

AUTISM SPECTRUM DISORDER

The word Autism comes from the Greek – “Aut” for self and “ism” for condition.

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History

The original paper describing autistic behaviour in a small number of children was published in 1943 by Dr. Leo Kanner, now described as the “Father of Child Psychiatry”. He was born in Austria, and fortunately for the medical world, left Austria in 1924 and settled in the US. In 1943, he described 11 children with “extreme autistic aloneness” delayed echolalia and an “anxiously obsessive desire for the maintenance of sameness”.

Up until the 1970s, autism was commonly regarded as an early presentation of childhood schizophrenia, the cause being a disturbance in child-parent relationship. Autism was considered mutually exclusive of mental retardation. In the 70s, the view moved to that of an inborn problem with development.

The Diagnostic and Statistical Manual (DSM III) (1980) sought to provide a clinical definition of autism. The diagnostic criteria included 3 areas of impairment: lack of response to other people (autism), gross impairment in communicative skills and bizarre responses to various aspects of the environment, all beginning by 30 months of age. The diagnoses fell under the umbrella of Pervasive Developmental Disorders (PDD) and had 3 specific diagnoses: Childhood Onset PDD, Infantile Autism and Atypical Autism.

DSM III-R (1987) presented a list of 16 criteria of which a child had to have at least 8 to fit the diagnosis, and had only 2 specific diagnoses: Autistic Disorder and the new category, Pervasive Developmental Disorder, not otherwise specified.(PDD-NOS)

DSM IV (1994) and DSMIV-TR (2000) had further refinement of criteria and had 5 different pervasive developmental disorders: Asperger Disorder, Rett syndrome, Autistic Disorder, Childhood Disintegrative Disorder and PDD-NOS.

Current Definition

DSM-5 (2013) defines autism spectrum disorder (ASD) in the terms of 2 criteria: “persistent impairment in reciprocal social communication and social interaction” AND “restricted, repetitive patterns of behaviour”. The symptoms must be present from early childhood but may not manifest until social demands exceed the capacity of the child to respond. The symptoms together limit and impair everyday functioning.

The diagnosis is then described with Specifiers:

1. Verbal abilities
2. Cognitive ability
3. Severity of symptoms in the 2 domains (communication and patterns of behaviour)
4. Associated with known medical, genetic or environmental factors: Eg. Tuberous sclerosis, Fragile X, intrauterine valproate exposure

Differences from previous diagnostic criteria

The term PDD is changed as the condition is not Pervasive to all areas of function and is limited to the above 2 spheres. The other PDD categories are eliminated as:

1. there is no biological distinction between high-functioning ASD and Aspergers Disorder
2. Childhood Disintegrative Disorder is nonspecific and given the regression, should prompt a dogged search for a neurologic disorder, including a metabolic disorder.
3. Rett Syndrome can present with autism but is a specific genetic diagnosis
4. PDD-NOS is very nonspecific

Office Approach

Clinical presentation

- Difficult temperament (difficulty with transitions, prickly, over or under responsive to sensations)
- Delays in socialization
- Delays in acquisition of receptive and/or expressive language
- Repetitive movements
- Unusual use of vision/smell/taste
- Fixation of certain toys or objects (e.g. running water, flushing toilets)
- Picky eater
- Difficulty with sleep

- Unusual movements

Approach

History

Start with parental concerns; open question format

- Pregnancy and birth history including exposures (anticonvulsants, ethanol, OTC and prescribed meds)
- Past medical history including allergies, immunizations
- Current meds
- Specific senses – hearing, vision and any testing done
- *Early* communication developmental milestones – particularly pointing, eye contact, response to name
- Overall development- gross motor, fine motor, receptive language (knows name, one part commands) expressive language, social skills
- Family history including intellectual delay, tuberous sclerosis, epilepsy, family members who are dysmorphic (“do not look like anyone else in the family”) anyone with neurologic, psychiatric or possible metabolic disorders (may need a special diet)
- Diet, toileting, daily routines, sleep issues
- Anyone else concerned? Extended family, daycare, teachers, friends?
- Any neurologic symptoms- tics, seizures, regression, etc.
- Any parental internet/library gleanings so far

Physical exam

This can be a significant challenge and might need a second appointment. The tendency to use voice to calm the child is often unhelpful and can make things worse (too much auditory stimulation). Having a toy in the room that can be examined as well can be very helpful. Using parallel activities can be helpful and less threatening. You may want to avoid direct eye gaze. Watch out for noisy toys, they can be frightening.

- Growth parameters
- Look for dysmorphic features
- General exam
- Use play, running and observation to glean information

Next steps

- Hearing test, if not done already
- Vision testing
- Involve your public health care providers – Community Health Nurse, local Infant Development Program, Speech Pathologist at the Health unit
- Paediatric consult – tell parents to bring along any *assessments* they have from the community; videotape of specific behaviours can be invaluable
- Follow-up visit while awaiting other services- parents often come back with more thoughts, the concern does not get lost in the black hole of waitlists, you develop rapport with the child and may glean more information

- If you believe that the child could have autism and do not have paediatric consultation services nearby, you can start the process of referral to the BC Autism Assessment Network: <http://www.phsa.ca/our-services/programs-services/bc-autism-assessment-network>
- You can refer the family to the website www.actcommunity.ca. The website has lots of information for families on proceeding if there is a possible diagnosis of ASD for their child
- If there are any dysmorphic features, strong family history, potential intrauterine exposure to a “toxin” – a referral to Medical Genetics may prove helpful
- If there is any questions of seizures, talk with a paediatrician or neurologist and ask for an EEG.
- If there are neurocutaneous findings (e.g. hypomelanotic area (Ash-leaf spot), facial angiofibromas, Shagreen patch (pebbly, thickened patch of skin, usually on the lower back) – these are all possible signs of tuberous sclerosis and you would request a Neurology consult.
- Review the guidelines at www.tidebc.org which is the Biochemical Diseases initiative at UBC to identify children with treatable causes of intellectual disability. The site gives an algorithm about how to identify children who may have an inborn error of metabolism that presents as intellectual deficit.
- The chapter in Up to Date: Autism Spectrum Disorder, Diagnosis is excellent for guiding further actions to be taken.

Differential Diagnosis:

- Hearing loss – conductive, sensorineural, auditory neuropathy – can have some features of autism but should have relatively normal intent to form social connections
- Global developmental delay/ cognitive delay
 - ~ 40% of children formally diagnosed with ASD will also have an IQ of 70 or less
 - the social delay is concordant with all of the other delays
- Developmental language disorder- should have normal social interactions
- Language based learning disability- should have normal social interactions
- Landau-Kleffner syndrome – acquired epileptic aphasia
- Rett disorder -Almost exclusively in females, typical development till 18 months and then regression, usually have mutations in MECP2 gene
- Severe early deprivation/attachment disorder- the history should reveal this scenario
- Anxiety disorder- normal communication skills and reciprocal interactions (at least with close caregivers)
- Obsessive –compulsive disorder – usually normal social and communication skills
- Social (Pragmatic) Communication Disorder - This is a *new* diagnostic category found in the DSM 5. It refers to persistent difficulties in the social use of verbal and nonverbal communication and is distinguished from ASD by the absence of restricted, repetitive patterns of behavior, interests or activities. The differentiation between the 2 disorders may be difficult, particularly as repetitive behaviours may vary over time.

Epidemiology

Prevalence

The Autism and Developmental Disabilities Monitoring (ADDM) Network reported a prevalence of 1 in 90 in 2007, then 1 in 68 in 8 year olds in 2010 (~ 1 in 42 boys, 1 in 189 girls). The prevalence variation may be related to changes in diagnostic criteria, study methodology, a true increase in the incidence of

autism or a combo of these factors. Decades ago, a child with autism might be labelled “mentally retarded” as the ability to assess intellect without using language based testing would not have been as well developed. Could the availability of funding have created a positive bias in identifying affected children? There was a problem with the wording of the diagnosis in DSM IV with the use of the word “or” for the criteria versus the word “and” which was corrected in DSM IV-TR. It is not clear what the effect will be of the revision of the diagnostic criteria in DSM 5. For research purposes, the diagnosis of ASD is made using the tools Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) and this will be important in comparing studies.

Rate in siblings

In the 2013 American College of Medical Genetics and Genomics practice guidelines, the risk is quoted at 4-7% if there is one previous child with ASD and the risk can be as high as 30% if there are 2 or more affected children.

Associated Conditions

- Intellectual disability (IQ 70 or less) 45-60% of kids with ASD
- Seizure disorder 11-39% of kids with ASD and risk is higher in kids with more severe intellectual disability
- Associated medical condition – 10-25% e.g.: Fetal alcohol syndrome, tuberous sclerosis, Fragile X, 15q chromosome abnormalities (deletions, duplications) Rett syndrome, Smith-Lemli Opitz syndrome, metabolic disorders/inborn errors of metabolism and a number of other chromosome markers
- Autism and macrocephaly – associated with *PTEN* mutations chromosome 10q23.3 – this is a gene that encodes for cell migration, apoptosis and is associated with growth of tumours.

Etiology, Research, MRI, Genetics – What causes autism?

Genetics

There are at least 230 genes identified so far that, when mutated, can result in an autistic phenotype. This area of research is exploding and has validated the opinion that autism is a collection of symptoms and signs but not a single disease. The majority of these gene disruptions are *de novo* and do not exist in the parents. Increasing parental age is a risk for autism in the offspring. This might be related to the increase in *de novo* mutations or changes in genetic imprinting or maybe the parents have a mild autism phenotype and take longer to find an appropriate mate.

- **Extreme prematurity and low birth weight** - increase the risk of autism, particularly birth before 27 weeks after the LMP. The specific factors are unclear, but there are many studies that look at the way the brain develops in the premature infant. The path of development is not just immature but is truly different than that of a child born at term. MRI studies have shown that a number of these studies include brain volumes, and also differences in areas of language processing.
- **Pregnancy** - Maternal obesity, gestational diabetes, hypertension are current areas of research.
- **Intrauterine exposures** - exposure to valproic acid and thalidomide increase the risk of ASD us.
- **Gender** – ~4:1 male to female ratio

SSRIs in pregnancy

- A review of 966 mother-child pair from the Childhood Autism Risks from Genetics and the Environment (CHARGE) (showed that boys with ASD were 3 times as likely to have been exposed to SSRIs in-utero, particularly the first trimester. (Harrington, RA et al 2014))

Anders Havid, et al Use of Selective Serotonin Reuptake Inhibitors during Pregnancy and Risk of Autism *N Engl J Med* 2013; 369: 2406-2415 - this study was conducted in Denmark and looked through data on more than 600,000 live births. They identified 3892 cases of autism and found the fully adjusted rate ratio to be 1.2 for exposure in pregnancy and 1.46 for SSRI use before but not during the pregnancy. These rates were not statistically significant.

Food for thought: New studies are emerging about the genetics of schizophrenia, bipolar disorder and other mental health diagnoses. There is some excitement about the discovery of how the genes are implicated in chromatin modification and there are some genes that overlap with those found in children with autism. Is the use of an SSRI for therapy a marker for these gene differences and therein lies the link, versus the actual exposure to the SSRI?

Environmental factors

These factors may constitute a “second hit” or additive factor but there have been few cases attributed to a specific element (lead, mercury).

Vaccines

All the vaccines routinely given to children less than 6 years of age (according to BC Immunization guidelines) are thimerosal free providing that one is using the single-dose seasonal flu vaccine or the nasal spray form.

If thimerosal was removed from paediatric vaccines starting in 2000 and being almost 100% gone by 2004, wouldn't the prevalence of autism have decreased with these manufacturing changes? (The prevalence did not go down)

- Paul Offit's paper *Thimerosal and Vaccines – A Cautionary Tale* is good review of the issue.
- Kirsten A. Blaine's *Your child's best shot: a parent's guide to vaccination (2nd edition)* is an excellent reference and is great reading for parents with questions

Brain Imaging and Functional Studies

Rather like the studies of the number of genes involved, there are a myriad of studies showing differences in brain volumes (e.g. macrocephaly in a number of people with ASD), smaller volumes in exprems, differences in activation of areas of communication, social reactivity and also in processing of sensory information. The results are variable, like the condition. For a thorough review on this topic, see Dichter, GS (2012).

Diagnostic Tools

For a thorough treatment of this topic, see Up to Date: ASD- Screening Tools.

There are a number of diagnostic tools, but for the purposes of BC government funding, a child must be diagnosed using 2 tools.

1. **Autism Diagnostic Interview-Revised** this is a 2-3 hr clinical interview with 82% sensitivity in children less than 3 yrs old and 91% in kids more than 3 years old.
2. **Autism Diagnostic Observation Schedule** - there is now a second version. The ADOS also has a Toddler Module that can be used for ages 12-30 months (or until phrase speech is acquired). The ADOS takes 40-60 mins to perform and requires substantial training to be able to administer and score the test.

Food for thought: Given that an appointment to rule in or rule out autism using these tests takes at least 3 hrs, you can see why there is a waitlist for the provincial resources to see children. Having the community resources apply their own standardized surveys, and provide copies to BCAAN in advance means that the time spent with BCAAN can be used more efficiently. Encourage parents to keep a binder with all assessments performed and results of any medical tests/consults and to bring this binder with them to any further assessments.

Funding and Therapy

If the child receives a formal diagnosis of ASD, application is made to the Government of BC for funding for therapy. Part of the paperwork is filled out by the parents and part is by the Qualified Specialist. (See websites noted in reference section of this handout). Part of the report from BCAAN includes a section documenting “next steps”.

BCAAN does not provide ongoing therapy but will provide the family with a list of resources. The Autism Community Training website provides a detailed guide on how families can move forward into developing a therapeutic team. This area can be VERY STRESSFUL for families as they learn about a multiplicity of resources and sometimes a service provider has a waitlist. Like many other chronic developmental issues, the GP might be a helpful sounding board for the parents to decide which areas of behaviour are the immediate priority.

Food for thought: There is a growing movement within the world of people with autism that distinguishes their world from that of us that are “neurotypical”. There has been a negative focus on autism to try and make the children “typical” without celebrating differences. Reading first- person accounts is very helpful to try and understand this area.

Intensive Behavioural Interventions

1. Discrete Trial Training – most structured form intensive therapy, developed by Ivar Lovaas
2. Applied Behaviour Analysis (ABA) seek to reinforce desirable behaviours and decrease undesirable behaviours, goal is to teach new skills and generalized learning skills by breaking them down into their simplest elements, uses reward based training

Best started before 5 yrs of age, can be individual or in group settings, time intensive (30-40 hrs per week). Generally improvements seen in the first 12 months of therapy, this therapy is supported for efficacy by a body of data but may not be indicated or effective for all kids with ASD. This form of therapy is somewhat controversial in older kids. Children requiring ABA at an older age may be more impaired than those who no longer need this intensive therapy.

TEACCH/Structured Teaching method

<http://teacch.com/about-us/what-is-teacch>

The goal is to modify the environment and improve skills, using an individualized person and family-centred plan with a predictable sequence of activities and using visual tools to help with activities. Some evidence to support improvement in cognitive and motor function but magnitude of effect unclear.

Development and Relationship models

This form of therapy focuses on teaching skills that are essential to development such as social communication, emotional relationships and cognitive abilities that were not learned at the typical time. Examples are: Milieu therapy, Responsive Teaching and “More than Words” program.

Integrative models

May use more than one form of therapy, e.g. SCERTS program, Early Start Denver Model (EDSM)

Cognitive Behavioural Therapy

CBT can be very effective in reducing anxiety symptoms in high-functioning individuals with ASD.

Parental role

While it might seem like common sense, there is a growing body of evidence showing that training parents, versus just educating them, produces great benefit to the child. At the least, it may help families interact, increase parental satisfaction, empowerment and mental health.

Communication Interventions

These interventions work best when they span settings and are incorporated into daily routines. The communication program may include:

1. Traditional speech therapy
2. Behavioural strategies to encourage the use of language
3. Augmentative communication strategies – sign language, gestures, electronic systems
4. Visual supports – visual schedules, choice boards , visual instructions

Some parents are worried that the use of communication techniques other than language could inhibit the development of language skills but at least one study shows that the use of symbolic language may stimulate the child with ASD to learn speech.

Social Skills Instruction

The National Autism Centers National Standards Report (US) in 2009 identified 4 therapies that have evidence to support benefit.

1. Joint Attention interventions – pointing, showing
2. Modelling – real life and video
3. Peer training
4. Story based intervention e.g. “Social Stories” approach

Occupational Therapy

The therapy may focus on fine motor skills such as self-care and participation in play. A specific form of therapy is **sensory integration therapy**, the theory being that various sensory experiences help to guide development, and children with ASD may have aberrations in sensory integration. The validity of this theory and therapy is controversial and the literature is inconsistent on results. It might be wise to avoid using sensory integration therapy as the sole form of therapy and to monitor for the child’s response to see if continued use is indicated.

I have only touched on some forms of therapy and there are different forms for toddlers and school aged children with ASD.

Complementary and Alternative Therapies- see Up to Date section for more detail on this

1. Melatonin – may be beneficial for initiating sleep
2. Secretin – INEFFECTIVE
3. Omega-3 Fatty Acids – benefit unclear in studies,
4. Gluten free and/or casein free diet – evidence is weak, could be unsafe as potential risk of lower intake of calcium, vitamin D and amino acids, decreased bone density. One study could not exclude that children with significant GI disease might benefit from the diet.
5. Vitamin B6 – often used with magnesium to reduce side effects of B6, data inconclusive
6. Dimethylglycine (DMG) - , thought to reduce lactic acid build up with stress and improve oxygen use - insufficient evidence
7. Sulforaphane – antioxidant from broccoli sprout extracts – one study was promising but the dose is much more than can be obtained from food, for now not recommended
8. Probiotics – evidence of efficacy is lacking but no studies demonstrating harm either
9. Antifungal agents – no evidence of efficacy and adverse effects may incl hepatotoxicity
10. IVIG - based on hypothesis that ASD related to immune system, no evidence of efficacy and significant risk of side effects- RISK
11. Chelation – given the concern for “toxins” – not well studied, hypothesis not supported and safety not ensured- RISK
12. Hyperbaric Oxygen – hypothesis – increase O2 delivery to brain – one study did show some positive effect in both kids with ASD and controls but only one assessment, RISK of side effects (one might also want to think about the risks of oxygen radicals, a hot topic itself)
13. Vitamin C, methylcobalamin, folic acid – some potential benefit but not sufficiently strong
14. Music therapy – 2014 review of 10 clinical trial – some benefit but needs more study

15. Horseback Riding – some evidence to support benefit, needs adequate supervision
16. Transcranial Magnetic Stimulation – needs further study, not recommended as yet- RISK
17. Facilitated communication- controlled studies revealed that the facilitator, rather than the child, is communicating. INEFFECTIVE
18. Auditory Integration Training – the American Academy of Peds considers this an investigational Tx

Medications

I myself would consult with a child psychiatrist before prescribing any psychoactive meds for a child with ASD other than a trial of a stimulant. The following paragraph is a summary of the information presented in the Up to Date: Pharmacologic Interventions article.

Some of the meds considered are:

1. Stimulants- methylphenidate, dextroamphetamine – for inattention, hyperactivity – side fx – sleep disturbance, decreased appetite, tics, sadness, dullness, social withdrawal
2. Alpha-2 adrenergic agonists – guanfacine, clonidine – for inattention, impulsivity, side fx - sedation, hypotension, dry mouth, increased aggression, noct enuresis, headache
3. Atomoxetine – for hyperactivity and inattention – side fx – mood swings, fatigue, dizziness, suicidal ideation, hepatotoxicity
4. Atypical Antipsychotics – risperidone, aripiprazole - can be used for inattention, hyperactivity, irritability, aggression, tantrums and self- injury, repetitive behaviours – side fx- weight gain, fatigue, drowsiness, tremor, constipation, metabolic disorder
5. SSRIs - to treat anxiety, repetitive behaviours, mood lability-

Summary

Autism Spectrum Disorder is a relatively common condition, characterized by atypical social communication and repetitive/rigid behaviours and areas of interest. Anyone working with children will see kids affected by ASD and having knowledge of the condition is helpful to the child and encouraging to the parents. Similar to the diagnosis of cerebral palsy, the term ASD alone does not delineate the child's strengths and weaknesses, and does not offer specific prognostication for the future. An approach that focusses on strengths and areas for therapy is valued by families as they move through this difficult journey.

References & Resources

1. www.actcommunity.ca "The mission of ACT – Autism Community Training is to provide excellent information and training, in accordance with international best practices. Our goal is to enable parents, professionals and para-professionals to support children and adults with Autism Spectrum Disorder to live productive, satisfying lives within their families and communities." This service is funded by MCFD and is a not-for-profit society. Excellent website for families and health professionals, some information in Chinese.
2. www.mcf.gov.bc.ca/spec_needs/index government website and includes a parent guide
3. www.health.gov.bc.ca/library/publications/year/2003/asd_standards This document describes the standards that must be met on diagnosis to qualify for funding. One can obtain a diagnosis of autism

privately but it must follow the standards set by MCFD to secure funding. See this topic in the ACT website.

4. www.uptodate.com/contents/autism-spectrum-disorder Extensive review of the current information
5. www.tidebc.org Treatable intellectual disabilities BC website
6. Anders, H. et al. Use of Selective Serotonin Reuptake Inhibitors during Pregnancy and Risk of Autism. *New England Journal of Medicine*. 2013; 369: 2406-2415
7. Baker, JP. Autism at 70 – Redrawing the Boundaries. *New England Journal of Medicine*. 2013; 369:1089-1091.
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9. Dichter, GS. Functional Magnetic Resonance Imaging of Autism Spectrum Disorders. *Dialogues in Clinical Neurosciences*. 2012; 14(3): 319-351.
10. Harrington, RA et al. Prenatal SSRI Use and Offspring With Autism Spectrum Disorder or Developmental Delay. *Pediatrics*. 2014;133:5.
11. Offit, PA. Thimerosal and Vaccines — A Cautionary Tale. *New England Journal of Medicine*. 2007; 357:1278-1279.
12. Volkmar, FR; Wiesner, LA. *Healthcare for Children on the Autism Spectrum: A Guide to Medical, Nutritional and Behavioural Issues*. 2004.
13. <http://www.autismconsortium.org/symposium-files/WalterKaufmannAC2012Symposium.pdf> Excellent review of the development of diagnostic criteria of ASD and interesting history of the evolution of the Diagnostic Statistical Manual and ICD criteria for mental disorders

First-hand accounts (reading list)

1. Fleischmann, A; Fleischmann, C. *Carly's Voice: Breaking Through Autism*. 2012.
2. Grandin, T; Panek, R. *The Autistic Brain: Thinking Across the Spectrum*. 2013.
3. Grandin, T. *Different...Not less*. 2012.
4. Grinker, RR. *Unstrange Minds: Remapping the World of Autism*. 2007.
5. Mukhopadhyay, TR. *How Can I Talk if My Lips Don't Move: Inside My Autistic Mind*. 2008.
6. Tammet, D. *Born on a Blue Day: Inside the Extraordinary Mind of an Autistic Savant*. 2007.