

# Medical Complications of Autism and The Autism Treatment Network

The 12th annual National Autism Conference:  
Progress Through Partnership

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# The Pathophysiology of Autism: The Many Layers of Autism

## **Autism As**

- A Behavioral Disorder
- A Cognitive Disorder
- A Neurologic or Brain Disorder
- A Developmental Neurobiologic Disorder
- A Genetic & Epigenetic Disorder
- Selective Gene Expression, Heteroplasmy
- A Multiple Organ System Disorder

# Sources of Slides: Two Clinicians Leading the Way

- Margaret Bauman, M.D.
- Ricki Robinson, M.D.

# Medical Issues in Autism

**ASD children and adults often have medical issues that go largely unrecognized and unaddressed:**

- Because autism is widely viewed only as a behavior disorder, and not as a medical disorder
- All abnormal behavior viewed as autism behavior
- Because ASD individuals may express pain and discomfort as negative behavior, rather than self-identify as pain or illness

# Medical Aspects of Autism & The Autism Treatment Network (ATN)

- Medical aspects or expressions of autism
- Underlying medical cause
- Medical complications of autism or its treatment
- Co-occurring disorders
- Ordinary illnesses, accidents, injuries

The Autism Treatment Network: seeing the whole disorder, the whole person, the whole family

# ASD: A Disorder Without A Medical Definition or Medical Home

## **Without a medical identity or home:**

- No accumulation or dissemination of knowledge on medical issues in ASD
- No uniform set of clinical measures to assess medical complications
- No evidence-based standards for assessment or intervention
- No vehicle for coordination across disciplines on health issues- actual disincentives

# Goals for 2008-2010 in Pennsylvania

- Establish state of the art assessment for diagnosis that includes structured instruments with national reliability, and definition of cognitive, language, social-emotional and behavior issues so that families have confidence in first evaluation & it is transportable geographically & across agencies
- Establish medical assessment that reflects scientific knowledge, and generates evidence to advance guidelines for assessment & treatment of medical issues in ASD; Update regularly

## Goals For 2010-2012

- Disseminate standards across state(websites)
- Educate med specialists, PCPs & families
- Increase availability of services
- Monitor & maintain standards
- Feasibility will depend on reimbursement rates reflecting cost of services!
- Update standards as science progresses

# The Autism Treatment Network (ATN)

- Began in 2003
- 5 academic sites: MGH, UW, OHSU, Baylor, Columbia
- Involved multi-disciplinary teams
- Committed to common protocols & sharing data
- To establish scientifically sound & meaningful standards of care

# Why A Consortium? Why Is This Initiative Important?

- It would take many experts & many families to advance understanding & develop national standards- pooling of knowledge and large #s.
- It would take many centers to disseminate these standards across the country so all families benefit.
- Bridge the gap between basic research funded by NIH, community services, and person needs.
- Improve quality of life.

## Why Is This Initiative Important?

- If ASD persons feel better, they are happier and can take better advantage of services provided.
- Subsets of ASD individuals at risk for specific problems may be identified for specific treatment.
- Understanding associated medical conditions could advance understanding of the neurobiology of ASD. For example, a recent animal model of a gene found in an ASD family had circadian rhythm problems.

# ASD and Associated Medical Disorders

- How often do they occur?
- Should anticipatory guidance in ASD include these issues?
- The role of the Autism Treatment Network

# Conclusion

- Individuals with ASD can have any / all medical conditions
- Presentation of usual medical symptoms can be masked by the increase of ASD symptoms
- Diagnosis requires a high index of suspicion and thorough evaluation utilizing all pediatric sub-specialist
- Research needed to document if prevalence of certain medical entities are increased in ASD
- The ATN will help develop standard of care and especially identify anticipatory guidance for associated medical issues

# Starting Points

ASD individuals who feel well will:

- Benefit more from treatments & interventions
- Be better learners
- Act better- have fewer behavior problems
- Enjoy life more

# Starting Points

- ASD individuals need & deserve appropriate medical care
- Many medical issues are treatable
- May not present with typical symptoms
- Changes in behavior or prolonged episodes of abnormal behavior merit a medical evaluation
- We need to learn the language and signs of pain/discomfort in nonverbal and sensory impaired children but also in verbal ASD individuals who cannot form concepts to evaluate how they feel MB

# Medical Issues

- May be an integral part of autism (seizures, MR)
- May be an underlying cause of autism (TS)
- May be a co-morbid condition
- May be a consequence (anxiety, accidents, stress)
- May be a complication of treatment (medications)
- May be a part of being a child (recurrent ear infections) or adult (HBP) or in a particular family
- What we don't know yet

# Neuropsychiatric Issues: Part of Autism, Co-Morbid, Familial, or Induced?

- Mental retardation/intellectual disability
- Attention Deficit Hyperactivity Disorder
- Anxiety Disorder
- Affective Disorder
- Obsessive Compulsive Disorder
- Tics-Tourette's-Other Movement Disorders
- Psychiatric misdiagnoses
- Medication-induced behavior

# Medical Issues That Are Part of Autism

- Seizures
- Sleep disorders (circadian rhythm, sleep apnea)
- Gastrointestinal Disorders
- Underlying medical disorders (disorders that rarely, sometimes, or frequently cause an autistic syndrome; may be infectious (fetal rubella in 1<sup>st</sup> trimester), genetic (tuberous sclerosis), or metabolic (untreated PKU))

# Medical Issues That Are Complications

- Medication induced medical problems (obesity, diabetes), medication interactions that produce toxicity or effect at lower doses or alterations in drug metabolism and hence dose requirements
- Beware impact of OTCs on prescription medications, also OTC side effects
- Stress: leads to irritability, depression, anxiety, gastrointestinal symptoms (ulcers of chronic disease, gastritis), deterioration in behavior etc

# Some Examples of Underlying Medical Issues

- Tuberous sclerosis
- Chromosome 15 deletions/duplications
- Fragile-X syndrome
- Rett syndrome
- Other chromosomal and gene abnormalities that have been identified (perhaps 18% of cases)
- Metabolic Disorders (IEM) (Untreated PKU to Mitochondrial enzyme deficiency)

# Associated Medical Conditions in Autism

Source: Gillberg & Coleman, *The Biology of the Autistic Syndromes*, 1992)

- Fragile X Syndrome
- Other sex chromosome anomalies (XYY)
- Marker chromosome syndrome
- Other chromosome anomalies
- Tuberous sclerosis
- Neurofibromatosis
- Hypomelanosis of Ito
- Goldenhar syndrome
- Rett syndrome
- Moebius syndrome
- Phenylketonuria
- Lactic acidosis
- Hypothyroidism
- Rubella embryopathy
- Herpes simplex encephalitis
- Cytomegalovirus infection
- Williams syndrome
- Duchenne muscular dystrophy
- Purine autism

# Other Medical Issues

- Hormonal imbalance (puberty)
- Endocrine dysfunction (diabetes)
- Immune system: PANDAS
- Allergies (food, environmental)
- Infections
- Genitourinary
- Headaches (migraine)

# Seizures: Persistent Recurring Stereotyped Episodes of Varying Length

- 30% with autism have seizures by 20's
- Predilection for those with low IQ, dysmorphic features, cerebral palsy
- List of known syndromes with mental retardation, seizures, and autism-pretty long
- Co-occurrence of autism and seizures is not chance, e.g., reflects shared biology
- Staring and irritability-aggression clinically
- Infantile spasms-hypsarrhythmia (old days)

# Risk Factors For Seizures in ASD

<u>Risk Factor</u>	<u>Seizure Rate</u>
• No risk factor other than ASD	6%
• Severe MR, motor deficit	25%
• Severe cognitive & motor deficits	42%
• Verbal auditory agnosia w/o MR	41%

# Seizures or Not – Persistent Recurring Stereotyped Episodes of Varying Length

- Often hard to tell - presentation may be atypical
- Routine EEG may not be helpful
- More prolonged EEG by high quality lab may help; study only as good as the person interpreting it
- Use of video monitoring, MEG, videotaping
- Abnormal EEGs exceeds seizure occurrence
- Medication trials should only come after clinical conviction; beware most psychotropic medications make seizures worse

# Sleep Disturbances: Multiple Origins

## **Problems with sleep onset or staying asleep:**

- Is this coming from brain arousal centers?  
Disturbed circadian rhythm, sleep apnea?
- Is this a GI disorder? GERD, gastritis, acid reflux
- Is this a respiratory problem? Mouth breathing due to enlarged tonsils and adenoids, sleep disordered breathing-snoring, obstructive apnea
- Is this related to allergies and nasal congestion?
- Is this related to sensory integration? A need for deep pressure, weighted blanket?

# Sleep Disordered Breathing in Non-ASD Preschoolers

## **Neurobehavioral issues:**

- Hyperactive/inattentive
- Daytime tiredness/sleepiness
- Emotional/social problems
- Behavior issues significantly associated with snoring
- Significant improvement with snoring cessation

Urschultz et al Ped 2004; 114: 1041-48

# Sleep Disordered Breathing in Typical Preschoolers

<u>Breathing Pattern</u>	<u>% Preschoolers</u>
Snoring/difficulty breathing	5-12
Waking during night	16-25
Difficulty getting to sleep	~9
Seems tired in a.m.	~1

# Sleep Disordered Breathing in Non- ASD School Age (8-11yrs)

<u>Sleep Disordered Breathing</u>	<u>8-11 yr olds</u>
Obstructive sleep apnea	5%
Primary snoring	15%
Neither	80%

SDB associated with significant increase in: hyperactivity, emotional lability, oppositional, aggressive, internalizing, somatic complaints, social behaviors

Rosen et al Ped 2004; 114:114:1640-48

# Polysomnography Results in ASD

## Ages 3-9 years

- REM behavior disorder
- Obstructive sleep apnea
- Periodic limb movements of sleep
- Seizures
- Bruxism

Thirumalai et al Jchild Neurol. 2002; 17;173-178

# ASD and Gastrointestinal Issues

## **Often overlooked diagnoses:**

- Gastroesophageal reflux disease (GERD)
- Constipation
- Motility issues
- Lactose intolerance
- Toileting issues (motor planning)

# Gastrointestinal Signs & Symptoms

- Chronic diarrhea or constipation
- Feeding/eating disorder/GE reflux
- Concern about food allergies
- Possible abdominal pain/discomfort
- Distress/behavior following eating or laying down
- Change in sleep patterns
- Behavior changes or increase in severity

# ASD and Gastrointestinal Issues

## **Increase in:**

- Repetitive behavior
- Anxiety
- Activity
- Aggression

# Gastrointestinal Causes

- Disaccharidase deficiency (lactose intolerance): may be familial, follow the flu or antibiotic use
- Gastric ulcers and reflux irritation (of chronic dis)
- Other considerations: dietary induced-lack of bulk, lack of frequency of eating, sugar loads, pica
- Medication side effects including OTCs (examples Mg, CoQ)
- Unknown

# Other Mechanisms of GI Disturbances

- Genes that code for brain development may also code for GI development or maintenance
- Every neurotransmitter in the brain is also in the gut; serotonin, GABA, dopamine, and acetylcholine have been connected with ASD
- All of these neurotransmitters affect GI motility and sensitivity
- Psychotropic medications may alter these neurotransmitter levels too
- Unknown

# ASD / Puberty Related

## **Males:**

- Increased testosterone production
- Secondary sex characteristics
- Possibility of increased aggression
- Brain Growth

# Girls & Women With ASD

- Worsening behavior at puberty
- Small subset with congenital adrenal hyperplasia
- All the feelings, pain, and issues that typical girls and women have across the life span

# ASD / Puberty Related

## Females:

- Increased estrogen / progesterone
  - Secondary sex characteristics
  - Periodic cycling
- Onset of menses
- PMS
- Period related issues
- Use of hormonal treatments (BCPs monthly vs long-term)
- Brain Growth

# GU Referral

- Previously continent child becomes incontinent and it is not due to a UTI
- Usually a preteen
- May be a spastic bladder
- Ditropan may be helpful

# ASD / Allergy

- Allergies occur in approx 20% pediatric population
- Allergic rhinitis, asthma, atopic skin disease
- Food & environmental antigens
- Needs to be diagnosed & treated vigorously
- Pediatric allergist referral if needed

# ASD / Infection

- High index of suspicion with ASD symptoms
- Consider untreated URI: may be acute or chronic
  - Otitis media
  - Sinusitis
  - Untreated Group A Streptococcal tonsillitis
- UTI
- Aggressively diagnose & treat
- Problem: under-served population

# GROUP A - Beta Hemolytic Streptococcal (GABHS) Tonsillopharyngitis (TP)

- School-aged children
- Sore throat, fever, headache, abdominal pain
- Winter & Spring months
- Diagnosis confirmed by throat culture
- Treatment: antibiotics
- Course: S/T Illness self-limited, resolved ~5d
- GABHS - serum antibodies Sinusitis
  - ASOT
  - Anti DNase B

# GABHS 2ary Effects

- Certain individuals AB production leads to end-organ damage
- AB cross-react with:
  - Kidney post GABHS glomerulonephritis-PSGN) -10 days
  - Heart (rheumatic fever-RF) - 18 days
  - Brain (Sydenhams Chorea) – months later
- Diagnosis depends on elevated titers of strep antibody (only 1 required)

# Pediatric Autoimmune Neuropsychiatric Disorder Associated with GABHS (PANDAS)

## Diagnostic Criteria

- Pediatric onset (pre-pubertal)
- Neuropsychiatric disorder (OCD) and/or TIC disorder
- Abrupt onset and relapsing/remitting course
- Association with GABHS and symptoms
- Association with neurologic abnormalities (motoric hyperactivity or adventitious movements, including choreiform movements, tics, clumsiness)
- Controversial Pediatric Concept

# Obsessive Compulsive Disorder (OCD)

## Characterized by:

- Obsessions: Intrusive and unwanted thoughts or images that cause anxiety or distress
- Compulsions: Actions performed to soothe the distress caused by obsessions
- Diagnose in adolescence (male) or early adulthood (female)
- Lifetime prevalence 2-3%
- Co-morbid depression, tics, anxiety disorders
- Slow insidious onset months - years before diagnosis
- Children with Sydenham's Chorea exhibit OCD
- 70% sudden onset OCD

# PANDAS: Proposed Etiology

(Swedo et al, J Child Psychol Psychiatry; 2005; 46 (3): 227-34)

- Post GABHS autoimmunity (e.g. Sydenhams Chorea)
- GABHS infection in susceptible host (?D8/17 marker) - incites AB to GABHS - AB cross reacts with cellular components of basal ganglia - AB interacts with neurons of basal ganglia - neuropsychiatric symptoms (OCD, tics)
- Controversial hypothesis but + MRI – inflammation thalami and basal ganglia
- Anti-basal ganglia antibodies found in some acute cases

# PANDAS: Prospective Study Results

- Positive GABHS
  - Throat Swabs
  - Rapid antigen detection
  - Culture
- GABHS serology +++ (anti-DNA se titers)
- Treatment: anti-GABHS antibiotics - PROMPT disappearance of OCD
- Recurrence OCD symptoms
  - 50% (6/12 patients)
  - Each responded to AB therapy

# PANDAS: Prospective Study Results (cont'd)

- OCD behaviors
  - Hand washing/ preoccupation with germs
  - Daytime urinary urgency/frequency (w/o dysuria, fever, incontinence) - 58%
    - Symptoms not present at night
    - UA/UC negative
    - More common than usual OCD series

# PANDAS: How to Diagnose

(Swedo et al, Am J Psychiatry 1998; 155: 264-271)

- History
- Physical Exam
- Evidence of GABHS infections
  - Throat swab test by rapid antigen-detection assay
  - Throat culture
  - GABHS antibody titers
    - ASO
    - Anti-DNase B
    - Anti-neuronal antibodies

# ATN Red Flags For Medical Evaluations

## Initial Guidelines:

Neurology

Sleep

Gastroenterology

Genetics

Inborn Errors of Metabolism

Infectious Disease

Psychiatry/Behavioral Neurology

# ATN Neurology Red Flags

- ✓ Seizures or seizure-like episodes
- ✓ Regression or loss of skills at any age but especially after 2 years of age (in conjunction with or after evaluation by Metabolic Genetics)
- ✓ Regular nighttime awakenings, daytime sleepiness (after appropriate interventions and evaluation by Sleep lab and Peds GI if needed)

**If Yes refer to the Peds Neurologist**

# Sleep BEARS

Domain	PRESCHOOL (2-5 Years)
<b>B</b> edtime problems	Does your child have any problems going to bed? Falling asleep?
<b>E</b> xcessive daytime sleepiness	Does your child seem over tired or sleepy a lot during the day? Does she still take naps?
<b>A</b> wakenings during the night	Does your child wake up a lot at night?
<b>R</b> egularity and duration of sleep	Does your child have a regular bedtime and wake time? What are they?
<b>S</b> leep-disordered breathing	Does your child snore a lot or have difficulty breathing at night?

# Sleep BEARS

Domain	SCHOOL-AGED (6-12 Years)
<b>B</b> edtime problems	Does your child have any problems at bedtime? (P) Do you have any problems going to bed? (C)
<b>E</b> xcessive daytime sleepiness	Does your child have difficulty waking in the morning, seem sleepy during the day or take naps? (P) Do you feel tired a lot? (C)
<b>A</b> wakenings during the night	Does your child seem to wake up a lot at night? Any sleepwalking or nightmares? (P) Do you wake up a lot at night? Have trouble getting back to sleep? (C)
<b>R</b> egularity and duration of sleep	What time does your child go to bed and get up on school days? Weekends? Do you think he/she is getting enough sleep? (P)
<b>S</b> leep-disordered breathing	Does your child have loud or nightly snoring or any breathing difficulties at night? (P)

# Sleep BEARS

Domain	ADOLESCENT (13-18 Years)
<b>B</b> edtime problems	Do you have any problems falling asleep at bedtime? (C)
<b>E</b> xcessive daytime sleepiness	Do you feel sleepy a lot during the day? in school? while driving? (C)
<b>A</b> wakenings during the night	Do you wake up a lot at night? Have trouble getting back to sleep? (C)
<b>R</b> egularity and duration of sleep	What time do you usually go to bed on school nights? Weekends? How much sleep do you usually get? (C)
<b>S</b> leep-disordered breathing	Does your teenager snore loudly or nightly? (P)

If Yes to 1 or more,  
refer to the Peds Sleep Physician

# ATN GI Red Flags

- Apparent pain/discomfort (how can the family tell?)
- Resists eating, although appears hungry
- Apparent abdominal pain after meals
- Discrete episodes of apparent abdominal pain occurring  $> 1/\text{week}$
- Nocturnal awakenings after appropriate interventions for behaviorally based sleep disorder

# ATN GI Red Flags

## Changes in stool pattern:

- 3 or more loose or watery stools per day for > 2 weeks
- Mucous and blood in stools
- 2 or fewer BM's per week that are hard in consistency (after appropriate interventions from PCP or Developmental Pediatrician)
- Regular stains in underwear between BM's

# ATN GI Red Flags

- Flatulence, bloating occurring 2-3 times per week for > 2 weeks
- Unexplained weight loss
- Persisting or unexplained severe behavior problems after appropriate management\*\*

**If Yes to 1 or more symptoms, refer to Peds GI**

\*\* (referral for severe and persisting behavioral problems only after discussion with the Peds GI)

# ATN Genetic Red Flags

## **Autism and developmental delay/MR with:**

- Multiple minor and/or major physical anomalies
- Unusual skin findings suggesting genetic or chromosomal disorder e.g., hyper or hypo pigmented patches, hypomelanosis of Ito
- Failure to thrive
- Multiplex family (2 or more affected members)

If Yes, refer to Genetics Clinic after obtaining blood chromosomal analysis with FISH (vs. microarray analysis) and Fragile-X DNA studies

# ATN Metabolic Red Flags

- Lethargic: seems tired during the day
- Sleeps too much: takes long daytime naps and sleeps more than 10 hour at night
- Fatigues easily, runs out of energy quickly
- Failure to thrive
- Spells of vomiting
- Regression or loss of skills at any age but especially after 2 years of age

# ATN Metabolic Red Flags

- Unusual odor
- Hypotonia, motor skills significantly delayed for developmental age
- Seizures
- Spells of vomiting
- Failure to show expected developmental progress
- Physical features suggesting metabolic disorder, e.g., cataracts/lens opacities, chronic or recurrent rash, coarse facies, joint contractures, organomegaly

# ATN Red Flags For Metabolic Work-Up MB

- Poor physical endurance
- Late walking (24 months)
- Repeated regression after 2 ½ years
- Dysmorphic features
- Qualitatively different
- Involvement of multiple organ systems
- Poor progress despite excellent services

If Yes to any of the above, obtain urine for metabolic screen, including amino acids, oligosaccharides and organic acids and refer to Metabolic Clinic (Inborn Errors of Metabolism)

# Follow-up Medical Evaluations Ricki Robinson

Intervening problems

# General Pediatrics Approach Ricki Robinson

## **If parent reports sudden change in behavior:**

- Repetitive/OCD/tic behavior
- Activity
- Aggression

## **DIR Approach**

- Take history
- Environmental changes (emotional, situation, physical-external/internal)
- PE / Floortime observation

## General Pediatrics Approach (cont'd)

### **Common entities happen commonly!**

- Infection
- Allergy
- Migraine
- Constipation
- Sleep changes
- Adverse response to meds

# General Pediatrics Approach (cont'd)

## Follow-up Considerations

- Change, bullying, seizures (especially if regression)
- Co-morbid psychiatric disorders (depression)
- Autoimmune issues

## Lab Tests

- GABHS
- ASOT
- Anti DNase
- UA/UC
- Abdominal XRay
- Sleep EEG if needed
- Others warranted by Hx/PE

# General Pediatrics Approach (cont'd)

## Treatment

- Appropriate to Dx
- Medicine trial often used (Anti-inflammatory: migraine)
- Neuropsychopharmacology

## If resolution

- Close follow up required
- Documentation/timeline very useful (seasonal affective disorder)

## If no improvement – Back to the Drawing Board!

- Search for individual patterns of response is KEY

# Early Signs of ASD, Screening, Initial Evaluation

# Key Clinical Milestones Observe By 18 Months

- Child's ability for warm, joyful relating
- Child's ability for engaging in a continuous back-and-forth pattern of emotional and gestural cueing
- Child's ability to engage with a caregiver in an intentional, complex, reciprocal interactive pattern (e.g., pushing the caregiver to the refrigerator and pointing to the desired food)

# THE CHAT

## (Checklist for Autism in Toddlers)

To be used during the 18-month developmental check-up

### Section A – Ask Parent

- Does your child enjoy being swung, bounced on your knee, etc.?
- Does your child take an interest in other children?
- Does your child like climbing on things, such as upstairs?
- Does your child enjoy playing peek-a-boo/hide-and-seek?
- Does your child ever pretend, for example, to make a cup of tea using a toy cup and teapot, or pretend other things?

## THE CHAT (cont'd)

6. Does your child ever use his index finger to point to ask for something?
7. Does your child ever use his index finger to point to indicate interest in something?
8. Can your child play properly with small toys (e.g. cars or bricks) without just mouthing, fiddling or dropping them?
9. Does your child ever bring objects over to you (parent) to show you something?

# THE CHAT (cont'd)

## Section B – GP'S Observation

- During the appointment, has the child made eye contact with you?
- Get the child's attention, then point across the room at an interesting object and say, "Oh, look! There's a (name a toy)!" Watch the child's face. Does the child look across to see what you are point at?
- Get the child's attention, then give the child a miniature toy cup and teapot and say, "Can you make a cup of tea?" Does the child pretend to pour out tea, drink it, etc.?
- Say to the child, "Where's the light?" or "Show me the light." Does the child point with his/her index finger at the light?
- Can the child build a tower of bricks? If so, how many?

# Level 2 - Neurodevelopmental Referral

**GOAL** - Make a diagnosis that will best prescribe the developmentally appropriate therapeutic intervention for the child.

**WHO** - Physician specialized and/or experienced with children on the spectrum (e.g., developmental pediatrician, pediatric neurologist, child psychiatrist)

## **TOOLS**

- √ Family, Medical and Developmental history
- √ Physical and neurologic exam
- √ Functional/emotional developmental level assessment
- √ Standardized diagnostic instruments (e.g., CARS, GARS, ADI R, ADOS)
- √ Evaluation by other team members

# ASD Diagnostic Concerns

## 1. Core Issues

- √ Language delay
- √ Social delay
- √ Repetitive behavior

## 2. Associative Issues

- √ Motor planning (oromotor dyspraxia, gross/fine motor delays, low tone)
- √ Sensory processing (auditory, visual-spatial, touch, taste)
- √ General regulatory/arousal (eating disorders, sleep disorders, pain response, hyperactivity)

# ASD Diagnostic Concerns (cont'd)

## 3. Other Medical Issues

- ✓ Regression
- ✓ Seizures (+/- “spacey episodes”) recurrent illness / immune status
- ✓ Allergies
- ✓ Gastrointestinal symptoms (constipation)

## 4. Targeted Issues

- ✓ Tics
- ✓ Mood disorders (bipolar)
- ✓ Self injurious behavior
- ✓ Anxiety
- ✓ Attention

# Level 2 Evaluation

## 1. Family History

- ✓ autism, mental retardation, Fragile-X, tuberous sclerosis, affective disorders, metabolic disorders, autoimmune disorders

## 2. Developmental History

- ✓ emphasis on regression and specific developmental level attainment

## 3. Medical History

- ✓ evidence of recurrent infections, response to immunizations, environmental exposures, review of systems, especially GI and neuro-related

## Level 2 Evaluation (cont'd)

### 4. Physical and Neurologic Examination

- ✓ longitudinal measurements of HC
- ✓ neurocutaneous abnormalities (Woods-lamp exam)
- ✓ dysmorphic features
- ✓ reflexes and cranial nerve functions
- ✓ muscle mass and tone
- ✓ gait, posture, facial movement (Moebius mouth), and generalized movement

## Level 2 Evaluation (cont'd)

### 5. Standardized Diagnostic Instruments

- ✓ Based on DSMIV definitions, (CARS, ADI-R, ADOS)

### 6. Evaluations by other team members

- ✓ Speech and language
- ✓ OT
- ✓ Education
- ✓ Visual/motor
- ✓ Neuropsychiatric