

Volume 8 Number 3 (Issue 227)

Friday, April 2, 2010

Guest Editors: Megan Peckham, Pharm.D. Candidate, Emily McLain, Pharm.D. Candidate, Wendy Herring, Pharm.D. Candidate, and Wesley T. Lindsey, Pharm.D.

# National Autism Awareness Month April 2010



### **Autism – An Introduction**

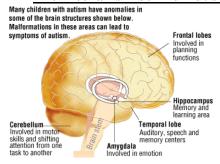
Autism is a neurodevelopmental condition that affects 1 out of 110 children in the U.S., although this is only one of many statistics currently available and the actual prevalence is not known. It is a lifelong, biologically based, neurobehavioral disorder that affects verbal and nonverbal communication, social interactions, and daily activities. The prevalence is increasing, with a male to female ratio of 4.3 to 1. In the U.S., as many as 483,000 people under age 20 are affected and 114,000 of those are children under the age of 5. Autism is a multi-faceted disorder and is often referred to as Autism Spectrum Disorder (ASD) because of the amount of variability between patients' symptoms. Along that "spectrum", are different types of autism ranging in severity. These include Classical ASD (the most severe) and Rett syndrome, to milder forms like Asperger syndrome, childhood disintegrative disorder and pervasive developmental disorder not otherwise specified (PDD-NOS). Although symptoms differ greatly between patients, here is a list of some of the most common, general signs and symptoms present in all types to some degree:

- The hallmark feature of ASD is impaired social interaction.<sup>3</sup>
  - O This is most often seen as early as infancy as the child fails to respond to people or focus intently on one item for long periods of time.<sup>3</sup>
  - As they grow older, the child may not respond to their name, develop rigid routines and avoid eye contact.<sup>3,4</sup>
  - o Children may refer to themselves by name instead of "I" or "me."<sup>3</sup>
  - May speak in a sing-song voice about a narrow range of topics with no regard for others' interest.<sup>3,4</sup>
  - They may also have difficulty interpreting what others are thinking and feeling due to not being able to understand tone of voice or facial expressions and cannot feel empathy.<sup>3,4</sup>
- Repetitive Movements:
  - o Many children will rock and twirl repetitively, have "tics" or sometimes engage in selfabusive behavior such as biting or head-banging.<sup>2,3</sup>
- Co-occurring conditions:
  - ASD appears to put children at a higher risk for certain conditions such as Fragile X syndrome (mental retardation), brain tumors, epilepsy (about 20-30% of children with ASD develop epilepsy by adulthood), Tourette's Syndrome, and Attention Deficit Disorder.<sup>3</sup>
- Data & Statistics [homepage on the internet] Centers for Disease Control and Prevention; [cited 16 Mar 2010]. Updated 18 Dec 2009. Available from: http://www.cdc.gov/ncbddd/autism/data.html
- West L, Waldrop J, Brunssen S. Pharmacologic Treatment for the Core Deficits and Associated Symptoms of Autism in Children. J Pediatr Health Care. 2009;23:75-89.
- Autism Fact Sheet [homepage on the internet] National Institute of Neurological Disorders and Stroke; [cited 15 Mar 2010]. Published Sept 2009. Available from: <a href="http://www.ninds.nih.gov/disorders/autism/detail\_autism.htm">http://www.ninds.nih.gov/disorders/autism/detail\_autism.htm</a>.
- 4. Autism [homepage on the internet] Mayo Clinic; [cited 15 Mar 2010] Available from: http://www.mayoclinic.com/health/autism/DS00348

# History 101 – Autism<sup>1</sup>:

- 1911-Eugen Bleuler (Swiss psychiatrist) coined the term, but he was referring to a group of symptoms associated with schizophrenia.
- 1943-Leo Kanner, doctor from Johns Hopkins University used the term to describe symptoms in children he was studying with emotional and social problems.
- 1940s-around the same time Hans Asperger (German scientist) identified a similar condition and called it "Asperger's syndrome."
- 1960s and 1970s-research for treatments of autism:
  - o LSD; Electric shock; Behavior therapy (pain & punishment)
- 1980s and 1990s-behavior therapy and learning environments became the primary treatment for autism and related conditions.
- Currently-behavior therapy is the cornerstone of treatment.
- Web MD [website]. New York: WebMD, LLC, c2005-2010; [updated 2009 Sep 3; cited 2010 March 15]. History of Autism; [about 3 screens]. Available from: <a href="http://www.webmd.com/brain/autism/history-of-autism?page=3">http://www.webmd.com/brain/autism/history-of-autism?page=3</a>

## The Mechanism behind Autism:



Neuropathologic studies of the brain reveal abnormalities in the amygdala, which could explain changes in recognition of emotional significance of stimuli, abnormalities in connections between behaviors and their consequences, in perception of the body's movements and eye gaze direction, in following social stimuli, and along with abnormalities in the hippocampus change the abilities of long-term memory. Deficits also exist in the septum, mamillary bodies, and the cerebellum. Changes in the cerebellum can explain rapid shifts in attention and impairment of modulating sensory input. Brains of autistic persons tend to be heavier and larger than normal brains. Head circumference can also be larger

than normal. The Limbic system has an excess of smaller than normal cells, which could possibly account for impairment in social cognition. Neuronal cells in general are immature. In the cerebellum, Purkinje cells are more widespread. Frontal lobe and basal ganglia abnormalities are noticed by changes in action plans, motor planning, execution, and working memory. It is important to understand that no one structural or neuronal deficit causes autism, instead the pathophysiology is extremely complex.<sup>1</sup>

- National Institutes of Health [website]. Bethesda: Department of Health and Human Services; [updated 2006 Aug 15; cited 2010 March 15].
   Pathophysiology of Autism: Brain Mechanisms; [about 6 screens]. Available from: <a href="http://www.nichd.nih.gov/publications/pubs/sos\_autism/sub6.cfm">http://www.nichd.nih.gov/publications/pubs/sos\_autism/sub6.cfm</a>
- Seattle PI: Special Reports [website]. Seattle: Hearst Seattle Media, LLC, c1996-2009; [updated 1999 Nov 15; cited 2010 March 15]. Autism's Effects
  on the Brain; [about 4 screens]. Available from: <a href="http://www.seattlepi.com/autism/info15.shtml">http://www.seattlepi.com/autism/info15.shtml</a>

## **Autism Diagnosis**

Diagnosing autism is a multiple step process which involves evaluating language development and child's behavior as they relate to age. Most patients with autism can be diagnosed by the age of 3. Approximately 75% of patients with autism will also be diagnosed with mild to profound mental retardation. Autism diagnosis is generally made using a combination of medical history, autism screening tools, and medical testing.<sup>1,2</sup>

• Symptoms: should include ≥6 of the following: significant impairment in nonverbal communications, inability to make friendships with peers, lack of spontaneous interactions with people or environment, delays in communication development, inability to use expressive language appropriately, lack of appropriate play for developmental level, ritualistic behavior, intolerability to change, lack of interest, limited scope of play, and repetitive, nonfunctional motor movements. In order to establish a diagnosis of autism, symptoms should be present before 3 years of age, at least two of the symptoms should be impairments in social interaction, one in communication and one in restricted interests or repetitive behaviors.¹

- Screening tools: used to assist clinicians in making a diagnosis of autism. Childhood Autism Rating Scale (CARS) is commonly used for children ≥2 years of age and evaluates body movements, listening response, verbal communication and relationships with people. The evaluator collects data from observing the patient as well as questioning the caregiver. The patient's behavior is then compared with the expected behavior of someone the same age.²
- **Medical testing**: generally done to rule out other medical possibilities. Patients with suspected autism should undergo hearing and vision testing because deficits in these areas can elicit symptoms similar to autism. Thyroid abnormalities can affect mood and activity levels; therefore, thyroid function testing should be done. Another common medical test performed is lead and heavy metal testing. Autistic children generally have elevated blood lead levels due to a prolonged oral-motor stage (place objects into mouth).<sup>1,2</sup>
  - Brahm N, McKee J, Brown RC. Developmental Disabilities. In: Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: a pathophysiologic approach. 7th ed. New York: The McGraw Hill Companies, Inc.; 2008. Pg O122-O128.
  - National Institute of Mental Health: transforming the understanding and treatment of mental illness through research [Internet]. Maryland: National Institutes of Health. Autism spectrum disorders (pervasive developmental disorders); 2009 July 22 [cited 2010 March 10].
     Available from: http://www.nimh.nih.gov/health/publications/autism/complete-index.shtml#pub3.

# **Autism Treatment**<sup>1,2,3</sup>

There is currently no cure available for autism and therefore the goal of treatment is symptom improvement and increased quality of life. There have been many treatment approaches suggested for autism, however, the two with the most evidence are behavioral/psychoeducational therapies and psychoactive medication intervention.

- **Behavioral therapies:** These therapies will help patients with autism interact socially, develop language, and behave more appropriately. It involves providing a structured environment with consistent feedback regarding various behaviors. This includes rewarding good behaviors (positive reinforcement), not rewarding bad behavior (negative reinforcement), punishment, and giving reward for getting closer and closer to good behavior (shaping).
- Psychoeducational therapies: If designed appropriately these therapies will help patients with autism develop social, communicative, self-care and cognitive skills.
   Educational services need to be consistent due to the patient's need for sameness in routine, therefore, year round school is often more effective.
   Patients with autism often require additional services such as occupational and physical therapy as well as speech pathology. The main focus of therapy is language skills.
- Psychoactive medication intervention: Medication treatment is focused on decreasing aggressive behaviors such as self-injury and severe tantrums. The only medication currently FDA approved for this indication in children and adolescents is risperidone (Risperdal®). Other antipsychotics studied include: olanzapine (Zyprexa®), quetiapine (Seroquel®), ziprasidone (Geodon®), and clozapine (Clozaril®). While these atypical antipsychotics may lessen aggression, self injury, irritability and anxiety, they do not show improvements in communication, social skills, or behavioral rigidity. Atypical antipsychotics have decreased extrapyramidal side effects but can cause weight gain and sedation in patients with autism. Selective serotonin reuptake inhibitors may help treat autistic symptoms such as ritualistic and repetitive behaviors. Naltrexone, an opioid antagonist, has been used in autistic patients with extreme self injurious behavior with modest efficacy at a dose of 0.5 to 2 mg/kg/day. Patients with co-morbid diseases such as seizures and attention-deficit disorder may benefit from valproate and psychostimulants (e.g. methylphenidate and dextroamphetamine), respectively.

Other treatments that are used with little or no evidence include secretin (polypeptide hormone), famotidine, chelation therapy, large doses of vitamin B6 in combination with magnesium, and casein and gluten free diets.

- West L, Waldrop J, Brunssen S. Pharmacologic treatment for the core deficits and associated symptoms of autism in children. J Pediatr Health Care 2009; 23:75-89.
- Brahm N, McKee J, Brown RC. Developmental Disabilities. In: Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: a pathophysiologic approach. 7th ed. New York: The McGraw Hill Companies, Inc.; 2008. Pg O122-O128.
- National Institute of Mental Health: transforming the understanding and treatment of mental illness through research [Internet]. Maryland: National Institutes of Health. Autism spectrum disorders (pervasive developmental disorders); 2009 July 22 [cited 2010 March 10].
   Available from: <a href="http://www.nimh.nih.gov/health/publications/autism/complete-index.shtml#pub3">http://www.nimh.nih.gov/health/publications/autism/complete-index.shtml#pub3</a>.

### From the Medical Literature:

In 2004, the CDC supported a report published by the Immunization Safety Review Committee that stated that the causal relationship between autism and vaccines (particularly measles mumps rubella vaccine) is theory only. It further stated that the causal relationship between any thimerosal-containing vaccine and autism is also only theory. The CDC released a chart containing all autism and vaccine studies published in the last 8 years and their results which showed no association between thimerosal or any other vaccine used in the study and autism. <sup>1</sup> Thimerosal is a mercury-containing preservative used in some vaccines and other products. There has been no causal relationship between thimerosal and autism however, in 1999, the Public Health Service agencies, and the American Academy of Pediatrics along with vaccine manufacturers agreed to reduce or eliminate the dose of thimerosal in their products as a precaution.<sup>2</sup> On February 2, 2010 the *Lancet* withdrew the original article that started the controversy. This article was published in 1998 and linked autism to vaccines in twelve children. Most recently on March 12, 2010, judges ruled in three separate cases that the thimerosal preservative in vaccines does not cause autism. This ruling comes from a longstanding case called the Omnibus Autism Proceeding that started in 2002 fighting for compensation from the federal vaccine injury fund for autism in children supposedly caused by the vaccines. The federal vaccine injury is a \$0.75 tax on every dose of vaccine.<sup>3</sup>

- Centers for Disease Control and Prevention [website]. Atlanta: CDC; [updated 2010 Jan 15; cited 2010 March 15]. Concerns about Autism: CDC
  Statement on Autism and Thimerosal; [about 3 screens]. Available from: <a href="http://www.cdc.gov/vaccinesafety/Concerns/Autism/Index.html">http://www.cdc.gov/vaccinesafety/Concerns/Autism/Index.html</a>
- Centers for Disease Control and Prevention [website]. Atlanta: CDC; [updated 2010 Feb 11; cited 2010 March 15]. Thimerosal; [about 2 screens].
   Available from: <a href="http://www.cdc.gov/vaccinesafety/Concerns/thimerosal/index.html">http://www.cdc.gov/vaccinesafety/Concerns/thimerosal/index.html</a>
- 3. McNeil DG. 3 Rulings find no link to vaccines and autism. The New York Times. 2010 March 12; A11.
- 4. The Editors of the Lancet. Retraction- ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. The Lancet [online publication]. 2010 Feb 2 [cited 2010 March 19]. Available from: <a href="http://press.thelancet.com/wakefieldretraction.pdf">http://press.thelancet.com/wakefieldretraction.pdf</a>

#### **For More Information**

- Autism Society of America: http://www.autism-society.org
- Autism Speaks, Inc.: http://www.autismspeaks.org
- Autism Research Institute: http://www.autismresearchinstitute.com

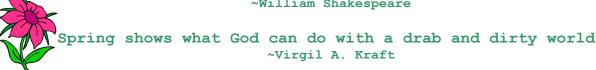
# **Other Important April Dates**

- April 1<sup>st</sup> April Fool's
- April 2<sup>nd</sup> Good Friday
- April 3<sup>rd</sup>, 5<sup>th</sup> NCAA Final Four
- April 4<sup>th</sup> Easter
- April 15<sup>th</sup> Income Taxes due
- April 22<sup>nd</sup> Earth Day



The last "dose" ...

"April hath put a spirit of youth in everything."
~William Shakespeare





An electronic bulletin of drug and health-related news highlights, a service of ...

Auburn University, Harrison School of Pharmacy, Drug Information Center

• Phone 334-844-4400 • Fax 334-844-8366 • <a href="http://www.pharmacy.auburn.edu/dilrc/dilrc.htm">http://www.pharmacy.auburn.edu/dilrc/dilrc.htm</a>

Bernie R. Olin, Pharm.D., Director