

**The Autism Treatment Network (ATN) in 2010:
Improving care for Children with ASD**



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Grand Rounds
Surrey Place Centre
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Outline

- 1) Review ATN/AIR-P Purpose and Accomplishments
ATN Staff, Statistics,
- 2) Building Capacity (10 min)
Symposiums, video clips, Paediatricians, Family Representatives
- 3) Clinical Guidelines from 2010 (10)
Constipation and Toileting Tool Kit; Sleep Guideline and Tools
- 4) Research Projects
Toileting, Sleep, Nurse follow up and QI (10)
Creatine, Neuroinflammation AL (10)
- 5) Looking ahead – 2011-2013 (5)
Questions (10-15 min)



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What is the Autism Treatment Network (ATN) ?

- Network, striving to define and implement the best practice standard of medical care for children with ASD, with an associated Data Registry
- 13 American Sites, 1 Canadian site
- Toronto completing first 3 year cycle, 2008-2010
 - Applying for next cycle, mentoring Edmonton
- Funded by Autism Speaks
 - Research Co-ordinator, Data Co-ordinator
 - Nurse Co-ordinator
- North American Collaborators
 - National Initiative for Children’s Healthcare Quality (NICHQ)
 - EMMES Corporation (Data), Clinical Co-ord Centre (Mass Gen Hos)
- Toronto Collaboration
 - Surrey Place Centre, Holland Bloorview Kids Rehabilitation Hospital, and the Hospital for Sick Children





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ATN Vision



“To improve the lives of all children and families with ASD by making a high quality, comprehensive, and multidisciplinary continuum of care accessible within local communities.”



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Goals

- Quality: Improve the quality of medical care for children and adolescents with ASD.
- Access: Increase the availability of a comprehensive, coordinated, longitudinal care model for all children with ASD.
- Research: Advance the evidence-base and research on medical issues in order to provide better care for children with ASD.
- Leadership: Becoming the leading clinical network on medical issues related to ASD



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Eligibility

- Ages 2 to 17.
- ASD diagnosis by Developmental Paediatrician (or NP) with ADOS within the last year.
- Parent able to read and speak in English.
- Child not deaf or blind.



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ATN Toronto Enrollment

- One of 14 sites in North America funded for first 3 year cycle: 2008-2010.
- Began enrolling Children in April 2008.
- Cycle 1 ends Dec. 31st, 2010

	ATN Toronto	ATN Total
April 2008 To Dec. 2008	34	529
Jan. 2009 To Dec. 2009	73	1319
Jan. 2010 To Dec. 2010	108	1267
Totals	215	3119



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Accomplishments in Cycle 1

- Building Capacity in the community
 - Expanded Nursing Role
- Involvement of Families in the work of the ATN



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Building Capacity in the Community

- ATN Symposiums
- Website Development
- Parent Newsletters AIR-P and ATN
- ATN Developmental Paediatricians (Lead Autism Specialists)
- ATN General Paediatrician Group
- Specialists:



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Helping Families – Counselling and Support

- Nursing Support
 - Nurse co-ordinators assigned to families
 - Provide education and support
- Behavioural therapy consults for toileting
- Advocacy in the Community and School
 - Mental Health issues prevalent in ASD
 - Identifying Service Gaps and advocating for children and families



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Family Involvement

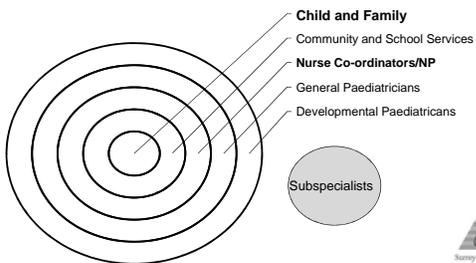


- The ATN was developed out of a need expressed by families to have medical issues addressed.
- Importance of family input in the work of the ATN.
- **Parent Representative** at each ATN site
- At the ATN Toronto Site, one of our Nurse Coordinators will work with 2 parent reps. to develop a plan for gathering input from families.
- ATN Toronto Parents piloted new ATN forms to be used for cycle 2.



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Building Capacity in the Community



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Clinical Highlights of the ATN

- Screening for sleep and GI disorders
 - Parent Handout for sleep
 - Algorithms for sleep difficulties and constipation
 - Algorithm for Referral to subspecialists
- Neurology algorithm for EEG and MRI
- Metabolic and Genetic testing in ASD
- Behavioural challenges
 - Psychopharmacology working group – ATN wide
- Local Referral network of Interested Expert Subspecialists
- GI, Sleep, Neuro, Genetics/Metabolics, Nutrition, Pain
 - Goals to develop and publish best practice guidelines for care



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Sleep Guidelines and Sleep Tool kit

- Algorithm for clinicians to follow in children with autism who have sleep problems
- Developed by sleep specialists in the ATN
- Is being piloted in some sites to determine effectiveness for use by all clinicians
- “tool kit” is being created to use with guidelines
- Includes handouts of sleep strategies for children and adolescents, bedtime pass, visual schedules for sleeptime



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Sleep Algorithm

- Starts with standardized parent questionnaire
- Children’s Sleep Habits Questionnaire
- Sleep red flags in questionnaire guide MD to further assess and rule out medical causes for sleep problems such as difficulty falling asleep, frequent night awakenings, snoring or apnea (not breathing for periods of time)
- Strategies for consistent sleep hygiene/sleep routines are provided with tools for implementation



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CSHQ targeted question #5

- **Child wakes up at least once during the night. If problem, ask (to get sense of severity):**
 - How many times does your child wake up in an average night?
 - How long does it take your child to fall back to sleep after waking up?
 - Does your child wander around the house after waking up?
- If family concerned or safety an issue, institute behavioral therapy
- If family in crisis, institute pharmacological therapy in conjunction with behavioral therapy.
- Consider referral to ATN sleep specialist for night wakings (consider wait list for specialist, severity of the problem, and expertise/comfort level of LAS in dealing with sleep problems)



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Evaluate and treat coexisting medical conditions contributing to sleep problems (checklist)

- Does child have poorly controlled seizures?
- Does child have acid reflux, constipation, diarrhea, or other digestive conditions?
- Does child have asthma or allergies?
- Does child have anxiety, depression, bipolar disease?
- Match list of medications against those that contribute to insomnia
- What else?



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ATN Constipation Guidelines

Background

- Approximately 3% of visits to general pediatric outpatient clinics and 25% of referrals to a pediatric gastroenterology clinic are prompted by a perceived defecation disorder
- The treatment of constipation in the US is estimated to cost over 3.9 billion dollars per year. This estimate only includes children covered by private health insurance (Liem et al., 2009)
- Chronic constipation is cited as one of the most common GI problems in persons with ASD (Buie et al. 2010a)
- The complexity of ASD and the specific characteristics commonly seen in children with ASD (e.g., behavioural rigidity, communication deficits, sensory sensitivities) pose challenges in the medical evaluation for constipation (Afzal et al., 2003; Buie et al, 2010a).



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Constipation Algorithm

- GI symptoms questionnaire to highlight red flags for constipation
- Definition of constipation < 3 stools per week or difficulty passing stools
- 1st step-Medical exam-physical and history
- If functional constipation-check for impaction and disimpact
- If medical cause-refer to GI specialist
- Next steps-parent education, diet changes, oral meds (PEG 3300), behavioural intervention



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Toileting Tool Kit

- Strategies and video developed in Denver
- A study by Dalrymple and Ruble found that, on average, children with autism spectrum disorders require:
- 1.6 years of toilet training to accomplish daytime continence
- More than 2 years to achieve bowel control
- Take-home message: **DON'T GIVE UP!**

Dalrymple, N.J. & Ruble, L.A. (1992). Toilet training and behaviors of people with autism: Parent views. *Journal of Autism and Developmental Disorders*, 22 (2), 265-275.



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Toilet Tool Kit Tips

- **1. Collect information** before beginning a toilet training program. Write down how much long it takes between when your child drinks and when he or she is wet. Checking your child's diaper frequently for wetness (e.g., every 15 minutes) will help you decide when to schedule toilet trips.
- **2. Consider dietary changes**, such as decreasing milk and dairy products and increasing fluids and fiber.
- **3. Think about small changes in daily habits.** Change diapers near the bathroom, if possible. Change your child as soon as he or she becomes wet or soiled. Have your child flush the toilet and wash hands after each diaper change. Dress your child in easy-to-remove clothing.
- **4. Make sure toilet trips are comfortable.** Your child should be comfortable and stable while sitting on the toilet. Your child may be more comfortable using a smaller potty seat and/or resting his or her feet on a stool. If your child won't sit on the toilet, work on this skill *before* beginning a toilet training program.
- **5. Ensure that the bathroom provides a positive sensory experience.** Watch your child - if he or she is sensitive to sounds, smells, or other sensations in the bathroom, try to find possible solutions. For example, if your child does not like certain noises in the bathroom, he or she may wear headphones to dampen the sounds, or listen to music to compete with the other noises in the bathroom.



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Toilet Tool Kit Tips

- **6. Have many pairs of underwear available.** When you are focusing on toilet training, it is important for your child to wear underwear during the day. Your child needs to feel when he or she is wet. Diapers or pull-ups may be used when the child is sleeping or is away from the home.
- **7. Use a visual schedule.** Pictures associated with each of the steps of the "potty routine" may be helpful in teaching the sequence of actions required for successful toileting. A schedule can also increase predictability so that your child knows what to expect. Actual objects (e.g., a roll of toilet paper) also may be helpful to use as a part of the schedule, if pictures aren't yet meaningful.
- **8. Use rewards.** Provide your child with a reward IMMEDIATELY after he or she urinates or has a bowel movement in the toilet. The more quickly you reward a behavior, the more likely that behavior is to increase. Rewards used for toileting should be "special" and used ONLY for toileting.
- **9. Include opportunities for generalization.** Assist your child to use toilets in different bathrooms in your home as well as bathrooms outside of your home (e.g., at school, in the homes of family members or friends, and/or in public restrooms).



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Research Projects

- Constipation and Toileting in Autism
- Team: Peggy Marcon, GI, SickKids, Lesley Barreira, Lianne Moroz, Pam Green, SPC, Jessica Brian, Holland Bloorview, Melanie Fenwick-Coordinator
- Funded by AIR-P Network from HRSA
- Goal- to describe and develop an effective and clearly defined behavioural treatment protocol to complement and enhance current medical treatment of constipation in children with ASD.
- This protocol would be used to develop a tool for primary health care providers



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Constipation and Toileting in Autism

- **Ten subjects diagnosed with ASD and difficulty with stool passage including constipation, refusal to stool anywhere but pull up and stool holding behaviors (including only stooling while sleep) between the ages of 4 to 9 years will be recruited prospectively from the Toronto ATN site.**
- Toileting Assessment
- Daily Tracking Record
- Toileting Plan with Behaviour therapist
- Implementation and Followup at 3 months and 6 months



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Sleep – Multicentre, Multiyear study

- “Parent Based Sleep Education Program for Children with ASD”
- AIMS
 - To determine the efficacy of a sleep education pamphlet compared to no sleep education in children with ASD
 - To compare 2 nurse led sleep interventions in children with ASD
 - To conduct a larger scale RCT comparing the more effective intervention developed in Phase 1, with the control intervention (sleep pamphlet)
 - To determine if the intervention improves sleep latency as measured by actigraphy
- PI – Beth Malow, Vanderbilt
- Collaborators – Cincinnati, Colorado, Toronto (Shelly Weiss)



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Sleep Study

- Phase 0 completed-use of sleep strategy handout (standard practice) had no effect on sleep problems
- Phase 1 in progress-comparison of parent education techniques-individual counselling with a nurse vs. group session with 4 parents with a nurse
- Phase 3 will be implementing the leading intervention of Phase 2 compared to handout in our popn in Toronto (Spring, 2011) Coordinator-Cathy Petta



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Nursing Followup Pilot/Quality Improvement

Background:
Children with ASD have many health related issues including sleep disturbances, GI problems, behaviour challenges and school issues.
Medical Followup is not consistently given after diagnosis to children with ASD
Nurses can provide holistic health expertise, system navigation skills and family support to bridge the followup gap and improve care



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Nurse Followup Pilot

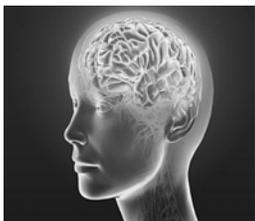
- Goal: To develop, pilot and evaluate a nursing model of followup for children in the ATN
- 4 month pilot from Jan, 2011- April, 2011: Dianne Davison and Cathy Petta, ATN Nurse Coordinators
- Outcomes include measures of parental advocacy, satisfaction and pediatric quality of life
- Meeting family needs for clarification of dx, navigating health care and school systems, accessing services, counselling for sleep, toileting, sensory and behavioural issues, referrals to specialty services, accessing respite, informed education about research, alternative treatments, supplements and nutrition



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**What is the Prevalence of Creatine Deficiency?
A treatable metabolic cause of DD, Seizures, and ASD**

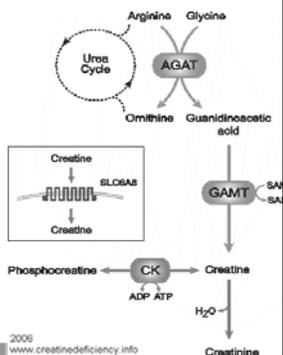
- Cases described in 1994, 2001
- X linked creatine transporter mutations in 1 % of males with MR
 - Clark AJ et al, Human Genetics, 2006
 - 478 males, 6 novel deletions
 - compared to 588 male controls
- 2.1% prevalence
 - (n=288, boys, familial cases)
- GAMT defects – 2.7%
 - (n=180, severe MR)
- Similar fragile X (2.5%)



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Creatine Metabolism

- Creatine - energy delivery
 - muscle and brain
 - Actively moved into brain by Creatine Transporter pump
- Brain also makes creatine
- Three disorders in CDS
 - GAMT, guanidinoacetate methyltransferase (1994)
 - AGAT, arginine:glycine amidinotransferase (2001)
 - CrT1, creatine transporter defect (2001)



2006 www.creatinedeficiency.info

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	GAMT (severe)	AGAT (mild)	Creatine Transporter Deficiency
Prevalence	< 2.7%	rare	0.3-2.7%
Genetics	AR	AR	X linked
Clinical	Dev Delay Speech Delay Hypotonia, Dyskinesia Refractory seizures Autistic Mannerisms/SIB	Dev Delay Speech Delay (Seizures)	Dev Delay Severe Speech Delay Autistic mannerisms (Mild seizures)
Pathophysiology	High GAA, Low creatine	Low creatine	Low creatine
Treatment	Creatine, restrict arginine	Creatine 400mg/kg/d	Diet
Outcome	Some improvement	Moder. Improvement	No clear changes

Testing for Creatine Deficiency

- Clinical Indication in Toronto
Global Delay, Poor Speech
(+/- abnormal movements, seizures)
- Research Indication
 - Child in ATN, Autism
- Screening
 - Urine, Sick Kids, Andreas Schulze's Lab
 - Repeat urine if + (12-24 hr collection ideal)
- Diagnostic Confirmation
 - Genetic (blood test): GAMT, AGAT, SLC 6A8
 - Brain Scan (MRS), Absent Creatine
- **Adults** – Genetic Metabolic Consultation at
TGH, Dr Hannah Fagfoury taking referrals

http://www.uhn.ca/Clinics_&_Services/services/adult_genetics/docs/agg_referral_form.pdf



Diet: False positives
- Oily fish or beef (100g)
at dinner, can raise urine
creatinine/creatinine levels
in adults into abnormal
range

Treatment of Creatine Deficiency

- GAMT
 - Supplement with creatine, restrict arginine
 - Seizures and neurological symptoms improve
 - More social and interactive and improved functioning
 - IQ and Language- clear change
- AGAT
 - Supplement with creatine
 - Milder phenotype, rare or underdiagnosed
 - Responsive to treatment
- Creatine Transporter Defect
 - Arginine and glycine and creatine supplements trialed
 - 3 boys seen at SPC



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STAR – Study of Toddlers with Autism and Regression: Biomarkers of immune activation and oxidative stress

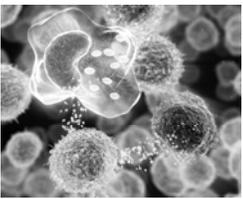
- Could Neuroinflammation be causing regression ?
 - Brain Pathology and fluid (CSF) studies, small sample (Vargas '05)
 - Increase in head circumference in ASD at 6-18 months of life
 - Mild MRI brain abnormalities: ?atypical cells ?edema (Dager '08)
 - Uncontrolled epilepsy associated with neuroinflammation (Choi '09)
- How can we detect this?
 - Brain imaging?
 - Too mild for MRI, SPECT scans with radioisotopes not ethical
 - EEG? not specific for inflammation
 - CSF? Some enthusiasm but challenging to obtain CSF
 - Is there a correlation between inflammation in blood and CNS
 - Funded: pilot study on biomarkers of immune activation



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Purpose of STAR protocol

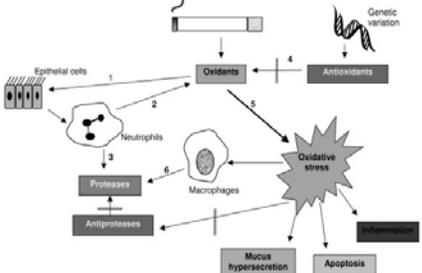
- To compare immune activation and oxidative stress markers in 18-36 month toddlers with autism and regression vs Controls (autism and no regression)
- Immune Dysfunction in ASD
 - CD 40L, chronic inflammation (Pardo 2009)




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Oxidative stress in ASD

- Glutathione (antioxidant) is decreased in ASD (James 2006)
- Oxygen reacts in our body leading to "oxidants"
- Potentially damaging "free radicals" are made and mopped up
- "an increase in production of oxygen molecules that can damage cells and impair their function" Jill James



Responding Quickly When Regression Occurs

- Make all MDs and early childhood centres aware
- Screen with Regression questionnaire
- Assessment with ASD testing (ADOS), and Developmental testing (Mullen), and Clinical History
- Clinical Tests (metabolic disorders, inflammatory markers)
- EEG
- Research Tests (immune overactivation, oxidative stress)
- Research Co-ordinator at SPC – Melanie Fenwick, x 2527



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Future Directions

- Toronto has applied for renewal in ATN for 2011-2013
- Quality Improvement
- Guideline Development and Piloting
 - When should you order an EEG for children with ASD ?
- Family Representation
- Building Capacity in the Community



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Acknowledgements

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- Salina Eldon
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- Johanna Lake
- Melanie Fenwick
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