What Causes Autism? An Epidemiologist's Approach to Searching for Clues

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What IS an Epidemiologist Anyway?

We don't study bugs!

Epidemiology is…

- The study of patterns of health and illness at the population level
- The identification of risk factors for disease
- It informs public health prevention strategies
- Ultimately leads to optimal treatment approaches at the individual level

Overview of Talk

- Definition of autism
- Descriptive epidemiology
  - Rates, trends
  - Demographic characteristics
- Risk factors
  - Genetic factors
  - Environmental factors
- Exciting, ongoing research

What is autism?

A brain disorder that results in a pattern of unusual development affecting an individual early in life and usually lasting throughout the lifespan

Core Features of Autism

- Communication impairments
- Social interaction impairments
- Restricted, repetitive, stereotyped behaviors and interests

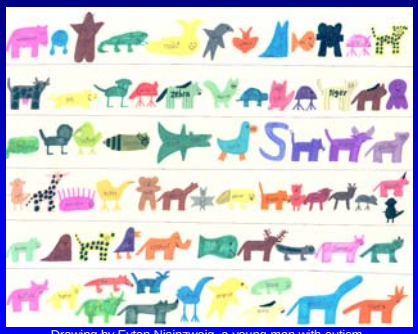
Autism Spectrum Disorders

- Autistic Disorder
- Asperger's Syndrome
- Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS)

Diagnosing ASD

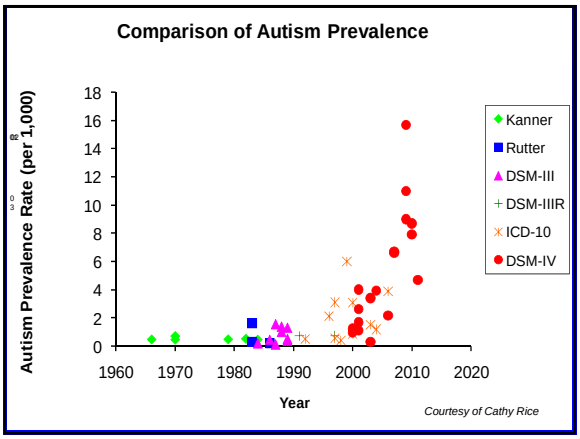
- Defined by behaviors
- No laboratory test
- Wide range of expression
- Mild to severe
  - Variability in who is considered 'affected' across different epidemiologic studies

"Autisms"



Drawing by Eytan Nisinzweig, a young man with autism

How many people have autism?



Best-estimate prevalence summary

- Prior to 1990: **1 in 2,000 children (autism)**
- Mid '90's: **1 in 500**
- Mid '00's: **1 in 150**
- Most recent: **~1% of children (ASD)**

The most recent studies from around the world

From areas in	ASD Prevalence per 1,000 1 in X children	Age Year(s) born	Reference
Canada	**7.9** 1 in 126	5-17 1991-2003	Lazoff et al, 2010
Norway	**8.7** 1 in 115	7-9 years est. 1998-1999	Posserud et al., 2010
US	**9.0** 1 in 110	8 years 1998	CDC, 2009
US	**11.0** 1 in 91	3-17 years 1990-2004	Kogan et al., 2009
US	**4.7** 1 in 213	Birth-9 years 1994, 1996	Windham et al., 2011
UK	**15.7** 1 in 67	5-9 years est. 1998-2004	Baron-Cohen et al., 2009

AVERAGE = 9.5 per 1,000 children; about 1%

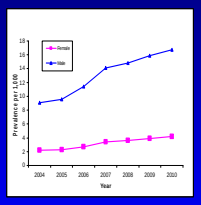
Courtesy of Cathy Rice

"Explanations" for increase

- **Change in how autism is defined**
  - DSM IV criteria broader than previous DSM
  - Milder ASD now being counted
- **Change in how autism is identified**
  - More awareness, recognition, services
- **Changes in risk factors**

Demographic Characteristics

- More males than females (4:1)
- Every race and ethnic group
- Lower rates among Hispanics
  - access to services?
- Higher rates among
  - premature infants
  - twins
  - first born
  - well-educated parents
  - older parents



Strong Genetic Component

Twin Studies:
- Identical twins (MZ) concordance ~70-90%
- Fraternal twins (DZ) concordance ~10-30%

Family Studies:
- Sibling recurrence risk 10-25% or more
- Broader Autism Phenotype in family members

Genetic Findings in 10%-20% of cases:
- Candidate genes
- Genetic syndromes
- Copy Number Variation (CNV)

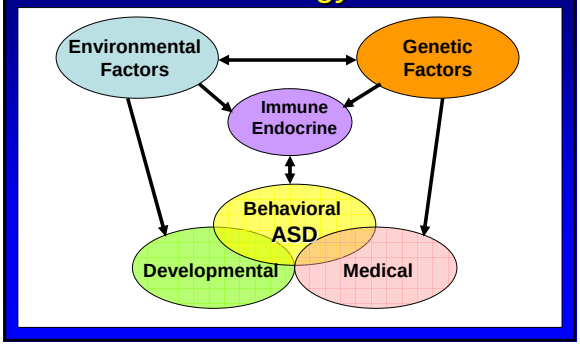
'Environmental' Component

- Identical (MZ) twins – 10%- 30% discordant for autism
- Prenatal exposures linked to autism
  - eg., thalidomide, valproic acid, infection
- Many chemicals are toxic to developing brain
- Increase in rate of autism...linked to changes in the environment?

Etiology (Cause)

- Combination of genetic and environmental factors
- A process that typically starts early in gestation...with later "second hits"?
- Different clinical subgroups may have different causes

Conceptual Model of Autism Etiology



Investigating relationship between

Exposure and Outcome

Do vaccines cause autism??

Exposure = vaccine

Outcome = autism

What about thimerosal?

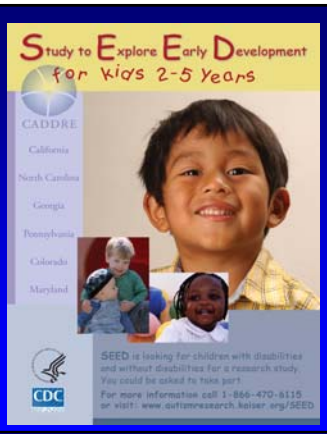
- Thimerosal is a preservative that was used in many vaccines until 1999
- Contains 49% ethylmercury
- Mercury is neurotoxic
- Prevalence of autism increased over time period that children received increasing numbers of vaccines
- Increased number of vaccines → increase in exposure
- Could mercury in vaccines cause autism?

IOM Report, May 2004

Immunization Safety Review: Vaccines and Autism

...the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism

"This study revealed no increased risk of ASD associated with receipt of thimerosal-containing vaccines. No increased risk was found for subtypes of ASD, including ASD with regression, and prenatal exposure was not associated with a risk of ASD."



California CADDRE

Study to Explore Early Development (SEED)

- SEED is the largest collaborative scientific study to date of **risks and causes of autism**.
- **2,700** children and their parents.
- Six areas across the country: California, Colorado, Georgia, Maryland, North Carolina, Pennsylvania.

California CADDRE

SEED Enrollment

- 2 to 5 year olds
- English and Spanish speaking
- 900 autism spectrum disorder
- 900 neurodevelopmentally impaired controls
- 900 general population controls

California CADDRE

SEED Research Questions

1. The ASD phenotype
2. Infection and immune function
3. Reproductive and hormonal features
4. Gastrointestinal features
5. Sociodemographics
6. Genetics

California CADDRE

SEED Data Collection

- Child development evaluation
- Child dysmorphology exam
- Biological samples: buccal cells, venous blood, hair
- Medical record abstraction
- Telephone interview
- Self administered questionnaires

EARLI

Early Autism Risk Longitudinal Investigation

Follow 1,200 mothers of children with autism at the start of a new pregnancy

Study environmental risk factors and biomarkers during different developmental windows (prenatal, perinatal, neonatal, postnatal)

Document the development of the new baby through age three

Explore interplay of genetic susceptibility and environmental exposure

Add to current knowledge of the natural history and progression of ASD

Autism Center of Excellence: Funded by NIH

- Four field sites (KPNC, UCD, Drexel, JHU)
- Data coordinating center (UC Davis)
- Central receiving lab and biosample repository (JHU)
- Scientific and community advisory committees

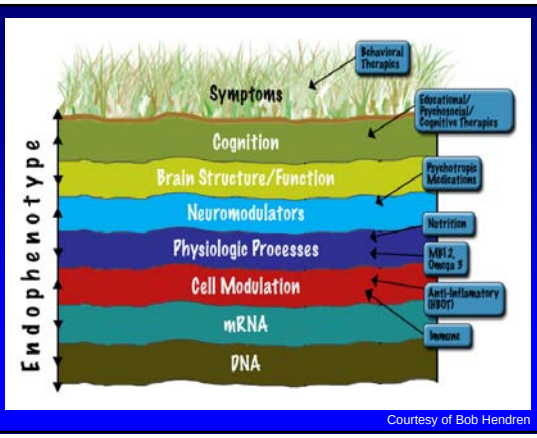
EARLI Data Collection Trajectory

Older Child with ASD
Mom
Dad
New Baby
Home

Pregnancy risk and contact information monitoring pre-pregnancy
Clinic visits in pregnancy (1st, 2nd, 3rd trimesters)
Home visits in pregnancy (2nd trimester)
Online weekly diaries during pregnancy
Telephone interview in pregnancy (1st, 3rd trimester)
Biologic sample collection at delivery (cord blood, placenta)
Home visit after delivery (3mo)
Clinical evaluation of baby (6mo, 12mo, 24mo, 36mo)
Online monthly and quarterly diaries after delivery
Telephone interview after delivery (3mo, 12mo)

Data collection domains include:

- Household demographics
- Maternal reproductive hx
- Pregnancy - symptoms, procedures, illness episodes, mood / depression, medications, personal care product exposure, diet, lifestyle
- Baby - symptoms, procedures, illness episodes, personal care product exposure, diet, lifestyle
- Residential hx
- Home pesticide use
- Other household chemicals
- Family medical history (ASD, DD, psychiatric, immune, sensory, other)
- Parental BAP
- Medical hx and dysmorphology of older child and baby
- Developmental hx of older child
- Clinical assessment of baby
- Environmental sample: dust from home
- Biologic samples:
  - Older child: blood
  - Mother: blood, hair, urine, saliva, placenta, cord blood, breast milk
  - Father: blood, semen
  - Baby: blood, hair, meconium, urine



Courtesy of Bob Hendren


THANKS to the Children and Families!!