Autism 2015: Overview and Update
Disclosure

- I have no financial interest or any relationship with any manufacturer of any commercial product or service. Sadly.
- I will be using the terms “autism” and “autism spectrum disorder” interchangeably for ease of speech.
Outline of Autism 2015 Overview and Update Part A

- Unit 1: Developmental Pediatrics
- Unit 2: Autism Spectrum Disorders (ASD) Diagnosis Overview
- Unit 3: ASD in the DSM-5 section I
- Unit 4: ASD in the DSM-5 section II
Unit 1: Developmental Pediatrics
Principle:

- Development unfolds across fetal, neonatal and postnatal time based on broadly conceived genetics and environment (both physical and experiential)
- This makes children the sum of all they inherit and experience.
For Developmental Concerns

- Find the right description of the developmental course
- Assist in finding the reason for it
- Figure out what can be changed or modified to maximize developmental potential.
Developmental Diagnosis

- Clinically determined condition
- A description of a particular pattern of developmental unfolding
- Can be wide variation among clinicians, with no one being “wrong”
Unit 2: ASD Diagnosis
Overview
Autism Diagnosis

- Rests on observations of behaviors in a limited time frame
- On ability or willingness of parents to give a supportive history
- On the ability or capacity of the diagnostician to see autism.
- On the developmental trajectory of autism--changes over time
These characteristics have to have a functional impact on life of the child.
The Ideal World
The Real World
We See What We are Trained to See

- Physical Therapists see hypotonia and motor planning problems
- Speech and Language Pathologists see central auditory processing problems
- Occupational Therapists see sensory processing problems
- Psychiatrists see anxiety, ADHD
Principle:

- Children are more complex than our diagnostic boxes
Autism is One Aspect of Complex Central Nervous System (CNS) Dysfunction

- Autism in premies: 25% fail screener
- Autism in cerebral palsy: 15% have an ASD
- Autism and ID/MR/CD: 10-18% have ASD
- Autism and ADHD
- Autism and LD
- Autism and epilepsy
History of Diagnosing Autism

- “Feral,” “possessed,” “changelings”
- 1943-44: Kanner and Asperger
- 1945-75: Psychodynamic period
- 1950-70: Only “classic” autism dx’d
- 1970-1980: Brain-based, MR, epilepsy
- 1980: “PDD” term introduced
- 1994: Asperger Syndrome
- 2000’s: Focus on impaired reciprocity
  - *Summary of talk by Isabelle Rapin, Johns Hopkins, 2006*
Autism Spectrum Disorders

(Previously called the Pervasive Developmental Disorders)
Autism is a developmental disability manifested by persistent deficits in social communication and social interaction co-existing with restricted, repetitive patterns of behavior, interests, or activities.
Early Signs of ASD

- Extremes of temperament
- Lack of connectedness
- Precocious labeling prior to useful language, which leads to parents saying “my child is SO smart.”
- Delayed cooing, babbling, meaningful words despite normal hearing
- Repetitive, unusual behaviors
- May not be any appreciable signs in infancy
Unit 3: ASD in the DSM-5 section I
What’s New in Diagnosis: DSM-5

- The Name: Autism Spectrum Disorder
- Gone are:
  - Autism
  - PDD-NOS
  - Asperger
  - Childhood disintegrative disorder
  - Rett syndrome is no longer in DSM
Lost criteria

- No longer criteria:
  - Delay or lack of language development
  - Lack of varied, spontaneous make-believe play or social imitative play
  - No age requirement (symptoms do not need to be recognized before 3 years) although symptoms must be present “early” whether or not they are recognized at that time.
DSM-5 Criteria: 2 Domains

- Deficits in social communication and social interaction: All 3 criteria in this section must be met.
- Restricted, repetitive patterns of behavior, interests, or activities: 2 of 4 criteria must be met.
Domain 1: Deficits in Social Communication and Social Interaction

A) Deficits in social emotional reciprocity:

- Abnormal social approach
- Failure of back and forth conversation
- Reduced sharing of interests, emotions or affect
- Failure to initiate or respond to social interactions
Domain 1: Social Communication and Social Interaction

B) Deficits in nonverbal communicative behaviors used for social interaction:

- Poorly integrated verbal and nonverbal communication
- Abnormalities in eye contact and body language
- Deficits in understanding and use of gestures
- Lack of facial expression and NV communication.
Domain 1: Social Communication and Social Interaction

C) Deficits in developing, maintaining and understanding relationships:

- Difficulty adjusting behavior to suit various social contexts
- Difficulty sharing imaginative play or in making friends
- Absence of interest in peers
Domain 2: “RRBs” (2/4)

A. Stereotyped or repetitive motor movements, use of objects or speech

-Simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases
Domain 2: RRBs

B) Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior

- Extreme distress at small changes
- Difficulty with transitions
- Rigid thinking patterns, greeting rituals
- Need to take same route or eat same food each day
Domain 2: RRBs

C) Highly restricted, fixated interests that are abnormal in intensity or focus

- Strong attachment to or preoccupation with unusual objects
- Excessively circumscribed or perseverative interests
RRBs

D) Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment

- Apparent indifference to pain/temperature
- Adverse response to specific sounds or textures
- Excessive smelling or touching of objects
- Visual fascination with lights or movement
Unit 4: ASD in the DSM-5 section II
Changes to Criteria

- Diagnostic criteria can be met by history OR chosen as ‘met’ by diagnostician
- Sensory issues got added to behavior domain
- In addition to choosing criteria, you have to choose a severity rating for each domain
Changes to Criteria

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DSM-5

- All those with current diagnosis migrate to “ASD” without further evaluation.
- You can now (officially) diagnose ASD and ADHD together
DSM-5

Say goodbye to the “axis” system (no more axis 1-4) and say hello to:

“SPECIFIERS”
Specifiers for ASD

- With or without intellectual impairment
- With or without language impairment
- Associated with a known medical or genetic condition or environmental factor
- Associated with another neurodevelopmental, mental or behavioral disorder
- With catatonia
Elements of Autism Diagnosis:

- Careful developmental history
- Program information
- Observations of the child
- Interactions with the child
- DSM-IV criteria
- Other available tools (e.g., ADOS)
- Audiology testing
- Cognitive and language testing
- Look for clues to medical diagnosis
- Explanation of the diagnostic process
- Documentation of thought processes
Unique Position of 299.00

• ASD is the only DSM diagnosis I know of that is beginning to require comprehensive developmental testing and specific “optimum” tests.

• This further limits the number of and type of providers, who can provide this type of evaluation.

• Many possible reasons
Absolute Indicators for Autism Evaluation:

- From Filipek, et al, 1999
- No single, meaningful words by 16 months
- No communicative gestures by 12 months
- No flexible 2 word phrases by 2 years
- ANY loss of ANY social or language skill at any age.
The New Numbers

- CDC currently reporting the prevalence of autism spectrum disorders at 1/68 children.
  - Some of the 11 states keep better records than others, some give access to educational records, while others do not
  - Some local effect of diagnosticians
  - There are ethnic/racial differences, probably access issues
  - Changes in the autism construct
Prevalence

- Everything we study increases in prevalence, as we learn about more and more mildly affected individuals: Alzheimer, Parkinson, Traumatic Brain Injury, Polycystic Ovarian Syndrome...and autism.
Outline of Autism 2015 Overview and Update Part B

- Unit 5: What Causes ASD section I
- Unit 6: What Causes ASD section II
- Unit 7: Treatment
- Unit 8: Updates in Prevention and Outcomes
What Does NOT Cause Autism

- Refrigerator mothers
- Immunizations/mercury poisoning
- Diet
- Immune deficiencies
- GI problems
- Lack of oxygen postnatally
Why Some Parents Insist that Vaccines Cause Autism

- Parents would like to see something outside themselves (their genes) as a cause.
- People create the narratives of their lives, which are their own true stories. That does not make the story true from a scientific point of view.
What Causes Autism?

- Genetic Clues:
  - Identical twins—90% both on spectrum
  - Fraternal twins—up to 30% both with autism—higher than expected, implicating prenatal environment
  - Siblings—up to 20% for autism, 10-15% S/L or spectrum issues
  - The Broader Autism Phenotype
# Speech and Language of Parents

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Piven, 1997
What Causes Autism?

- Single gene or chromosomal disorders:
  - Tuberous Sclerosis
  - Smith-Magenis Syndrome
  - Smith-Lemli-Opitz
  - Rett Syndrome
  - Metabolic disorders
  - Angelman Syndrome
  - Fragile X syndrome
  - And dozens more
Fragile X Syndrome
Rett Syndrome

- Used to be the only PDD with specific test.
- Vast majority are girls.
- More profound loss of skills.
- NOT neurodegenerative
- 96% due to MECP2 mutation
- Classical phenotype by 2-3 years.
The Hands
Fetal Alcohol Syndrome

Discriminating Features
- short palpebral fissures
- flat midface
- short nose
- indistinct philtrum
- thin upper lip

Associated Features
- epicanthal folds
- low nasal bridge
- minor ear anomalies
- micrognathia

In the Young Child
Williams Syndrome
Why We Cannot find “the Gene”?

- Because we cannot verify who has autism and who doesn’t
- If you misidentify a relative, all genetic calculations are off
- The current use of ADOS/ADI-R is a circular definition: If you score high on an ADOS, you have autism, thus defining who has it, without a way to verify
- We may miss identifying people who have had enough cognitive ability to adapt, and over identify those who cannot
A recent article by Eric B London in Trends in Neurosciences (2014) puts forth the case that the categorical diagnosis of “autism” is not biologically useful. Autism traits are distributed throughout the population with no clear boundaries. This affects translational research.
Neurodevelopmental Theories

- Broken or intact “mirrors”
- Disordered “connectivity”
- Theory of mind

- No Grand Unification Theory that explains everything. This could be because our underlying constructs are wrong.
“My son has islands of intelligence, but they don’t seem to be connected to each other.”

-Father of little boy with autism
Unit 6: What Causes ASD
section II
What’s New in Etiology?

• Cortical disorganization
• Epigenetics
• Prenatal Depakote exposure
• Advanced paternal age
Cortical Disorganization

- Eric Courchesne is the senior author for a New England Journal Manuscripts (NEJM) article that identified focal disruption of the cortical layers, indicating prenatal timing of onset of autism.
New Study Consistent with Prevailing View of ASD

- General agreement that autism is caused by multiple genetic factors that interact with environmental factors, primarily in prenatal life.
- This pushes those who blame postnatal, environmental factors even further from the mainstream of scientific thought.
Epigenetics

- Epigenetic modifications alter gene expression without changing the primary DNA sequence
- These factors may integrate genetic and environmental influences to dysregulate neurodevelopmental processes.
  - Grafodatskaya, et al, review, 2010
Epigenetic Terms

- **Epigenome** - network of chemical compounds that surrounds the DNA and determines which genes are active

- **Epigenotype** - inherited potential to express a particular type of differentiation
Epigenetic Definitions

- Epimutations—errors in duplication of epigenome during mitosis—errors can be genetic or environmental
- Epigenetic syndromes—dysregulation of genes that control epigenetic mechanisms
The epigenome can be inherited, which goes against much of what we learned about maternal experience during pregnancy affecting the outcome of the fetus in a heritable way.
Epigenetic Syndromes and Risk of ASD

- Rett syndrome-hard to dx c severe ID
- Fragile X syndrome-60-67% M/23%F
- Prader-Willi-19-36.5% (MatUPD higher)
- Angelman-hard to dx with severe ID
- Maternal duplication of 15q11-13->85%
- Beckwith-Wiedemann-6.8%
- CHARGE-15-50%
- Turner-3% X^o higher risk
  - Grafodatskaya, 2010
Valproate

- Risk of ASD in children of mothers who took VPA during pregnancy is 8.9-10.8% with monotherapy and 11.7% VPA+AED

- Possible mechanisms:
  - Inhibition of histone deacetylases—increases gene expression
  - Altered folate metabolism
Paternal and Grandpaternal Age

- Advanced paternal age known to be associated with increased risk of ASD in offspring (Reichenberg, 2006)
- Advanced grandpaternal age: Men who became fathers after 50 were more likely to have a grandchild with autism than men who fathered children at 20-24. (Frans, 2013)
- Possible epigenetic mechanism.
Unit 7: Treatment
Evidence-based Treatment

- Early Intensive Behavioral Intervention
  - Behavior-based
  - Play-based
  - Social communication based

- Medications
There is data to support intensive intervention (>20 hours/week) for children with autism, using “ABA” or “Lovaas” and more recently for social-communication based therapy
Principle:

- There are interventions with both theoretical and evidence-based support and these are BETTER than interventions without either. For those that lack evidence, use the concept of “plausible” or “implausible” to help parents pick and choose.
Other Plausible Interventions

- Teaching joint attention
- Use of social stories
- Visual strategies
- Treatment for sensory processing disorders
- Teaching parents tools to teach children
- Some psychotropic medications
Placebo = Drug Rx in DD

- Matches my clinical impression that prescribers of psychotropic meds often do not investigate a disruptive behavior fully enough before turning to meds.

Why It’s Hard to Evaluate Effectiveness in Autism:

- Placebo may be more effective than study drug in autism: the lessons from the secretin trials
- Using parent report or clinician report of improvement is unreliable. We all see what we are hoping to see.
Psychotropic Medication use Among Medicaid-enrolled Children with ASDs

- University of PA study looked at over 60,000 children with an ASD dx
- 56% used at least one
- 20% were on 3 or more meds
- 18% of 0-2 year olds were on meds
- Fewer inner city children

2008, Pediatrics
Risperidone (Risperdal)

- FDA approval for autism
- Absence of clinical trials comparing risperidone to haloperidol
- Better (75%) than placebo (30%) in RCT
- In France, cost Ris.7x haloperidol
- Risks: sleepiness, weight gain, extrapyramidal movements (25% at 1 year, less in other studies)
Overuse of Medication

- Too many meds prescribed without adequate investigation
- Good problem solving by teachers and parents needed.
- Disruptive behaviors are often communicative—the nonverbal child may be hungry, tired, in a demanding environment, in need of a break, etc. We don’t want to just “medicate” the behaviors
- We may be asking too much.
What’s New in Treatment?

- Early Start Denver Model
- Not new but important:
  - Positive parenting
  - Challenging behaviors are delays (Greene)
Early Start Denver Model (ESDM)

- Comprehensive behavioral early intervention approach for children with ASD between 12-48 months.

- Focus on:
  - ABA strategies
  - Developmental sequence
  - Parental involvement
  - Shared engagement in joint activities
  - Interpersonal relationships
ESDM

- Developed by Sally Rogers and Geraldine Dawson
- Shown to be effective in randomized clinical trial (Pediatrics, 2009)
- Only intervention with evidence for children as young as 12-18 months.
- Local providers: IDS, Family PATH, and (stay tuned) Waisman Center
Positive Parenting I

- Discipline is not about punishment, but about teaching children to be the people we want them to be.
- Teach what we WANT, not only what we don’t want.
- Positives should outweigh negatives by 10:1 (my estimate)
Positive Parenting II

- Most children respond to verbal praise and parental approval.
- This may not work as well for the child with ASD.
- Most children with ASD do have things they care about, however, and we have to use those things to reward positive behaviors.
Examples of Using Interests

- Thomas the Tank Engine stickers
- Pokemon cards
- Videogame model (9 points for level one, 12 points for level two, etc)
- Earned screen time
- Treasure chest
- When there is no other way, use food to get started
- Disney article in NY Times
My Personal Parenting Rules

- Never fight with a child when you don’t control the outcome—so never fight over orifices

- The ‘4 C’s’ of parenting:
  - Be Clear (and specific)
  - Be Concise (do not talk too much)
  - Be CALM (model behavior you want to see)
  - Be Consistent
Challenging Behaviors I

- Ross Greene, PhD, has articulated this best in Lost at School.
- Challenging behaviors are a form of development delay—if a child had another way to respond, s/he would
- Challenging behaviors result from a gap between adult expectation and child ability
Challenging Behaviors II

- Challenging behaviors are the result of a dynamic process between a child and his/her environment.
- We need to stop thinking about labeling the child’s behavior and start thinking about how to modify the adult’s expectations.
- Bill of Rights for Behaviorally Challenging Kids
Unit 8: Updates in Prevention and Outcomes
Periconceptual Folic Acid

- Suren P, et al, Norway
- 85,176 births between 2002-2008
- End of follow-up 2012
- 270 children with ASDs (114 Autism, 56 Asperger, 100 PDD-NOS)
  - Folic Acid users: 0.1% had autism
  - Non-users: 0.2% had autism
  - No association of ASD with fish oil users
Does it Make Sense?

- If folic acid were protective, why would ASD be higher now compared to era before FA fortification of foods?
- Estimates suggest maybe not enough FA to protect?
- Not sure, but *probably* not harmful.
What’s New in Outcomes?

- Adaptive behavior is an important predictor of adult function
- Definition: how we use our intelligence in everyday life
- Standardized measures include the Vineland Adaptive Behavior Scales and the ABAS
- Diagnosis of ID requires both cognitive and adaptive measures
Outcomes in ASD I

- While IQ is an important predictor of adaptive behavior, children with ASD can have a significant gap between IQ (higher) and adaptive (lower).

- This could explain poor adult outcomes with only 10% of adults with autism and average IQ having a good/fair outcome.
  - Gillberg 2009
Outcomes in ASD II

- It does not make sense unless you look at adaptive skills
- Important implication of this is to encourage parents to work diligently on the skills that will help the child have the best independence, be a good employee (be on time, well-groomed, polite to others), care for living needs
Creating the Future

- Nothing is easy, but it is essential that we are leaders in creating a full life for all children.