




Special Populations Etiologies

Dominick M. Maino, OD, MEd, FFAO
Professor, Illinois College of Optometry/Illinois Eye Institute
Chicago, IL USA



Etiologies

The etiology of special needs infants includes genetics, physical and neurological trauma, and the various influences of the environment. Resources, such as Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=CIMM>), lists thousands of genetic causes. Many of those anomalies due to traumatic etiologies are also known. The role of the environment and those set of factors that contribute to the developmental of a child with special needs described as being “multifactorial” have only recently been studied in-depth, however. This presentation offers up to date information on the commonly encountered genetic causes of special needs children (Down Syndrome, Fragile X Syndrome), traumatic etiologies (Cerebral Palsy), and the multifactorial basis for disability (Autism).






Etiologies

Genetics

Trauma

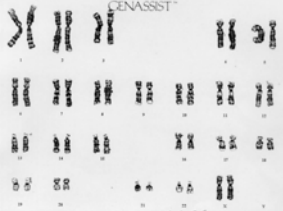

Environment

Etiologies

Chromosomes & Genes



The basic unit of heredity
Genes code for proteins
Made up of sequences of DNA
(humans have ~100,000 genes)

Etiologies

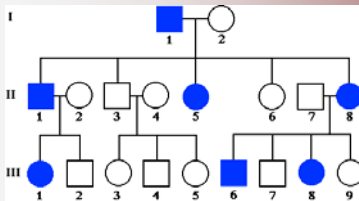
Chromosomes & Genes

Genes occupy specific locations on chromosomes
 Humans have 46 chromosomes (23 pairs)
 22 pairs of autosomes
 1 pair of sex chromosomes (XX, XY)
 Half of the chromosomes come from each parent



Diagnostic Tests

Pedigree Analysis



Helps determine inheritance pattern
 Can help determine chances of passing a trait to offspring
 Need information on 3 generations of the family

Pedigree 1. An idealized pedigree of a family with hypercholesterolemia, an autosomal dominant disease where the heterozygote has a reduced number of functional low density lipoprotein receptors.



Diagnostic Tests

Ultrasound

Evaluates



- fetal health
- size
- levels of amniotic fluid
- maternal and placental anatomy

Early diagnosis of fetal structural abnormalities

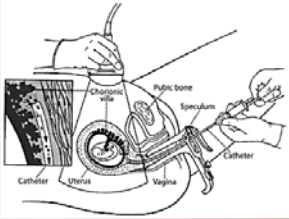
Diagnostic Tests

Ultrasound

Diagnostic Tests

Chorionic Villi Sampling

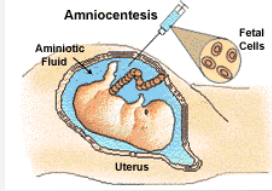


Can be performed at 7-11 weeks
Diagnostic information in 24 hours

Procedure
small sample from chorion frondosum cells are cultured
cells are karyotyped (chromosome analysis)
detects chromosomal abnormalities, metabolic, blood disorders

Diagnostic Tests

Amniocentesis

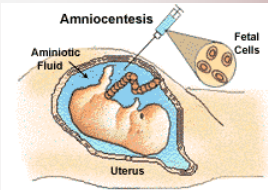


Performed at 16 weeks gestation
Genetic work-up takes 2-4 weeks

Procedure
ultrasound to find pockets of amniotic fluid
20-22 gauge needle used to withdraw amniotic fluid
cells can be cultured and karyotyped
metabolic studies/chemistry of fluid

Diagnostic Tests

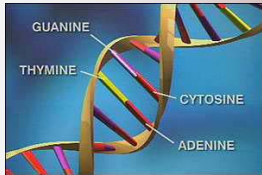
Amniocentesis



Uses of amniocentesis
chromosomal abnormalities
neural tube disorders
blood disorders
sickle cell anemia, thalassemia
metabolic disorders (> 100 disorders)
Tay-Sachs, Lesch-Nyhan, Hunter's, Hurler's

Diagnostic Tests

DNA Analysis



Detects the specific sequence of DNA that causes abnormality

Diseases include
aniridia
retinitis pigmentosa (at least 7 genes)
macular dystrophy
Norrie's disease
choroideremia

Diagnostic Tests

Percutaneous Umbilical Blood Sampling PUBS

This test obtains **fetal blood**.

Used in addition to an ultrasound and amniocentesis


Main advantage: speed

Used after an abnormality noted on an ultrasound or when amniocentesis results aren't conclusive

Exposure to an **infectious disease**

Testing between 18 and 36 weeks.

Results Available **In 3 days**.



Diagnostic Tests

Triple Screen

Results Available: 1 week for Down syndrome and 2 weeks for thorough analysis.

Use this to test the mother's blood only for **alpha-fetoprotein (AFP)**. This test has been expanded, however, to also detect two pregnancy hormones - **estriol** and **human chorionic gonadotropin (HCG)** - which is why it's now sometimes called a "**triple screen**" or "triple marker." The test is called a "quadruple screen" ("quad screen") or "quadruple marker" ("quad marker") when the level of an additional substance - **inhibin-A** - is also measured. The greater number of markers increases the accuracy of the screening and better identifies the possibility of a birth defect.


This test, which also is called a multiple-marker screening or maternal serum screening, calculates a woman's individual risk of **trisomy** defects based on the levels of the three (or more) substances plus: her age, her weight, her race, whether she has diabetes requiring insulin treatment

It's important to note, though, that this screening test determines risk only - it **doesn't diagnose a condition**.

Test at 16 to 18 weeks.

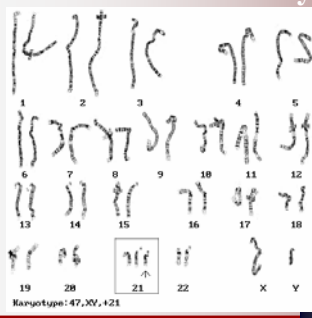
Blood is drawn from the mother.

Results Available 3 to 5 days, although it may take up 2 weeks.





Genetic anomalies

Down Syndrome

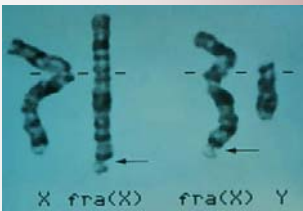


Karyotype: 47,XY,+21






Genetic anomalies

Fragile X Syndrome



X fra(X) fra(X) Y



Genetic anomalies

Mental Retardation

5000 known genetic anomalies

1000's unknown

Go to Online Mendelian
Characteristics in Man

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>



Trauma

Cerebral Palsy

Traumatic
neurological event
just before, at or
just after birth



Environment

Teratogens

“.....is a drug, chemical, infectious, or environmental agent which by acting during the embryonic or fetal period alters morphology or subsequent function in the postnatal period.”



Environment

Teratogens

Teratogens

Humans susceptible thru out gestation

Genetics determine susceptibility

No human teratogen has ever been identified by animal studies

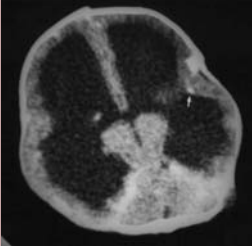


Environment


Infections

Infections

- Congenital Cytomegalovirus
- Rubella
- Herpes Simplex
- Toxoplasmosis
- HIV



Cytomegalovirus Brain with hydrocephalus




Environment


Infections

Infections

- Congenital Cytomegalovirus
- Rubella
- Herpes Simplex
- Toxoplasmosis
- HIV



Infant with Rubella



Environment

Infections

Infections

- Congenital Cytomegalovirus
- Rubella
- Herpes Simplex
- Toxoplasmosis
- HIV



Infant with Rubella



Environment

Drugs, chemicals, & environmental agents

Alcohol

- Fetal Alcohol Syndrome
- Fetal Alcohol Effect

FAS Facial Characteristics

- epicanthal folds
- small eye openings
- flat midface
- upturned nose
- smooth philtrum
- thin upper lip



©1999 Teresa Kelleman, Community Resource Center

Infant with FAS



Environment

Drugs, chemicals, & environmental agents

Cigarette Smoking
Decreased length (1.3 cm less)
? Reading, math, cognition, behavior?






Environment

Anti-Seizure Medications (Fetal Hydantoin Syndrome)

Dilantin

- Short nose
- Hypertelorism
- Cleft lip and Cleft Palate
- Mild MRDD
- Digit and Nail anomalies


10% risk for complete syndrome
33% risk for some features


Environment

Heroin/Methadone/Cocaine

anatomical defects, intrauterine growth, retardation, prematurity, microcephaly, ED/BD, perceptual anomalies, learning problems





Turning children everywhere into psychotic little monsters



Autism

The incidence of autism has increased from 1 in 10,000 in the 1970s to 1 in 150 today, an increase of over 6,000%. Many more children have been diagnosed with other neurodevelopmental disorders all considered to be on the same spectrum including Asperger's, ADHD/ADD, speech delay, and many other developmental delays and learning disabilities.



Autism

Do Parents cause their children to be autistic ?

There are autistic children born to parents who do not fit the autistic parent personality pattern.

Parents who do fit the description of the supposedly pathogenic parent have normal, non-autistic children.

Frequently siblings of autistic children are normal.

Autistic children are behaviorally unusual "from the moment of birth." ***



There is a consistent ratio of three or four boys to one girl.

Virtually all cases of twins reported in the literature have been identical, with both twins afflicted. ***

Autism can occur or be closely simulated in children with known organic brain damage. ***

The symptomatology is highly unique and specific.

There is an absence of gradations of infantile autism which would create "blends" from normal to severely afflicted.



Autism Etiology

Yeast infections

Intolerance to specific **food** substances


Gluten intolerance ("**Leaky Gut Syndrome**" / **Casein** intolerance causing intestinal permeability and allowing improperly digested peptides to enter the bloodstream and cross the blood-brain barrier which may mimic neurotransmitters and result in the scrambling of sensory input. I've also heard "Leaky Gut Syndrome" described as lack of the beneficial bacteria that aids digestion, and that the resulting matter in the bloodstream invokes an unnecessary immune reaction)

Phenolsulphotransferase (PST) deficiency--theory that some with autism are low on sulphate or an enzyme that uses this, called phenol-sulphotransferase-P. This means that they will be **unable to get rid of amines and phenolic compounds** once they no longer have any use for them. These then stay in their body and may cause adverse effects, even in the brain.

Autism Etiology

- Brain injury
- Constitutional vulnerability
- Developmental aphasia
- Deficits in the reticular activating system
- An unfortunate interplay between psychogenic and neurodevelopmental factors
- Structural cerebellar changes
- Genetic causes
- Viral causes
- Immunological ties
- Vaccines
- Seizures




Autism Etiology

My Goodness!

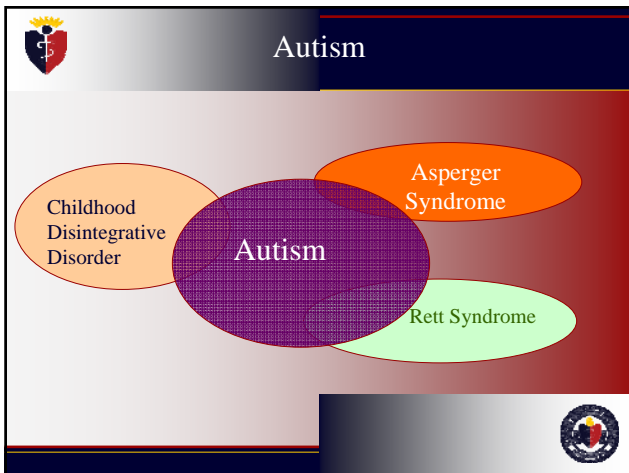


Autism Etiology

What the research shows...

Autism


- Impairment in social interactions
- Impairment in communication
- Restricted repertoire of activities



Autism

Disorder	Onset/Course	Delay	Severity	Domains affected
Autism	Prior to 3 years ^a	May or may not be associated with general delays ^a	Exceeds standard thresholds of number of features ^a	Social, communication, and repetitive ^a behaviors
Childhood disintegrative disorder	Typical development up to 2 years; loss of speech and/or at least one other skill ^b	Usually associated with mental retardation requiring extensive supports ^b	Thresholds not specified but appear same as autism	Abnormalities in two of three domains of autism
Asperger syndrome	Onset may be before or after 3 years ^b	No general delay in cognition or language ^c	Must exceed threshold in social area ^b	Social and circumscribed interests ^b
Atypical autism (ICD-10)/pervasive developmental disorder - not otherwise specified (DSM-IV)	May fail to meet autism onset criteria ^b	May or may not be associated with developmental delays	May fall below threshold in one or more areas ^b	Social and either communication or repetitive behaviors or both ^c

^aAutism criteria.
^bMay differ from autism.
^cAlways differs from autism.





Autism

Cohly HH, Panja A.
Immunological findings in autism.
Int Rev Neurobiol. 2005;71:317-41.s

Mercury and an infectious agent like the measles virus are currently two candidates for immune dysfunction in autism..."



Childhood Disintegrative Disorder - Elevated brain specific antibodies in autism support an immune mechanism. Viruses may initiate the process but the subsequent activation of cytokines is the damaging factor associated with autism. Virus specific antibodies associated with measles virus have been demonstrated in autistic subjects. Environmental exposure to mercury is believed to harm human health possibly through modulation of immune homeostasis. **A mercury link with the immune system has been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines."**

Autism

Adams JB, George F, Audhya T. Abnormally high plasma levels of vitamin b(6) in children with autism not taking supplements compared to controls not taking supplements.
J Altern Complement Med. 2006 Jan-Feb;12(1)



Childhood Disintegrative Disorder - Total vitamin B(6) is abnormally high in autism, with previous reports of an impaired pyridoxal kinase for the conversion of pyridoxine and pyridoxal to PLP. This may explain the many published studies of benefits of high-dose vitamin B(6) supplementation in some children and adults with autism.

Autism

Strambi M, Longini M, Hayek J, Berni S, Maciari F, Scalacci E, Vezzosi P.
Magnesium profile in autism.
Biol Trace Elem Res. 2006 Feb;109(2):


Childhood Disintegrative Disorder - Present study was to determine and compare plasma and concentrations of magnesium in 12 autistic children (10 boys, 2 girls), 17 children with other autistic spectrum disorders (14 boys, 3 girls), 5 girls with classic Rett syndrome, and 14 normal children (7 boys, 7 girls) of the same age. No differences in intracellular Mg were found between controls and pathological subjects; however, **autistic children and children with other autistic spectrum disorders had significantly lower plasma concentrations of Mg than normal subjects (p=0.013 and p=0.02, respectively).** Although our study population was small, we conclude that **children with autistic spectrum disorders require special dietary management. If these cases are diagnosed at an early stage, they can be helped through diet.**





Autism

Palmer RF, Blanchard S, Stein Z, Mandell D, Miller C.
Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas.
Health Place. 2006 Jun;12(2)

Childhood Disintegrative Disorder - Environmental mercury release, special education and autism was investigated using data from the Texas Education Department and the United States Environmental Protection Agency. A Poisson regression analysis adjusted for school district population size, economic and demographic factors was used. There was a significant increase in the rates of special education students and autism rates associated with increases in environmentally released mercury. **On average, for each 1,000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism.** The association between environmentally released mercury and special education rates were fully mediated by increased autism rates. This ecological study suggests the need for further research regarding the association between environmentally released mercury and developmental disorders such as autism. These results have implications for policy planning and cost analysis.





 Autism

Demicheli V, Jefferson T, Rivetti A, Price D.
Vaccines for measles, mumps and rubella in children.
 Cochrane Database Syst Rev. 2005 Oct 19;(4)

Childhood Disintegrative Disorder

RESULTS: MMR was associated with a lower incidence of upper respiratory tract infections, a lower incidence of irritability, and similar incidence of other adverse effects. The vaccine was likely to be associated with benign exanthema, febrile convulsions, febrile convulsions within two weeks of vaccination and aseptic meningitis (mumps)... **Exposure to MMR was unlikely to be associated with Crohn's disease, ulcerative colitis, autism or aseptic meningitis (mumps).** We could not identify studies assessing the effectiveness of MMR that fulfilled our inclusion criteria even though the impact of mass immunisation on the elimination of the diseases has been largely demonstrated. AUTHORS' CONCLUSIONS: The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate. The evidence of adverse events following immunization with MMR cannot be separated from its role in preventing the target diseases.





 Autism

Zimmerman RK, Wolfe RM, Fox DE, Fox JR, Nowalk MP, Troy JA, Sharp LK.
Vaccine criticism on the World Wide Web.
 J Med Internet Res. 2005 Jun 29;7(2):

Childhood Disintegrative Disorder

OBJECTIVE: A common characteristic of vaccine-critical websites was the inclusion of specific allegations with specific adverse reactions, especially idiopathic chronic fatigue syndrome, multiple sclerosis, autism, and diabetes. Other common attributes were links to other vaccine-critical websites; charges that vaccines contain contaminants, mercury, or "hot lots" that cause adverse events; claims that vaccines provide only temporary protection and that the diseases prevented are mild; appeals for responsible parenting through education and resisting the establishment; allegations of conspiracies and cover-ups to hide the truth about vaccine safety; and charges that civil liberties are violated through mandatory vaccination. CONCLUSIONS: Vaccine-critical websites frequently make serious allegations. With the burgeoning of the Internet as a health information source, an undiscerning or incompletely educated public may accept these claims and refuse vaccination of their children. As this occurs, the incidence of vaccine-preventable diseases can be expected to rise.




 Autism US FDA Statement


IOM Report: No Link Between Vaccines and Autism
 By Michelle Meadows

There is no link between autism and the measles-mumps-rubella (MMR) vaccine or the vaccine preservative thimerosal, according to a report released by the Institute of Medicine's (IOM) Immunization Safety Review Committee. The report, released in May 2004, was prepared by a committee of independent experts and requested by the IOM in 2001 at the request of the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) to evaluate evidence on potential links between childhood vaccines and health problems. The agencies explored the issue because of growing controversy and questions from the public about vaccine safety. ... Other concerns the committee looked at include the use of thimerosal, a mercury-based compound used as a vaccine preservative, because many forms of mercury are known to damage the nervous system in high doses.

Childhood Disintegrative Disorder

http://www.fda.gov/fdac/features/2004/504_iom.html




 Autism

Siklos S, Kerns KA.
Assessing the diagnostic experiences of a small sample of parents of children with autism spectrum disorders.
 Res Dev Disabil. 2006 Jan 24

Childhood Disintegrative Disorder


All previous studies have been conducted, studies suggest parents of children with autism experience difficulties obtaining a diagnosis for their child. Fifty-six parents of children with autism completed three questionnaires providing information on the families' demographics, parents' experiences throughout the diagnostic process, and their child's autistic symptomatology. These parents experienced significant difficulties obtaining a diagnosis for their child. Parents saw an average of 4.5 professionals, and waited almost 3 years to receive a diagnosis following their first visit to a professional regarding their child's development. The impact of autistic symptomatology on the diagnostic process is discussed.






Autism Etiology

We are back
to....
My Goodness!



Autism

Bottom line...
We just don't know



Autism

Questions?

Contact

Dominick M. Maino, OD, MEd, FAAO
Professor of Pediatrics, Illinois College of Optometry
3241 S. Michigan Ave. Chicago, IL 60616 USA

dmaino@ico.edu

