)</td>
</tr>
</tbody>
</table>
Antipsychotics: Side Effects & Monitoring

Potential Side Effects

- Increased appetite and weight gain
- Dyslipidemia
- Diabetes
- Sedation
- Constipation
- Extrapyramidal symptoms
- Prolactin elevation
- Increased liver enzymes (less common)

Recommended Monitoring (Varies)

- BMI
- HbA1c
- Fasting blood glucose
- Fasting lipids
- Prolactin (+/-, depends on drug)
- Baseline, Repeat labs at 3 m, then annually
  - LFTs baseline, 3 m only
- Monitor for EPS (AIMS, DISCUS)
Atypical Antipsychotics: Side Effects

- SE: antihistamine (dry mouth, sedation) & anticholinergic (↑ HR, constipation)
- Extrapyramidal symptoms, dystonia, akathisia (restlessness— from the Greek “not to sit”)
- Tardive dyskinesia: involuntary lip smacking, tongue rolling, grimacing, spasms, choreiform movements
- Clozaril: seizures, agranulocytosis-✓ CBC weekly
Atypical Antipsychotics: Metabolic effects

• All carry a risk of metabolic disturbance
  – Clozapine, olanzapine >> quetiapine, risperidone
  – Weight gain: clozapine, olanzapine highest; aripiprazole, ziprasidone lowest

• If any parameter abnormal, consider the following:
  – Switching to an agent that is less risky
  – Decreasing dose or discontinuing therapy
  – Recommend diet and exercise
  – Refer to clinician with expertise in weight management, diabetes, or lipids

Zeier K et al, Current Psychiatry 2013:12 (9): 51-56
### Comparison of Metabolic Effects of Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Weight gain</th>
<th>Dyslipidemia</th>
<th>Hyperglycemia</th>
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</thead>
<tbody>
<tr>
<td>clozapine</td>
<td>Clozaril</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>olanzapine</td>
<td>Zyprexa</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>risperidone</td>
<td>Risperdal</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>quetiapine</td>
<td>Seroquel</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>ziprasidone</td>
<td>Geodon</td>
<td>+/-0</td>
<td>+/-0</td>
<td>+/-0</td>
</tr>
<tr>
<td>aripiprazole</td>
<td>Abilify</td>
<td>+/-0</td>
<td>+/-0</td>
<td>+/-0</td>
</tr>
<tr>
<td>paliperidone</td>
<td>Invega</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</table>