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Thursday, June 10, 2021

08:30 AM - 10:30 AM WS #5: Integrative Medicine Masterclass - Part 1 11:00 AM - 01:00 PM WS #13: Integrative Medicine Masterclass - Part 2 02:00 PM - 04:00 PM WS #20: Integrative Medicine Masterclass - Part 3 04:30 PM - 06:30 PM WS #27: Integrative Medicine Masterclass - Part 4

INZMA Rotorua GP CME General Practice Conference & Medical Exhibition



Dr Daniel Quistorff Millhouse Medical Centre



Tessa Jones

Room 1

Autism How can we help?

Dr Debbie Fewtrell MB ChB, Dip Obs, RNZCGP, FACNEM June 2021







OVERVIEW

1. Nutritional interventions – Fe, Zn, Vit D, Omega 3 2. Diet – Gluten free casein free 3. Gl assessment in ASD 4. Sleep - melatonin

- ASD's diagnostic features
 - Issues with speech and communication and social interaction
 - Restrictive and repetitive and ritualised behaviours, stimming
 - Restricted interests and excessive resistance to change and need for routines

Autism spectrum – a complex disorder: There are simple interventions that may help the child



Autism Rates



- - years has ASD dx
- Adolescents, 2014-2016
- alWei Bao, MD, PhD¹
- Author Affiliations Article Information •
- JAMA. 2018 •

Higher rates in Maori than European

Causes: genetic 38% and environmental 58%

Increase in cases of autism in USA from 1:2500 in 1990 to 1:68 in 2012. In 2015 1:45 children between aged 3-17

1 in 36 children(2.76%) (95% CI, 2.20%-3.31%) in 2016 USA

Prevalence of Autism Spectrum Disorder Among US Children and

<u>Guifeng Xu, MD¹</u>; Lane Strathearn, MBBS, PhD²; Buyun Liu, MD, PhD¹; et

Causation Theories and the Web of Interactions





Oxidative Stress Gut Dysfunction Immune Dysregulation Inflammation

The autism web

TOXICOLOGICAL

Methylation issues Oxidative stress

Blutathione depletion

eavy metal toxicity

IMMUNOLOGICAL

Environmental allergies

Chronic inflammation Autoimmune reactions

Frequent infections False neurotransmitters

Neuronal inflammation

Dysregulated neurotransmitters Autonomic dysfunction

NEUROLOGICAL

ASTROINTESTINAL Nutritional deficits Food sensitivities Intestinal dysbiosis GI inflammation Motility issues

3D SCIENCE.com

Simplistic approach to ASD



"Clean up environment" Patient info sheet

"Low additive diet" Patient info sheet

"Healthy gluten free casein free diet" Patient info sheet

Complex spectrum but there are some simple steps that may help

- Clean up environment
- Assess nutrient deficiencies and supply missing nutrients
 - Fe, Zn,
 - vitamin D
 - Omega 3
- Trial of gluten and casein free diet
- Assess GI problems constipation, diarrhoea, pain and treat -Treat as you would a neurotypical child!



Developmental origins of disease. Consensus PPTOX 2012

NUTRITIONAL INTERVENTIONS

- Are they safe? • Are they effective? Are they available? • What is the evidence?





IRON

- Low iron: pale, tired child, no energy
- Very common deficiency lacksquare
- Low iron can cause problems with lacksquare
 - Development (if iron low in first year) \bullet
 - Focus, attention and hyperactivity ۲
- Sleep problems trouble falling asleep, waking in the night ${\color{black}\bullet}$
- Fingernails spoon shaped koilonychia lacksquare

Iron Deficiency Anemia



anemia



normal blood





IRON



- Meats especially liver lacksquare
- Plant sources non-heme iron most people consume more non-heme iron: lacksquarelegumes, dark green vegetables, enriched cereals
- Increased absorption with vitamin C \bullet



Which deficiency ?









ZINC DEFICIENCY

- Frequent infections: ears, throat, skin...
- Irritable child
- Poor memory, slow processing
- Poor appetite or very restricted diet
- Acne
- White spots on nails
- Stretch marks
- Poor growth

Food source: whole grains, meat, seeds

Testing not great for mild deficiency.



Zinc Rich Foods

Vitamin D

PSYCHOLOGY AND **PSYCHIATRY**

Journal of Child Psychology and Psychiatry **:* (2016), pp **-**

Randomized controlled trial of vitamin D supplementation in children with autism spectrum disorder

Khaled Saad,¹ Ahmed A. Abdel-Rahman,² Yasser M. Elserogy,² Abdulrahman A. Al-Atram,³ Amira A. El-Houfey,⁴ Hisham A. K. Othman,⁵ Geir Bjørklund,⁶ Feiyong Jia,⁷ Mauricio A. Urbina,^{8,9} Mohamed Gamil M. Abo-Elela,¹⁰ Faisal-Alkhateeb Ahmad,¹ Khaled A. Abd El-Baseer,¹⁰ Ahmed E. Ahmed,¹⁰ and Ahmad M. Abdel-Salam¹¹

- Most children on the spectrum are low
- Treatment for 4 months
- Supplements improve autism symptoms esp if ended up with level > 100nmol/L



doi:10.1111/jcpp.12652



VITAMIN D

- <u>Conclusion of Meta-analysis 2020 Song et al</u>: Vitamin D supplementation improves the typical symptoms of autism spectrum disorder, as indicated by reduced Social Responsiveness Scale and Child Autism Rating Scale scores; thus, it is beneficial for children with autism spectrum disorder.
- Vitamin D deficiency during pregnancy and childhood: known risk factor for developing ASD

Mechanism-

- Reduces inflammation
- Production of neurotransmitters: serotonin
- Neuroplasticity



OMEGA 3 fatty acids

Keratosis pilaris, bumpy, dry skin on upper arms: low EFA





Omega 3 fatty acids:



- 50-60% of brain made up of lipids
- 35% of those lipids are HUFA highly unsaturated fatty acids Essential - not produced by humans – have to be ingested
- Signs of low omega 3 in children:
- Problems with focus and attention Ι.
- Low mood; mood swings ||.
- Fatigue
- IV. Poor memory
- Aggression and violent behaviour V.
- Suppressed immunity VI.
- VII. Increased auto-immunity

OMEGA3

- Omega 3 needed for brain structure and function • EPA antinflammatory • DHA neuroprotective
- Omega 3: low dose studies show moderate improvement: speech, sociability, repetitive behaviours
- Need more than 3 months Rx



Suggested treatments for deficiencies

	Aim	Dose if deficient	Recheck	
Zinc	12-20umol/L	1 mg/kg	3 months Clinical assessment	Zinc chelate, picolinate,gluconate Avoid zinc oxide and sulphate
Vitamin D	50-150nmol/L	Mild (30-49)- 2000iu/day Mod-severe (<30) 4000iu/day or equivalent	3-6 months	
Ferritin	>35	Usual approach	3 months	
Fish oil	Monitor clinical response	5 mls twice daily (20Kg child)	By observation	

Dietary interventions for autism:

- Some diets seem to work clinically for some children
 - Organic diet
 - Additive free diet
 - Gluten free casein free diet
- Proposed mechanism of action:
 - Abnormal gut flora
 - GI inflammation
 - Opioid theory
 - Mitochondrial dysfunction



Increased risk of food allergies in children with autism

The odds ratio (OR) of ASD increased in association with

- food allergy (OR, 2.29; 95% CI, 1.87-2.81),
- respiratory allergy (OR, 1.28; 95% CI, 1.10-1.50), and
- skin allergy (OR, 1.50; 95% CI, 1.28-1.77)

when comparing children with these conditions and those without.

Association of Food Allergy and Other Allergic Conditions With Autism Spectrum Disorder in Children 2019 Guifeng Xu, JAMA Netw Open. 2018;1(2):e180279. doi:10.1001/jamanetworkopen.2018.0279

How to test?

Difficulty with dietary research

- Research is very limited and hard to do
- Diet has to be kept 100% all of the time
- How to ensure that?
- Subset of children with more GI problems more likely to respond
- Can take 3-6 months to see full response

SPECIAL DIET – Gluten free Casein Free

- Gluten and dairy free diet
 - Peptides with endorphin/opioid effect
 - inflammation
 - Best responders have GI symptoms







Cellular Space



Neuronal Receptors for Casein and Gliadin Peptides

GFCF diet – **Gut-Peptide theory**

- Peptides are short chains of amino acids derived from incomplete digestion of proteins especially -gluten (wheat, oat, rye and barley) -casein (milk protein)
- Interfere with neurotransmission in brain perception- opiate-like activity behaviour mood 26 emotion



Opioid Peptide Theory

- Abnormal peptides can be measured in the urine of many ASD kids
- Insufficient gut enzyme DPP4 in intestinal brush border
- Inability to fully digest gluten and casein
- Gluteomorphine and caseomorphine with opioid activity cross into the blood stream and into the brain and attach to endorphine receptors
- Opioids from gluten and casein cause behaviour changes in rats
- Removing offending proteins from diet may help
 - Knivsberg, Reichelt. Can the pathophysiology of autism be explained by the nature of the discovered urine peptides? Nutr Neurosci. 2003 Feb;6(1):19-28
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LATEST META-ANALYSIS OF GFCF DIET: OCT 2020

- 9 RCT were included (521 participants) with age range between 2 to 18 years. Four of these studies did not show a significant improvement regarding the symptoms of ASD. The rest of these studies (n=5) showed improvement in communication, stereotyped movements, aggressiveness, language, hyperactivity, tantrums, and signs of attention deficit hyperactivity disorder compared to control group.
- The studies that showed a benefit were >12 months long; the negative studies 12 weeks - Alamri, 2020



Considerations

- Nutrient density some children eat GFCF junk food diet
- Diet needs to be unprocessed, whole food based, with plenty of vegetables
- Calcium intake may be a concern in dairy free diets



GI DISORDERS - THE GUT - BRAIN AXIS

- GI disorders are common in children with ASD
- Severity of GI symptoms correlates with ASD behaviours
- Abnormal microbiome
 - Endotoxins cause inflammation
- Diarrhoea reduces absorption of nutrients
- Constipation may cause pain and reduce appetite



h ASD ASD behaviours

e appetite

Increased risk of GI problems in children with autism

- Meta-analysis 2014: About 4 fold increase in gastrointestinal symptoms, diarrhoea and constipation
- Increased behaviour problems in ASD children with GI problems
- Autism symptom severity correlated with higher odds of GI problems
 - McElhanon BO, McCracken C, Karpen S, Sharp WG.Pediatrics. Gastrointestinal symptoms in autism spectrum disorder: a metaanalysis. 2014 May; 133(5):872-83.
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Symptoms of gastro-intestinal problems in children with ASD



Abdominal pain

- -Crying
- -Night time wakening
- -General irritability
- -Vocalizing complaints
- -Posturing
- -Irritability just prior to bowel movement
- -Hyperactivity and distractibility
- -Self injurious behavior

-Unexplained tantrums

Pediatrics

January 2010, VOLUME 125 / ISSUE Supplement 1

Evaluation, Diagnosis, and Treatment of Gastrointestinal Disorders in Individuals With ASDs: A Consensus Report

Timothy Buie, Daniel B. Campbell, George J. Fuchs III, Glenn T. Furuta, Joseph Levy, Judy VandeWater, Agnes H. Whitaker, Dan Atkins, Margaret L. Bauman, Arthur L. Beaudet, Edward G. Carr, Michael D. Gershon, Susan L. Hyman, Pipop Jirapinyo, Harumi Jyonouchi, Koorosh Kooros, Rafail Kushak, Pat Levitt, Susan E. Levy, Jeffery D. Lewis, Katherine F. Murray, Marvin R. Natowicz, Aderbal Sabra, Barry K. Wershil, Sharon C. Weston, Lonnie Zeltzer, Harland Winter

New Zealand Autism Spectrum Disorder Guideline



New recommendations relevant to gastrointestinal problems in children and young people with ASD

Reference	New recommendations	Grade
4.1.4a	Gastrointestinal problems, specifically constipation, chronic diarrhoea, altered bowel habits, and encopresis (faecal soiling), are more common in children and young people with ASD compared with typically developing peers.	В
4.1.4b	Children and young people with ASD should have a full evaluation that includes a thorough assessment of gastrointestinal function. Some children, particularly those with social communication difficulties, may have atypical presentations such as increased anxiety, irritability, disordered sleep patterns, and unusual vocalisations and movements.	C

Faecal retention

- Approximately 50% of ASD children
- Incomplete emptying of the bowel
- Child may still "go" daily
- May have alternating constipation and diarrhoea
- Sometimes dramatic improvements in ASD behaviour when treated.

35



Treating constipation



- Clean 'em out
- Magnesium oxide
- Vitamin C
- Increased fiber
- Diet changes

Sleep

Revised recommendations

4.4.7 Melatonin may be useful for improving sleep in ch itimg guidelines group recommendation 2014 Changed to:

4.4.7 Melatonin can be recommended for use in children ASD who are experiencing significant sleep problems.

New recommendations

4.4.7a Benefits and adverse effects of longer term treatr further investigation.

4.4.7b Behavioural strategies (eg, sleep hygiene) should conjunction with melatonin.

Placebo controlled double blind trial – 13 weeks 2-17

Schroder, C. M., Malow, B. A., Maras, A., Melmed, R. D., Findling, R. L., Breddy, J., Nir, T., Shahmoon, S., Zisapel, N., & Gringras, P. (2019). Pediatric prolonged-release melatonin for sleep in children with autism spectrum disorder: Impact on child behavior and caregiver's quality of life. *Journal of Autism and Developmental Disorders*, *49*(8), 3218-3230. <u>https://doi.org/10.1007/s10803-019-04046-5</u>

	Grade	
nildren with ASD who have	в	
n and young people with		

	Grade
ment of melatonin require	С
l always be used in	С

Slow release melatonin in for sleep in ASD – Impact on ASD behaviour and caregivers quality of life

- Sleep issues more common in ASD
- Sleep hygiene addressed first
- Placebo controlled double blind trial 13 weeks
- 2-17yrs 125 subjects
- 2(-5)mg melatonin SR
- 54% improvement in treatment group- 27% in placebo
- 1 hour longer sleep on average v placebo
- Fell asleep 40 mins quicker on average v placebo
- Particular improvement in hyperactivity and inattention •
- Caregivers life improved



Schroder, C. M., Malow, B. A., Maras, A., Melmed, R. D., Findling, R. L., Breddy, J., Nir, T., Shahmoon, S., Zisapel, N., & Gringras, P. (2019). Pediatric prolonged-release melatonin for sleep in children with autism spectrum disorder: Impact on child behavior and caregiver's quality of life. Journal of Autism and Developmental Disorders, 49(8), 3218-3230. https://doi.org/10.1007/s10803-019-04046-5

Sienna presenting picture Age 3 (refs) ATEC 76

- 1. Head banging bruises if didn't get her own way
- 2. Screaming episodes may last up to 30 mins
- 3. Sleep pattern sleeping 7pm-2am

Symptom assessment

Stimming- rubbing soft ribbons, repetitive behaviour particularly with musicPoor eye contactSideways glancingSpeech delay particularly receptiveEcholaliaScriptingPoor socialisation,
Debble FewtrellACNEM AugScriptingLack of imaginative play and inappropriate playWill not eat all colours of food.Fidgety , inattentivePoor fine and gross motor skillsFidgety , inattentivePoor wound healingNot toilet trained – stool

Sienna

Past medical history

Pregnancy

Moderate stress 2 fish meals per week Mother 8 amalgams- no dental work whilst pregnant Painted house whilst pregnant Some first trimester bleeding

Birth

Full term LSCS foetal distress CPD

0-1

Dr Exclusively breastfed 10 weeks then diary formula introduced with breast. First solids 5 months Reflux Dry skin from birth No antibiotics received.

Sienna

Age 1-3

No obvious regression just slow development in language

Dry skin continues

Food intolerances develop

Alternating diarrhoea and constipation – could go 3 days between bowel motions

No significant illnesses or admission

Family History

Mother has food intolerances

Dr DLives with mother and father in UK . Father – pop star Younger sister neurotypical with some food intolerances





Sienna non-regressive ASD Treatment 6 weeks GFCF + additive free diet only

Before

• Few single labeling words

After

- sentences, "Hello spelling "Amici
- BO every 3rd day, fowl loose
- Could only sit for 2 mins • Able to sit for 30mins

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    200 words and 2 word

 Mummy", counting 1-20,
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• BO daily , less offensive

Sienna ASD- the power of GFCF diet

- Rosier glow • Pale doughy complexion, dark circles
- Tantrums at least daily lasting • Tantrums alt days 5 mins 30mins
- Minimal eye contact

- Eye contact increased

Summary

- Nutritional interventions look for clinical signs
- Diet consider gluten free casein free
- GI assessment in ASD don't overlook
- Sleep !

cal signs casein free on't overlook

Where do I learn more?

ACNEM

- Australasian College of Nutritional and Environmental Medicine
- <u>www.acnem.org</u>
- RNZCGP accredited education





20% discount for 3 months access

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