THE AUTISM EXPLOSION: MYTH OR REALITY?
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New Orleans, LA

Roundtable/Poster abstract
Deadline: November 1, 2012
IF YOU CAME HERE TO FIND OUT WHAT CAUSES AUTISM...
If you can’t explain it **simply**, you don’t understand it well enough.

— Albert Einstein
WHAT IS AUTISM?

- Diagnosis is *behaviorally* based
  - No specific genetic, medical or laboratory tests are diagnostic
- Autism is a *spectrum disorder*
  - Wide variety of behavioral characteristics, ranging from mild to very severe involvement
WHAT IS AUTISM?

• The Autistic Spectrum Disorders (ASD), aka Pervasive Developmental Disorders (PDD) are characterized by deficits in 3 major areas:
  
  • Social interaction/relatedness
  • Verbal/nonverbal communication
  • Restricted interests, repetitive/stereotyped behaviors, resistance to change

*American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV)*
AUTISTIC SPECTRUM DISORDERS: CLASSIFICATION (DSM IV)

- Childhood Autism or Autistic Disorder
- Asperger Disorder
- Pervasive Developmental disorder, NOS
- Rett Syndrome
- Childhood Disintegrative Disorder
COMMON CHARACTERISTICS OF AUTISM

- Insistence on sameness; resistance to change
- Stereotypical (repetitive, non-productive) movements
- Not responsive to verbal cues
- Difficulty in expressing needs
- Difficulty interacting in social situations
- Inappropriate attachments to objects
- Little or no eye contact
COMMON IMPAIRMENTS

- Sensorimotor deficiencies
- Echolalia
- Deficiencies in symbolic thinking
- Self-injurious behaviors
- Mental retardation (70%*)
- Seizure disorders (approx 30% of adolescents have had two or more seizures*)

(American Psychiatric Assoc. Diagnostic and statistical manual of mental disorders, 4th ed.)
HISTORICAL PERSPECTIVE

- 1943 - Kanner described a group of children with symptoms of “an extreme aloneness...and an obsessive desire for the preservation of sameness.” He used the term *autism* to describe the condition.

- 1944 – Asperger described 4 children with normal IQs and verbal abilities who had behavioral characteristics consistent with autism.
1960s – 1970s: Neurobiologic studies associating convulsions and abnormal EEGs in children with autism

1980s: Bauman demonstrated abnormalities in the frontal brain, hippocampus and cerebellum suggesting abnormal fetal brain development occurring between 12-30 weeks of fetal life
HISTORICAL PERSPECTIVE

1985: Fragile X Syndrome identified
1990s: Genetic studies in autism
- Monozygotic twin studies – 70-90% concordance for autism
- Dizygotic, same-sex twins – 5-10% concordance
- Sibling recurrence risk – 4-8%
- Associations of tuberous sclerosis, Prader-Willi & Angelman Syndromes with autism demonstrated
A measure of the risk of developing some new condition within a specified period of time.

The rate of occurrence of new cases.

Incidence conveys information about the risk of contracting the disease.

http://en.wikipedia.org/wiki/INCIDENCE
Measure of the total number of cases of disease in a population,
Indicates how widespread the disease is

http://en.wikipedia.org/wiki/
- Original survey-1966
  - 4 cases per 10,000
    (Lotter V, Soc Psychiatry 1966;1:124-37)

- From 1966 – 2003: 54 studies that reported disease frequency statistics
  (Blaxill M. Public Health Reports 2004 Nov-Dec;119:536-551)
EPIDEMIOLOGY:
MORE RECENT STUDIES

- Childhood autism: 27.2 per 10,000

- Autism: 7 cases per 10,000
  (Fombonne E, Psychol Med 1999;29:769-86)

- Autistic Spectrum Disorders: 30-60 cases per 10,000
  (Rutter M, Acta Paediatrica 2005;94:2-15)

- CA Dept of Developmental Services: 31.2 per 10,000
  (Cal HHS Agency, Dept of Devel Services;2003)
PREVALENCE OF ASD IN THE UNITED STATES

- 2000: 4.5-9.9/1,000 (CDC data)
- 2011: 1 in 80 and 1 in 240 with an average of 1 in 110 children in the U.S.
- Dx growing 10-17% per year (U.S. Dept of Ed est.)
- DATA last 5 years (2006–2011) is 2 to 4 times greater than some estimates: 45 to 110/10,000.
Review on epidemiological studies on the prevalence in ASD globally

- 62/10,000 (estimate)
- Need more info internationally & prevalence will be more accurate
  

- 3 to 17 years to be 47 per 10,000
  

(Remember: **Prevalence** is the measure of the total number of cases of disease in a population, indicates how widespread the disease is)
PREVALENCE & INCIDENCE OF ASD IN TAIWAN FROM 1996 TO 2005

- **Incidence:**
  - 0.91/10,000 in 1997 to 4.41/10,000 in 2005.

- **Higher incidence in**
  - the 0 to 5 age group
  - males
  - those in northern, southern, and eastern regions & urban areas

*(Chien et al J Child Neurol 2011 26: 830)*
Baseline prevalence for future comparison
Common case definition
Standardized data abstraction
Clinician review
Quality assurance procedures

1/152 children

(more common than childhood cancer, diabetes and AIDS combined).
Gender
- Male:Female
- 3.4:1 (MD, SC & WI)
- 6.5:1 (UT)

Females more likely to be cognitively impaired

Skewed ratio remains unexplained: despite the contribution of a few well characterized X-linked disorders, male-to-male transmission in a number of families rules out X-linkage as the prevailing mode of inheritance.
<table>
<thead>
<tr>
<th>STATE</th>
<th>1992-93</th>
<th>2000-01</th>
<th>% increase</th>
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<tbody>
<tr>
<td>California</td>
<td>1,605</td>
<td>10,557</td>
<td>558</td>
</tr>
<tr>
<td>Florida</td>
<td>582</td>
<td>3,926</td>
<td>527</td>
</tr>
<tr>
<td>Illinois</td>
<td>5</td>
<td>3,103</td>
<td>Almost infinite</td>
</tr>
<tr>
<td>New York</td>
<td>1,648</td>
<td>5,943</td>
<td>260</td>
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<tr>
<td>Texas</td>
<td>1,444</td>
<td>6,023</td>
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Changes in Prevalence of ASDs among Children 8 Years Old, 2002 to 2006

<table>
<thead>
<tr>
<th>State</th>
<th>2002</th>
<th>2006</th>
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<tbody>
<tr>
<td>AL</td>
<td>2.0</td>
<td>2.5</td>
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<tr>
<td>AZ</td>
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<td>8.0</td>
</tr>
<tr>
<td>CO</td>
<td>4.0</td>
<td>6.0</td>
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<tr>
<td>GA</td>
<td>6.0</td>
<td>8.0</td>
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<tr>
<td>MD</td>
<td>4.0</td>
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<tr>
<td>WI</td>
<td>6.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Average</td>
<td>5.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>
WHY THE INCREASE?

- Better diagnosis
- Broader definition
- Marked increase in rate of individuals with ASD with normal intelligence (i.e. Asperger’s)
DIFFERENCES IN SURVEY DESIGN

- Definition of condition
  - Nomenclature
  - Diagnostic criteria
  - Spectrum diagnoses
  - DSM-III 1987 PDD-NOS
  - Measurements (incidence v. prevalence)
  - Case ascertainment (health v education systems)
  - Cultural differences
Overall prevalence of ASDs:
11.3 per 1,000 (or 1 in 88)
**ADDM 2008**

- **8-Year-Old Children**: 337,093 (8.4% of all the 8-year-old children in the US in 2008)

- **Range of prevalence estimates across sites**: 4.8/1,000 to 21.2/1,000

- **Boys**: 18.4/1,000 (or 1 in 54)

- **Girls**: 4.0/1,000 (or 1 in 252)

CHANGES IN PREVALENCE OF ASD

- Difference between 2006 ADDM Network and 2008: 23% increase
- Difference between 2002 report and 2008: 78% increase
Diagnosis & Screening

- Diagnosis can be made before age 3

- AAP recommends autism specific screening tool for all children at 18 and 24 month visits

- Only 8% of pediatricians regularly screen for autism
MEASUREMENTS/TOOLS

- The Modified Checklist for Autism in Toddlers (M-CHAT)
- Autism Diagnostic Observation Schedule (ADOS)
No medical tests for autism

DX based on observation, and requires that the patient exhibit abnormal behavior in 3 categories:

- Impairment of social interaction
- Impairment of communication skills
- Restricted and repetitive interests and behaviors
5 behaviors in young children that signal a need for further evaluation:

- No babbling, cooing by 12 months
- Does not point, wave, grasp by 12 months
- No single words by 16 months
- No 2 word phrases by 24 months
- Loss of previously acquired language and/or social skills
Approximately **40%** of children with an ASD do not talk at all.

Approximately **25%–30%** of children have some words at 12 to 18 months of age and then lose them.

Others may speak later in childhood.

Epilepsy occurs in at least 30% of cases of traditional autism, usually in the preschool years or around puberty.

20% children with autism, a history of regression is present.

MORTALITY IN INDIVIDUALS WITH AUTISM, WITH AND WITHOUT EPILEPSY

- Population of California with Autism vs patients with comorbid epilepsy
- Mortality rates were higher when epilepsy was present as a co-morbid disease

CDC found 91% increase in prevalence among black children (5.5-10.5 in 1000)
110% increase among Hispanic children (3.7-7.7 per 1000)
70% increase among white children (7.0-11.9 per 1000)
Suggests: better diagnosis?

“...odds of a boy being diagnosed with ASD are approximately 4 times greater than girls”

ETIOLOGY

- UNKNOWN
- Proposed theories:
  - Genetic
  - Neurotransmitters (seratonin)
  - Infection
  - Metabolic errors
  - Immunologic
  - Inflammation
10% of ASD cases associated with genetic disorders
- e.g. tuberous sclerosis, Prader-Willi & Angelman Syndromes

GENETIC DISORDERS ASSOCIATED WITH AUTISTIC BEHAVIORS

- Fragile X (5% of people with an ASD have fragile X; 10% -15% of those with fragile X show autistic traits)
- Rett Syndrome
- Tuberous sclerosis (1-4% of people with ASD)
- Prader-Willi Syndrome
- Angelman Syndrome
- Various deletion, translocation and duplication syndromes

http://www.cdc.gov/ncbddd/autism/data.html
Monozygotic twin studies – 60% concordance
Dizygotic, same-sex twins – 0% concordance

Reevaluation of broader phenotype
including communication and social disorders
MZ twins 92%
DZ twins 10%
Sibling recurrence risk – 2-8%

Concordance of ASD was reported to be significantly greater among monozygotic twins (88.1%) than dizygotic twins (30.5%)

MARCUS AND LUKE
“This suggests that interactions between multiple genes cause “idiopathic” autism but that epigenetic factors and exposure to environmental modifiers may contribute to variable expression of autism-related traits. The identity and number of genes involved remain unknown.”

“the study of heritable genetic factors that are not part of the DNA sequence”

Epigenetic mechanisms may be responsible for changes in gene expression due to methylation, not mutation in the DNA sequence

Heritable AND influenced by the environment

Lopez-Rangel E, Lewis ME. Clinical Genetics 2006;69:21-22
2193 genes, 2806 SNPs/VNTRs, 4544 copy number variations (CNVs) and 158 linkage regions have been associated with ASD.

Core data set of 434 high-confidence genes.

Xu LM. Et al Nucleic Acids Research, 2012, Vol. 40, Database issue, Published online 1 December 2011
26 high-penetrance, high-risk genes that have arisen as de novo mutations and have been associated with ASD phenotype, with 13 involving gene expression in the synapse.

Gillis & Rouleau, 2011
Teratogens such as valproic acid & thalidomide in early prenatal life can effect developing CNS or may act to influence phenotypic expression.

Autism Research Institute recommendations for safe dental care.

“Donald Robbins, DMD, FAGD, AIAOMT, is a bio-safe dentist protecting patients’ overall health, practicing in Exton, Pennsylvania.”

www.autism.com
www.donaldrobbinsdmd.com
Both maternal and paternal age were independently associated with autism.

Firstborn offspring of 2 older parents were 3 times more likely to develop autism than were third- or later-born offspring.

Fathers >50 y.o: 2.2X more likely for child w/ASD than a father <29 y.o.

Risk increased significantly with each 10-year increase in maternal & paternal age

Maternal age at the time of conception & delivery may be associated with an increased risk

860 cases in the birth cohort study were examined.

Risk started to increase at the paternal age of 30, plateau after age 40; further increased from the age of 50 years.

Fathers >50 years had 2.7X increased risk of having an offspring with ASD.

Hultman CM et al. Molecular Psychiatry (2011) 16, 1203–1212
“Global variation in gene expression that could explain the multi-systemic effects of autism exploring the regulation of genes globally, rather than a link to specific individual genes or SNPs. (single nucleotide polymorphisms)"

Alter MD, et al 2011
Decrease in variance in the distribution of gene expression levels in ASD & increased paternal age

Suggest the presence of epigenetic paternally transmitted factors in both mice & humans that can influence brain development and global levels of gene expression regulation
Prevalence of autism in low birth weight (<2500g) or preterm (33 wks) children
- markedly lower than in other developmental disabilities.

Approximately twofold increased risk for autism

Gender variation: (higher in girls) and also autism subgroup (higher for autism accompanied by other developmental disabilities).

Schendel D, Karapurkar Bhasin T. Pediatrics Vol. 121 No. 6 June 2008, pp. 1155-1164
529 participants in Israel (comparison to newborn data)

Advanced parental (M and P) age was associated with ASD,

ASD cohort had significantly higher % of low birth weight (<2500g) and very low birth weight (VLBW < 1500 g)

Itzchak EB etal Research in Developmental Disabilities 32 (2011) 1776–1781
MATERNAL INFECTION

- Viral?
  - Congenital rubella, congenital cytomegalovirus, perinatal herpes

  “Maternal Influenza Infection During Pregnancy Impacts Postnatal Brain Development in the Rhesus Monkey”

  Example of the experiments being done on primate models to evaluate the effect that maternal infection can have on brain development.

Compared results obtained with those from animal models of autism or with clinical data on the biochemical profile of autistic patients.

Neurotoxicity of PA as an environmental factor could play a central role in the etiology of autistic biochemical features.

El-Ansary AK et al Journal of euroinflammation 2012, 9:74
The enteric bacterial metabolite propionic acid alters brain and plasma phospholipid molecular species: further development of a rodent model of ASD

MCFABE’s Group

JENNY MCCARTHY

Louder than Words
A Mother's Journey in Healing Autism

Jenny McCarthy
New York Times Bestselling author of Baby Laugh
“leaky gut”? Allows some toxins from gluten containing foods to get into the brain? Anecdotal improvements

(IAN Autism Speaks, online parental survey)
“All this gluten intolerance, and using the diet to treat autism, ADHD ... there's no documented scientific reason for that at all. However, patients without celiac disease often do notice an improvement in a whole spectrum of gastrointestinal or neurological symptoms when they start a gluten-free diet. But it's not defined by any medical diagnosis.”

Dr. Peter Green, director of the Celiac Disease Center at Columbia University

*Newsweek Web Exclusive Dec 3, 2008*
"However, these are the facts: celiac disease is present in roughly 1 percent of the general population and maybe can affect twice as much [of the population] among autistic kids." That means perhaps 2 percent of autistic kids have it. “

"I don't think there's too much scientific basis to justify [the] broad intervention of a gluten-free diet.”

Dr. Alessio Fasano, pediatric gastroenterologist, University of Maryland.

Newsweek Web Exclusive Dec 3, 2008
“With the present data, we are forced to agree with the previous work by Pavone et al., who concluded that concomitant occurrences of autism and CD in the same individuals are most likely due to pure coincidence.”

Children with (ASD) who exhibit chronic GI symptoms & marked fluctuation of behavioral symptoms exhibit distinct innate immune abnormalities & transcriptional profiles of peripheral blood (PB) monocytes

Mothers exhibit some of the same things. (PB monocytes)

Evaluation of different recommendations of studies on children with ASD and GI disorders.

CONCLUSION: more info is needed on all topics before recommendations can be made.

Buie T et al. Pediatrics 2010;125;S1

Examines the roles that immunology may have in the etiology of ASD
Differences between ASD immune responses (with T cells and cytokines, etc.) as compared to a control group.

Small subject group, but good info linking the immune system to the aberrant behaviors seen in ASD

Cross-sectional study looked at mother’s cytokine levels during mid-gestation, & then related it to the children with ASD, DD, and general population.

Elevated serum IFN-g, IL-4 and IL-5 (cytokines) was more common in women who gave birth to a child subsequently diagnosed with ASD.

Goines PE et al Molecular Autism 2011, 2:13
“An alternative profile of increased IL-2, IL-4 and IL-6 was more common for women who gave birth to a child subsequently diagnosed with DD without autism. Further investigation is needed to characterize the relationship between these divergent maternal immunological phenotypes and to evaluate their effect on neurodevelopment.”
ENVIRONMENT: METABOLIC IMBALANCE AND METHYLATION

- 68 children with ASD, 54 age-matched control children & 40 unaffected siblings
- Both methionine & SAM were significantly decreased in children with autism. The SAM/SAH ratio, an indicator of methylation capacity, was decreased in children with autism compared to their siblings but not different between siblings and controls.

“redox biomarkers are specific for autistic disorder and not present in unaffected siblings who share similar genes and environmental exposures, not possible to discern whether the observed deficits in methylation and redox capacity contribute to autism pathogenesis or are simply a reflection of on-going autism pathophysiology.”
MMR VACCINE

“It is clear that none of the epidemiological findings provide support for an association between MMR vaccine and ASD.”

(Rutter M, Acta Paediatrica 2005;94:2-15)
Controversial figure in GI research at the Royal Free Hospital in London

1998 Press Conference: announced that he had concerns about the safety of the measles-mumps-rubella vaccine (M.M.R.) and its relationship to the onset of autism
Did not claim to have *proved* that the M.M.R. vaccine caused autism

Based on a study with *n=12*

Proposed that three vaccines, given together, can alter a child’s immune system by allowing the measles virus in the vaccine to infiltrate the intestines; certain proteins, escaping from the intestines, could then reach and harm neurons in the brain.
2003 paper in The Archives of Pediatrics and Adolescent Medicine, which reviewed a dozen epidemiological studies, concluded that there was no evidence of an association between autism and M.M.R.
Britain’s General Medical Council revoked Wakefield’s medical license

Lengthy hearing

Cited numerous ethical violations (like failing to disclose financing from lawyers who were mounting a case against vaccine manufacturers!)
Published the original Wakefield paper, retracted it

2011: The British Medical Journal concluded that the research was not just unethically financed but also “fraudulent” (ie: timelines were misrepresented, to suggest direct causality of the vaccine).
REPERCUSSIONS

- Vaccination rates plunged
- Re-emergence of Childhood diseases once essentially eradicated here such as [**whooping cough**] and measles
12 publications of original data evaluating the design of the studies

Concludes that the studies do not demonstrate a link between thimerosal-containing vaccines & ASD.

Evidence supporting the link was found to have major flaws in their design.

Parker SK et al. PEDIATRICS Vol. 114 No. 3 September 2004
Immunization Safety Review Committee

- new epidemiological evidence from the U.S., Denmark, Sweden, & U.K., and studies of biologic mechanisms related to vaccines and autism since its report in 2001

Conclusion:

“that this body of evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism, and that hypotheses generated to date concerning a biological mechanism for such causality are theoretical only.”

http://www.fda.gov/CBER/vaccine/thimerosal.htm
- Benefits of vaccination are proven
- Hypothesis of susceptible populations is presently speculative
- Widespread rejection of vaccines would lead to increases in incidences of serious infectious diseases like measles, whooping cough and bacterial meningitis.

http://www.fda.gov/CBER/vaccine/thimerosal.htm
Thimerosal was eliminated from routinely administered childhood vaccines manufactured after 2001, yet autism rates have continued to climb.

-Dr. Julie Gerberding, director of the Centers for Disease Control and Prevention (CDC) 2008

www.time.com/time/health/article/0,8599,1721109,00.html
- 71 families
- 26% of parents answered ‘yes’ to the question concerning a belief that something specific had caused or contributed to their child’s autism
- 45% answered ‘maybe’: most commonly immunizations, genetic predisposition, and environmental exposure of the mother or child

Harrington J et al. Autism 2006; 10; 452
PARENTAL BELIEFS ABOUT AUTISM: IMPLICATIONS FOR THE TREATING PHYSICIAN

- Most frequent responses involved delaying or withholding immunizations
- 29% of parents cited Immunizations as the cause of their child’s autism
Commentary:

“Save the public from outbreaks of terrible diseases such as Measles. It urges government research to focus on improving the lives of the autistic and what actually causes it and stop flooding money into research on something that has been completely refuted.”

Review on mitochondrial disease & autism suggesting the prevalence of a subgroup of ASD having mitochondrial disorder

HANNAH POLING, LEFT, STANDS WITH HER PARENTS TERRY AND JON POLING, RIGHT, AT A NEWS CONFERENCE IN ATLANTA ON MARCH 6, 2008.
Developmental Regression and Mitochondrial Dysfunction in a Child With Autism

Retrospective study of 159 patients w/autism previously undx w/metabolic disorders

- J Child Neurol 2006;21:170–172
- 38% elevated aspartate aminotransferase (control 15%)
- 47% elevated serum creatinine kinase
- Recommend further metabolic eval in autistic pts. Defects of oxidative phosphorylation might be prevalent
AUTHORS

- Jon S. Poling, MD, PhD  Department of Neurology and Neurosurgery Johns Hopkins Hospital Baltimore, MD
- Richard E. Frye, MD, PhD  Department of Neurology Boston Children's Hospital Boston, MA
- John Shoffner, MD  Horizon Molecular Medicine Georgia State University Atlanta, GA
- Andrew W. Zimmerman, MD,  Department of Neurology and Neurosurgery Johns Hopkins Hospital Kennedy Krieger Institute Baltimore, MD
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- 68 children with ASD, 54 age-matched control children & 40 unaffected siblings,
- Both methionine & SAM were significantly decreased in children with autism. The SAM/SAH ratio, an indicator of methylation capacity, was decreased in children with autism compared to their siblings but not different between siblings and controls.

ASD is most likely multifactorial in etiology with genetic factors and to a lesser extent, environmental factors to blame.

First recognized as distinct disorder in 1994 (DSM-IV)

Accounts for 14-19% of ASD cases

Qualitative impairment in social interaction, manifested by at least 2 of the following:

- Impairment in use of nonverbal behaviors (i.e., eye contact, facial expression)
- Failure to develop appropriate peer relationships
- Lack of seeking to share enjoyment or interests with other people
- Lack of social or emotional reciprocity
Restricted repetitive or stereotyped behaviors, interests and activities, as manifested by:

- Preoccupation with one activity or interest that is abnormal either in intensity or focus
- Inflexible adherence to specific, nonfunctional routines or rituals
- Repetitive and stereotyped motor mannerisms
- Persistent preoccupation with parts of objects.
No clinically significant delay in language
No clinically significant delay in cognitive development or age-appropriate self-help skills
Criteria not met for another PDD or schizophrenia
PDD - NOS

- Impairment in social interaction
- Impairment in verbal and non-verbal communication
- Stereotypical behaviors often present
- However, the child does not meet all the diagnostic criteria for autism
Children exhibit normal development for the first few years of life.

Regression of language, interest in social interaction and self-care abilities.

Prognosis is worse than that for other PDDs.

Unknown etiology. Possible central nervous system pathology.
RETT SYNDROME

- X-linked genetic abnormality (MECP2 gene)
- Full syndrome seen only in girls. A few reports of males with mutated MECP2 gene who have similar symptoms to females
- Early development is normal
- Progressive CNS involvement – symptoms include autistic behaviors, intellectual disability, stereotypical hand wringing, spontaneous apnea
BEHAVIORAL CHALLENGES

- Short attention span
- Rigidity of routines
- Hyperactivity
- Easily frustrated
- Tantrums
- Echolalia
"Take one of these whenever you get the cap off."
MEDICATIONS

- Hyperactivity
  - Methylphenidate (Ritalin, Concerta)
    - CNS stimulant, use vasoconstrictors with caution
  - Side effects: tics, irritability, anorexia, insomnia
  - More effective in children with Asperger than other ASDs
- Repetitive behaviors
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
- Side effects of all SSRIs (selective serotonin reuptake inhibitors): agitation, insomnia, increased motor activity
Risperidone (Risperdal)
Olanzapine (Zyprexa)

- Both are antipsychotics
  - Increase sedation of other CNS depressants
  - Increase orthostatic hypotension
  - Weight gain
  - Can rarely cause extrapyramidal (movement) disorders
• **Aggressive behaviors**
  • Lithium (Eskalith)
    • NSAIDs can increase renal clearance time
    • Increased sedation when used with benzodiazepines
    • EKG changes, weight gain, hypothyroidism
  • Carbamazepine (Tegretol)
    • Decreased WBC and platelet counts
  • Valproic Acid (Depakote, Depakene)
    • Can cause liver function problems
    • Leukopenia, thrombocytopenia, decreased fibrinogen
- Risperidone (Risperdal)
- Recently approved by FDA for irritability & aggression in children with ASD.
- Only drug approved specifically for ASDs
- Olanzapine (Zyprexa)
  - Both:
    - Increases sedation of other CNS depressants
    - Orthostatic hypotension
    - Motor disturbances (akathisias)

Applied Behavior Analysis (ABA)
- Based on principles of learning and behavior
- Used for >30 years
- Efficacy established, n
- Normal functioning achieved in almost half of children treated with INTENSIVE ABA 25-40 hrs/week
- Less effective 5-10% of children improve with less intensive ABA (<20 hrs/week)

Practical Approaches to Treating Patients with Autism
23% of parents with children with ASD reported unmet dental needs. (Massachusetts)

Nelson L et al PEDIATRIC DENTISTRY. V 33 / NO 1 JAN / FEB 11. Pgs 29-36
BEHAVIOR MANAGEMENT

- Ask parent/caregiver about patient’s
  - Peculiarities/ stereotypic behaviors
  - Communication level
  - Reactions to noise
  - Reactions to touch (light and deep pressure)
  - Reactions to bright light
  - Previous visits to doctors
Standard Techniques

- Tell-Show-Do
- Immediate positive and negative reinforcement (paired with firmness, if necessary)
- Hand-over-mouth not appropriate
- NEED TO BE FLEXIBLE IN TRYING DIFFERENT TECHNIQUES
SORRY FOR THAT OUTBURST EARLIER ... I KNOW ONCE IT COMES OUT, THERE'S NO WAY TO TAKE IT BACK...
Other Recommendations:

- Modeling
- Positive reinforcement (praise) after every successful step of procedure and a prize at the end of the visit
- Clear, short, simple sentences
- Ignore inappropriate behavior
Here's the deal...If you cooperate with me I'll use the good-boy-drill. Jerk me around and you get this.
To papoose or not?

- McDonald & Avery and Zisserman advocate using it
  

- Lowe & Ledyrchowski and Kamen disapprove
  

- Lindemann reported comforting effect of physical restraint on some ASD children
  
  *(Lindemann R, Henson JL, Spec Care Dent 1983;3:72-76)*
Grandin reviewed literature on deep touch pressure to patients with ASD

- Relaxing calming effect of deep pressure (light touch alerted nervous system)
- Overall results that firm touch, pressure have calming and comforting effect

(Grandin T, Thinking in pictures. 1995; New York: Doubleday)
Repetitive conditioning and reinforcement process before treatment is actually started.

D-Termined Program: Repetitive Tasking & Familiarization in Dentistry

- DVD and CD-Rom available from Specialized Care Co. 800-722-7375 or www.specializedcare.com
DESENSITIZATION

- Limitations
  - Manpower
  - Time
  - Financial concerns
DESENSITIZATION

- Slow, step-wise approach described by many authors: i.e. Kamen, Kopel, Burkhart
- Allow patient to visit office, get used to people and place*
- Establish ROUTINE*
- Gradual, slow exposure to the environment with non-threatening contacts
PARENTS IN OR OUT?

- Parental presence discouraged by Klein & Nowak (Klein U, Nowak A, Ped Dent 1998;20:5, 312-317)
- Parents/aides in the operatory is helpful and appears to comfort them and augments cooperation according to Friedlander, et al. (Friedlander A, et al, California Dental Journal 2003;31:9, 681-691)

BOTTOM LINE
- Every patient is an individual
- Get good history, ask questions about other doctor visits
TIPS

- Let patient sit in chair (in your chair, stool, etc.)
- Use a toothbrush to get patient to open for exam, (patients do better with familiar items)
- Do not touch or pat if patient has tactile issues
- Avoid sensory overload; use a quiet, private area
- Short appointments, esp. 1st visit
- Well planned appointment, be organized
- Don’t make patient wait in waiting area a long time
- Routine, sameness, same time, day, personnel
- Music can be played if patient enjoys it
Minimize sudden movements, patients are easily distracted
Don’t crowd patient
Be careful with light, some patients are very sensitive
At home rehearsals for visit
Compassion, empathy
Realize dental visit is one small part of this family’s issue dealing with the outside world.
Always ask the caregiver about patient’s
- Communication abilities
- Reactions to sensory stimuli such as noise, touch, and light
- Stereotypic behaviors
- Previous dental experiences?

Does parent or caregiver have any suggestions for techniques that may help to distract patient during treatment?
- Listening to music
- Playing with a portable video game machine
- Anything else!!
“If you have seen one patient with autism, you’ve seen one patient with autism.”
Hey everybody, look out! It's one of those... Um... you know... Uhh, with the fire and stuff...

Despite its name, the thesaurus was quite often at a loss for words.
THE FUTURE
CDC will continue its population-based surveillance of ASD and intellectual disabilities through 2020 through its ADDM Network. (est. 2000)

The Combating Autism Act authorized nearly $1 billion over 5 years for research.

Autism Speaks and the Simons Foundation (SFARI) add significant research dollars (autismspeaks.org)
CDC Study to Explore Early Development

Largest collaborative study to date on causes of autism

5 year study

2,700 children, ages 2-5, includes parents

Six diverse sites CADDRE Network (Centers for Autism & Developmental Disabilities Research & Epidemiology)
BROTHERS!
RESOURCES

- **BOOKS**
RESOURCES

WEB SITES

- Special Care Dentistry.  www.scdonline.org
- Southern Association of Institutional Dentists (SAID).  www.saiddent.org
- American Academy of Developmental Medicine & Dentistry.  www.aadmd.org
- United Cerebral Palsy.  www.ucp.org
- Autism Speaks.  www.autismspeaks.org
RESOURCES

- WEBSITES
  - FDA: [www.fda.gov/CBER/vaccine/thimerosal.htm#intro](http://www.fda.gov/CBER/vaccine/thimerosal.htm#intro)
  - CNN: [www.cnn.com/2008/HEALTH/conditions/03/06/vaccines.autism/index.html#cnnSTCVideo](http://www.cnn.com/2008/HEALTH/conditions/03/06/vaccines.autism/index.html#cnnSTCVideo)
THANKS!
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