



## CHANGE OF DIET FOR CHILDREN WITH AUTISM SUFFERING FROM GI PROBLEMS

### Databases used:

File 155: MEDLINE(R) 1950-2009/Feb 20

File 5: Biosis Previews(R) 1926-2009/Feb W3

File 45: EMCare 2009/Feb W1

### Search terms:

S1 30315 AUTIS?

S2 1600915 GASTRO? OR GUT? OR BOWEL? OR STOMACH

S3 27807 DIGESTIVE?(2W)TRACT?

S4 1615952 S2 OR S3

S5 7948 GI?(2W)TRACT?

S6 1617208 S4 OR S5

S7 687 S1 AND S6

S8 3071817 DIET? OR NUTRI? OR FOOD? OR FEED? OR EAT?

S9 155 S7 AND S8

S10 3182325 PEDIATRIC? OR PAEDIATRIC? OR CHILD???? OR INFANT? OR BAB? OR TODDLER?

S11 124 S9 AND S10

S12 90 RD (unique items)

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## **Altered amino acid excretion in children with autism.**

Evans Craig; Dunstan R Hugh; Rothkirch Tony; Roberts Tim K; Reichelt Karl L ; Cosford Robyn; Deed Gary; Ellis Libby B; Sparkes Diane L  
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Nutritional neuroscience ( England ) Feb 2008 , 11 (1) p9-17 , ISSN: 1476-8305--Electronic Journal Code: 100892202

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Autism is a complex and life-long behavioural disorder of unknown aetiology. Recent reports have indicated the involvement of digestive tract dysfunction and possible complications from inadequate nutrition. In this study, 34 autistic children (12 untreated and 22 receiving therapeutic treatments related to digestive function and nutritional uptake) and 29 control subjects (all 5-15 years of age) were investigated to determine whether there were any anomalies in the urinary excretion of amino acids, glucose, sucrose, arabinose and tartaric acid using GC/FID and GC/MS analysis techniques. Significantly lower relative urinary levels of essential amino acids were revealed for both the untreated (mean +/- SEM, 32.53 +/- 3.09%) and treated (31.98 +/- 2.87%) autistic children compared with the controls (37.87 +/- 1.50%). There were no significant differences in measured excretions of sugars or tartaric acid. It was concluded that the untreated autistic children had evidence of altered metabolic homeostasis.

Tags: Female; Male

Descriptors: \*Amino Acids--urine--UR; \*Autistic Disorder--urine--UR ;

Adolescent; Amino Acids, Essential--urine--UR; Arabinose--urine--UR; Autistic Disorder--drug therapy--DT; Child; Child, Preschool; Glycosuria; Homeostasis; Humans; Sex Characteristics; Sucrose--urine--UR; Tartrates --urine--UR

CAS Registry No.: 0 (Amino Acids); 0 (Amino Acids, Essential); 0 (Tartrates);  
147-81-9 (Arabinose); 526-83-0 (tartaric acid); 57-50-1 (Sucrose)  
Record Date Created: 20080530  
Record Date Completed: 20090209

## **[Autism and gastrointestinal disease: a different point of view]**

Autismo e patologia gastroenterica: un punto di vista inconsueto.  
La Pediatria medica e chirurgica - Medical and surgical pediatrics ( Italy ) May-  
Jun 2008 , 30 (3) p141-5 , ISSN: 0391-5387--Print Journal Code: 8100625  
Publishing Model Print  
Document type: Journal Article; Review  
Languages: ITALIAN  
Main Citation Owner: NLM  
Record type: MEDLINE; Completed  
Subfile: INDEX MEDICUS  
( 19 Refs.)

Descriptors: \*Autistic Disorder--complications--CO; \*Autistic Disorder--therapy--  
TH; \*Gastrointestinal Diseases--complications--CO; \*Gastrointestinal Diseases --  
therapy--TH ; Abdominal Pain--etiology--ET; Autistic Disorder--diagnosis--DI;  
Autistic Disorder--diet therapy--DH; Child; Child, Preschool; Colonoscopy;  
Endoscopy, Gastrointestinal; Food Hypersensitivity--complications--CO;  
Gastroenteritis--complications--CO; Gastrointestinal Diseases--diagnosis --DI;  
Gastrointestinal Diseases--diet therapy--DH; Humans; Treatment Outcome  
Record Date Created: 20081124  
Record Date Completed: 20081219

## **Intestinal involvement in autistic disorder: PRogress of research**

Author: Familiari Valeria; de Magistris Laura; Sapone Anna; Riegler Gabriele;  
Carteni Maria; Iardino Patrizia; Caravelli Giancarlo; Bravaccio Carmela; Frolli  
Alessandro; Militerri Roberto; Pascotto Antonio  
Journal: Gastroenterology 134 ( 4, Suppl. 1 ): p A407 APR 2008 2008  
Conference/Meeting: Digestive Disease Week Meeting/109th Annual Meeting of  
the American-Gastroenterological-Association San Diego, CA, USA May 17 -22,  
2008; 20080517  
Sponsor: Amer Gastroenterol Assoc  
ISSN: 0016-5085  
Document Type: Meeting; Meeting Abstract  
Record Type: Abstract  
Language: English  
Abstract: We already demonstrated that IP is altered in a consistent % of autistic  
patients and their first-degree relatives. AIM of the present progress of research  
was to increase the number of investigated subjects and to correlate IP values to  
gastrointestinal (GIs) and behavioural symptoms (ADI). MATERIALS AND  
METHODS: 90 consecutive children with autism (mean age +/- SD=7,4 +/- 5,1;  
F=14, M=76) diagnosed according to the DSM-IV criteria, most of them naive and  
without any dietary restrictions; 146 of their first degree relatives (mean age +/-  
SD= 40,2 +/- 8,7; F=72, M=74); 160 normal adult subjects (mean age +/-  
SD=31,8 +/- 12,3; F=98, M= 42) and 20 normal children (mean age +/-  
SD=10,1 +/- 3,9; F=11, M=9) were recruited. The IP was evaluated by means of

lactulose and mannitol test (LA/MA). Faecal calprotectin was performed to evaluate intestinal inflammation, Serum anti-trans-glutaminase (tTG) and HLA-DQ2/8 were determined to rule out celiac disease in all subjects. GIs were evaluated as: constipation(C), diarrhoea (D), alternating diarrhoea/constipation and abdominal pain (P). RESULTS: tTG resulted normal in all autistic patients. HLA-DQ2/8 distribution reflected that of general population. 36,7% of autistic patients showed LA/MA values higher than the cut off range (0,030). 21,7% of first-degree relatives had LA/MA higher than normal. LA/ MA mean values resulted statistically different ( $p < 0,05$ ) among the groups: a) autistic, 0,042 +/- 0,084; b) relatives, 0,028 +/- 0,050; c) adult 0,014 +/- 0,014 and children controls 0,016 +/- 0,006. GIs resulted present in 48,1% of the autistics, being: C=46,2%, D= 34,6%, P= 19,2%. The presence of referred GIs was independent on IP alteration: no correlation was found between LA/MA values and GIs ( $p = 0,275$ ). Moreover, no correlation was found between LA/MA and typical autistic behavioural symptoms (ADI) such as: lack of communicative skills ( $p = 0,163$ ), deficits in social interaction ( $p = 0,88$ ) and restricted repetitive behaviour ad interests ( $p = 0,246$ ), neither between GIs and ADI. Calprotectin values indicated that inflammation was present in 24,6% of autistic patients and in 11,7% of their relatives. As already described, we found no correlation between IP and faecal calprotectin values ( $r = 0,0177$ ). CONCLUSION: A statistically significant increase of IP has been confirmed in larger groups of autistic patients and first degree relatives compared to controls, thus suggesting a genetically-determined defect of intestinal barrier function. GIs are moreover present in almost 1:2 autistic children, thus confirming the importance of GI tract involvement in autistic disorder. The still unknown genetic intestinal factor seems anyway independent from behavioural symptoms.

Registry Numbers: 87-78-5: mannitol; 4618-18-2: lactulose

DESCRIPTORS:

Major Concepts: Psychiatry--Human Medicine, Medical Sciences;

Gastroenterology--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child, female, male

Organisms: Parts Etc: intestine--digestive system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: autistic disorder--behavioral and mental disorders

Mesh Terms: Autistic Disorder (MeSH)

Chemicals & Biochemicals: mannitol; lactulose; calprotectin

## **Absence of urinary opioid peptides in children with autism.**

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Archives of disease in childhood ( England ) Sep 2008 , 93 (9) p745-50 ,

ISSN: 1468-2044--Electronic Journal Code: 0372434

Publishing Model Print-Electronic

Document type: Journal Article; Multicenter Study; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS; Toxbib

**OBJECTIVE:** It has been claimed for a number of years that the urine of children with autism contains exogenously derived opioid peptides. This finding is said to reflect a disturbance in the integrity of the gut epithelium, act as a diagnostic marker for autism and predict treatment response to a diet excluding gluten and casein. The aim of the present study was to determine whether exogenous or endogenous peptides were present in the urine of children with autism or of control children. **DESIGN:** Case-control study **SETTING:** Cases were recruited from two tertiary referral centres specialising in autistic spectrum disorders, while controls were recruited from mainstream primary and secondary schools in the same geographical area. **PARTICIPANTS:** 65 boys with autism, mean age 7.4 years (range 5-11) and 158 control boys, mean age 7.8 years (range 4.2-11). **INVESTIGATIONS:** Urine samples were examined by high pressure liquid chromatography (HPLC) and matrix assisted laser desorption ionisation-time of flight mass spectrometry (MALDI-TOF MS) for the presence of a number of putative opioid peptides. **OUTCOMES:** There were no significant differences between the HPLC urinary profiles of the children affected by autism and the typically developing controls. In those cases where HPLC showed peaks in the locations at which opioid peptides might be expected to be found, MALDI-TOF established that these peaks did not, in fact, represent opioid peptides. **CONCLUSIONS:** Given the lack of evidence for any opioid peptiduria in children with autism, opioid peptides can neither serve as a biomedical marker for autism nor be employed to predict or monitor response to a casein- and gluten-free diet.

**Tags:** Male

**Descriptors:** \*Autistic Disorder--urine--UR; \*Opioid Peptides--urine--UR ; Biological Markers--urine--UR; Case-Control Studies; Caseins--adverse effects--AE; Child; Child, Preschool; Glutens--adverse effects--AE; Humans; Opioid Peptides--deficiency--DF; Treatment Outcome

**CAS Registry No.:** 0 (Biological Markers); 0 (Caseins); 0 (Opioid Peptides); 8002-80-0 (Glutens)

**Record Date Created:** 20080822

**Record Date Completed:** 20080929

**Date of Electronic Publication:** 20080312

## **Intestinal permeability and glucagon-like peptide-2 in children with autism: a controlled pilot study.**

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Journal of autism and developmental disorders ( United States ) Jul 2008 , 38 (6) p1066-71 , ISSN: 0162-3257--Print Journal Code: 7904301

**Publishing Model** Print-Electronic

**Document type:** Journal Article; Research Support, Non-U.S. Gov't

**Languages:** ENGLISH

**Main Citation Owner:** NLM

**Record type:** MEDLINE; Completed

**Subfile:** INDEX MEDICUS

We measured small intestinal permeability using a lactulose:mannitol sugar permeability test in a group of children with autism, with current or previous gastrointestinal complaints. Secondly, we examined whether children with autism had an abnormal glucagon-like peptide-2 (GLP-2) response to feeding. Results were compared with sibling controls and children without developmental disabilities. We enrolled 14 children with autism, 7 developmentally normal siblings of these children and 8 healthy, developmentally normal, unrelated

children. Our study did not detect differences in these measures of gastrointestinal function in a group of children with autism.

Tags: Female; Male

Descriptors: \*Autistic Disorder--physiopathology--PP; \*Glucagon-Like Peptide 2--blood --BL; \*Intestinal Absorption--physiology--PH ; Autistic Disorder--diagnosis--DI; Autistic Disorder--psychology--PX; Child ; Child, Preschool; Humans; Intestine, Small--physiopathology--PP; Lactulose--diagnostic use--DU; Lactulose--metabolism--ME; Mannitol --diagnostic use--DU; Mannitol--metabolism--ME; Pilot Projects; Reference Values; Satiety Response--physiology--PH  
CAS Registry No.: 0 (Glucagon-Like Peptide 2); 4618-18-2 (Lactulose); 69-65-8 (Mannitol)

Record Date Created: 20080609

Record Date Completed: 20081104

Date of Electronic Publication: 20080229

## **Autism spectrum disorders: concurrent clinical disorders.**

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Journal of child neurology ( Canada ) Jan 2008 , 23 (1) p6-13 , ISSN: 0883-0738--Print Journal Code: 8606714

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Individuals with autism spectrum disorder are heterogeneous in clinical presentation, concurrent disorders, and developmental outcomes. This study characterized the clinical co-occurrences and potential subgroups in 160 children with autism spectrum disorders who presented to The Autism Center between 1999 and 2003. Medical and psychiatric co-occurrences included sleep disorders, epilepsy, food intolerance, gastrointestinal dysfunction, mood disorder, and aggressive and self-injurious behaviors. Sleep disorders were associated with gastrointestinal dysfunction ( $P < .05$ ) and mood disorders ( $P < .01$ ). Food intolerance was associated with gastrointestinal dysfunction ( $P = .001$ ). Subjects with mood disorder tended to develop aggressive or self-injurious behaviors ( $P < .05$ ). Developmental regression was not associated with increased co-occurrence of medical or psychiatric disorders. Medical co-occurrence did not present as a risk factor for psychiatric co-occurrence, and vice versa. These results showed a high prevalence of multiple medical and psychiatric co-occurrences. There may be common pathophysiologic mechanisms resulting in clinical subgroups of autism spectrum disorders. Recognition of the co-occurrence of concurrent disorders may provide insight into the therapeutic strategy.

Tags: Female; Male

Descriptors: \*Autistic Disorder--epidemiology--EP; \*Epilepsy--epidemiology--EP; \*Gastrointestinal Diseases--epidemiology--EP; \*Mental Disorders --epidemiology--EP; \*Sleep Disorders--epidemiology--EP ; Adolescent; Aggression--psychology--PX; Child; Child Behavior Disorders --epidemiology--EP; Child, Preschool; Comorbidity; Developmental Disabilities--epidemiology--EP; Humans; Mood Disorders--epidemiology--EP; Prevalence; Regression (Psychology); Retrospective Studies; Self Mutilation --epidemiology--EP

Record Date Created: 20080110  
Record Date Completed: 20080307  
Date of Electronic Publication: 20071203

## **Intestinal permeability in autistic disorder**

Author: Familiari Valeria; De Magistris Laura; Carteni M; Bravaccio Carolina; Frolli Alex; Riegler R; Militerni Roberto; Pascotto Vincenzo; Fasano Alessio

Journal: Gastroenterology 132 ( 4, Suppl. 2 ): p A369 APR 2007 2007

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Sponsor: Amer Gastroenterol Assoc

Amer Assoc Study Liver Dis

Amer Soc Gastrointestinal Endoscopy

Soc Surg Alimentary Tract

ISSN: 0016-5085

Document Type: Meeting; Meeting Abstract

Record Type: Abstract

Language: English

Abstract: **BACKGROUND:** There have been indications that autistic children have an impaired barrier function of the gastrointestinal tract leading to elevated intestinal permeability. According to the leaky gut hypothesis, the intestinal mucosa is abnormally permeable in autistic children. Digestion products of natural food could gain access to the bloodstream through the leaky mucosa and induce antigenic responses as well as interfere directly with the central nervous system **AIM** to evaluate barrier function and intestinal inflammation in children with autistic disorder and their first degree relatives. **MATERIALS AND METHODS:** 25 (mean age SD = 5.8 +/- 3.7; F=3, M=22) consecutive outpatient children with autistic disorder, diagnosed according to the DSM-VI criteria, and 50 (mean age +/- SD=38.5 +/- 8.3; F=28, M=22) first degree relatives were recruited, The intestinal permeability was evaluated by means of lactulose and mannitol test (LA/MA). Faecal calprotectin was performed to evaluate an eventual intestinal inflammation. In all patients serum tissue transglutaminase and HLA DQ2 DQ8 were determined to rule out celiac disease. **RESULTS:** In 48 % of patients with autistic disorder the LA/MA values were higher than the cut off range (0.030). In the group of first degree relatives 34% resulted higher than normal. Calprotectin values indicated inflammation in 7/25 patients (28%) and only 3/50 (6%) relatives. The tissue transglutaminase was normal in all patients. HLA haplotype resulted DQ2 positive in only one of the seven patients investigated so far. **CONCLUSIONS:** Our results showed that a subgroup of autistic patients and their family members showed altered intestinal permeability, sometimes associated to biochemical signs of intestinal inflammation. These results suggest a genetically-determined defect of intestinal barrier function in a subgroup of large spectrum autistic disorder patients and their family members.

Registry Numbers: 87-78-5: mannitol; 4618-18-2: lactulose; 137741-97-0: transglutaminase

**DESCRIPTORS:**

Major Concepts: Clinical Chemistry--Allied Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences; Psychiatry--Human Medicine, Medical Sciences; Pediatrics--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child

Organisms: Parts Etc: serum--blood and lymphatics; feces--digestive system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
Diseases: autistic disorder--behavioral and mental disorders; celiac disease--digestive system disease, metabolic disease  
Mesh Terms: Autistic Disorder (MeSH); Celiac Disease (MeSH)  
Chemicals & Biochemicals: mannitol; lactulose; calprotectin; transglutaminase; HLA-DQ2-DQ8  
Miscellaneous Terms: Concept Codes: haplotype; intestinal permeability; antigenic response; cut off range; Meeting Abstract

## **Autistic enterocolitis; is it a histopathological entity?**

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Journal: Histopathology (Oxford) 50 ( 3 ): p 371-379 FEB 2007 2007  
Item Identifier: doi:10.1111/j.1365-2559.2007.02606.x  
ISSN: 0309-0167  
Document Type: Article; Editorial  
Record Type: Abstract  
Language: English  
Abstract: Aims: To review the literature on the histopathological diagnosis of the condition termed 'autistic enterocolitis'. Methods and results: We have reviewed all published works where mucosal biopsy specimens from autistic children have been examined histopathologically. Abstracts were excluded. Our review of the published works, nearly all from a single centre, identifies major inconsistencies between studies, lack of appropriate controls and misinterpretation of normal findings as pathology. Ileal lymphoid hyperplasia may be more prevalent in children with regressive autism but is also seen in children with food allergies and severe constipation, the latter being an extremely common finding in autistic children. Conclusions: The histopathological diagnosis of autistic enterocolitis should be treated with caution until a proper study with appropriate methodology and controls is undertaken.  
DESCRIPTORS:  
Major Concepts: Psychiatry--Human Medicine, Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences; Pediatrics--Human Medicine, Medical Sciences  
Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia  
Organisms: human (Hominidae)--child  
Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
Diseases: autism--behavioral and mental disorders; constipation--digestive system disease; allergy--immune system disease; autistic enterocolitis--digestive system disease  
Mesh Terms: Autistic Disorder (MeSH); Constipation (MeSH); Hypersensitivity (MeSH)  
Miscellaneous Terms: Concept Codes: ileal lymphoid hyperplasia; Editorial

## **Agitation and weight loss in an autistic boy.**

Conyers Rachel; Efron Daryl

Department of General Paediatrics, The Royal Children's Hospital, Parkville, Vic., Australia.

Journal of paediatrics and child health ( Australia ) Mar 2007 , 43 (3) p186-7 , ISSN: 1034-4810--Print Journal Code: 9005421

Publishing Model Print

Document type: Case Reports; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

An 11 year old boy with autism presented with a 2-month history of agitated behaviour with associated weight loss. On examination he was wasted and distressed. He had severe hypoalbuminaemia. Gastrointestinal imaging revealed a gastric bezoar. At operation a large phytobezoar extending into the jejunum was identified and removed. Postoperatively he required intensive nutritional resuscitation and support, including treatment of multiple micronutrient deficiencies. Malnutrition is common in children with developmental disabilities, with a number of possible contributing factors. Gastric bezoar is a rare cause, which should be considered in mobile children who may engage in pica.

Tags: Male

Descriptors: \*Autistic Disorder; \*Psychomotor Agitation; \*Weight Loss ; Bezoars--diagnosis--DI; Child; Humans; Pica; Victoria

Record Date Created: 20070223

Record Date Completed: 20070416

## **Relationship of dietary intake to gastrointestinal symptoms in children with autistic spectrum disorders.**

Levy Susan E; Souders Margaret C; Ittenbach Richard F; Giarelli Ellen; Mulberg Andrew E; Pinto-Martin Jennifer A

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Biological psychiatry ( United States ) Feb 15 2007 , 61 (4) p492-7 , ISSN: 0006-3223--Print Journal Code: 0213264

Contract/Grant No.: 2T73 MC 00035 09; PHS HHS United States; 3P30 HD26979-04S2; HD; NICHD NIH HHS United States; 541247; PHS HHS United States; RR00240; RR; NCRR NIH HHS United States

Publishing Model Print-Electronic

Document type: Clinical Trial; Comparative Study; Journal Article; Randomized Controlled Trial; Research Support, N.I.H., Extramural; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

**BACKGROUND:** Gastrointestinal (GI) symptoms and abnormalities in stool consistency are frequently reported by parents of children with autism spectrum disorders (ASD). The purpose of this study was to 1) describe dietary intake of a cohort of children with ASD compared with normative data and 2) determine whether GI symptoms and stool consistency are related to dietary intake.

**METHODS:** Data from diet diaries of children (3-8 years) with ASD (n = 62) were analyzed by a registered pediatric dietician to compare to RDA standards for total calories, protein, carbohydrate, and fat. Dietary intake was correlated with descriptors of stool consistency using cumulative logistic regression methods.

RESULTS: Intake of calories, carbohydrates, and fat were in the average range; protein intake was increased (211% of RDA). Reported frequency of GI abnormalities, including abnormal stool consistency (e.g., bulky or loose), was increased (54%). No statistically significant relationships between stool consistency and dietary intake were observed. CONCLUSIONS: In this sample, there was a high rate of reported gastrointestinal symptoms, despite lack of medical causes. Intake was adequate for calories and carbohydrates and increased for protein. The children did not exhibit excessive carbohydrate intake. There was no association of nutrient intake to changes in stool consistency.

Tags: Female; Male

Descriptors: \*Eating--drug effects--DE; \*Energy Intake--drug effects--DE; \*Gastrointestinal Agents--therapeutic use--TU; \*Gastrointestinal Diseases --drug therapy--DT; \*Gastrointestinal Diseases--physiopathology--PP; \*Secretin--therapeutic use--TU ; Autistic Disorder--complications--CO; Child; Child, Preschool; Cohort Studies; Cross-Over Studies; Double-Blind Method; Energy Intake--physiology --PH; Gastrointestinal Diseases--etiology--ET; Humans CAS Registry No.: 0 (Gastrointestinal Agents); 1393-25-5 (Secretin)

Record Date Created: 20070205

Record Date Completed: 20070327

Date of Electronic Publication: 20070103

## **Beneficial behavioural effects of IBD therapy and gluten/casein-free diet in an Italian cohort of patients with autistic enterocolitis followed over one year**

Author: Balzola Federico; Clauser Daniela; Repici Alessandro; Caldognetto Marina; Barletti Claudio; Sapino Anna; Barbera Cristiana; Calvo Pierluigi; Reggio Dario; Gennari Fabrizio; Nonnato Antonello; Forni Marco; Morra Isabella; Gandione Marina; Rigardetto Roberto; Rizzetto Mario

Journal: Gastroenterology 130 ( 4, Suppl. 2 ): p A211 APR 2006 2006

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Record Type: Abstract

Language: English

Abstract: Autism diagnoses alone have risen from 1:5000 in 1980 to a frightening 1:120 today, that cannot only be the result of better diagnostic variation or recognition of the disease. A substantial proportion of pts with regressive/late onset autism showed evidence of a previously unrecognized IBD, labelled autistic enterocolitis characterized by lymphoid nodular hyperplasia and chronic ileocolitis. Although improvements in autistic behaviour has been reported when gluten and casein exclusion diets was introduced, no data is available on the effect of specific bowel therapy on the psychiatric symptoms. We aimed to evaluate the effects of specific IBD therapy together with the gluten/casein free diet on specific gastrointestinal and autistic symptoms in a cohort of regressive/late onset autistic pts with autistic enterocolitis, followed over 12 months. Among the 85 consecutive autistic pts observed, 40 presented with severe constipation or diarrhoea. In 12 of them (male, median age 16 yrs, 4-30) an endoscopy and wireless capsule examination were performed because of the permission of the parents and then enrolled in the follow-up study. Macroscopic lesions were observed in 55% of the pts in both the upper and lower

gastrointestinal tract. Microscopic involvement was observed in 70%, 60% and in 100% of pts in the upper gastrointestinal tract, in the terminal ileum and in the colon respectively, with different histological grade. Mesalazine (8 pts), steroids (2 pts) and 6-mercaptopurine (2 pts) were prescribed according to the histological/clinical score, Casein-free diet and successively gluten-free diet were introduced within the first 3 months by a dietician. A Behavioural Summarized Evaluation (BSE, a score with 29 behavioural items with a degree of frequency validated with a statistical correlation with the Childhood Autism Rating Scale) was used to blindly evaluate the pts at entrance and after 12 months. After 1 year treatment, 80% of pts with severe constipation or diarrhoea had normal stool movements and in 75% an evident reduction of abdominal pain was also observed, The total BSE score showed a global improvement after 12 months that ranged from 10 to 32% ( $p=0.00388$ ) in all the pts evaluated. When selected symptoms were compared before and after the treatment a reduction of deep anxiety (53%), agitation (35%), mood disturbance (24%), etero-aggressivity (14%), self-aggressivity (13%) as well as an improvement of attention (77%) and sleep (44%) were also observed ( $p=0.009796$ ). In conclusion, these results proved for the first time a beneficial effect of the combination of drug and dietetic therapy on both bowel and psychiatric symptoms in autism.

Registry Numbers: 89-57-6: mesalazine; 50-44-2: 6-mercaptopurine

**DESCRIPTORS:**

Major Concepts: Clinical Immunology--Human Medicine, Medical Sciences; Nutrition; Psychiatry--Human Medicine, Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child, preadolescent child, adult, adolescent, female , male

Organisms: Parts Etc: colon--digestive system; ileum--digestive system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: diarrhea--digestive system disease; constipation--digestive system disease; autism--behavioral and mental disorders, complications; autistic enterocolitis--digestive system disease, drug therapy, diet therapy, symptom; lymphoid nodular hyperplasia--blood and lymphatic disease, immune system disease; chronic ileo-colitis--digestive system disease; inflammatory bowel disease {IBD}--digestive system disease, diet therapy

Mesh Terms: Diarrhea (MeSH); Constipation (MeSH); Autistic Disorder (MeSH); Inflammatory Bowel Diseases (MeSH)

Chemicals & Biochemicals: mesalazine--gastrointestinal-drug; 6-mercaptopurine--enzyme inhibitor-drug, immunosuppressant-drug, gastrointestinal-drug, immunologic-drug; steroids--hormone-drug, gastrointestinal-drug

Methods & Equipment: gluten-free diet--therapeutic and prophylactic techniques, clinical techniques; casein-free diet--therapeutic and prophylactic techniques, clinical techniques

## **Frequency of gastrointestinal symptoms in children with autistic spectrum disorders and association with family history of autoimmune disease.**

Valicenti-McDermott Maria; McVicar Kathryn; Rapin Isabelle; Wershil Barry K ; Cohen Herbert; Shinnar Shlomo

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Journal of developmental and behavioral pediatrics - JDBP ( United States ) Apr  
2006 , 27 (2 Suppl) pS128-36 , ISSN: 0196-206X--Print Journal Code:  
8006933

Contract/Grant No.: K12 NS048856; NS; NINDS NIH HHS United States;  
RR17672-01; RR; NCRR NIH HHS United States

Publishing Model Print

Document type: Journal Article; Research Support, N.I.H., Extramural; Research  
Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

This is a cross-sectional study that compares lifetime prevalence of gastrointestinal (GI) symptoms in children with autistic spectrum disorders (ASDs) and children with typical development and with other developmental disabilities (DDs) and examines the association of GI symptoms with a family history of autoimmune disease. A structured interview was performed in 50 children with ASD and 2 control groups matched for age, sex, and ethnicity-50 with typical development and 50 with other DDs. Seventy-four percent were boys with a mean age of 7.6 years (SD, +/-3.6). A history of GI symptoms was elicited in 70% of children with ASD compared with 28% of children with typical development ( $p < .001$ ) and 42% of children with DD ( $p = .03$ ). Abnormal stool pattern was more common in children with ASD (18%) than controls (typical development: 4%,  $p = .039$ ; DD: 2%,  $p = .021$ ). Food selectivity was also higher in children with ASD (60%) compared with those with typical development (22%,  $p = .001$ ) and DD (36%,  $p = .023$ ). Family history of autoimmune disease was reported in 38% of the ASD group and 34% of controls and was not associated with a differential rate of GI symptoms. In the multivariate analysis, autism (adjusted odds ratio (OR), 3.8; 95% confidence interval (CI), 1.7-11.2) and food selectivity (adjusted OR, 4.1; 95% CI, 1.8-9.1) were associated with GI symptoms. Children with ASD have a higher rate of GI symptoms than children with either typical development or other DDs. In this study, there was no association between a family history of autoimmune disease and GI symptoms in children with ASD.

Tags: Female; Male

Descriptors: \*Autistic Disorder--genetics--GE; \*Autistic Disorder--  
physiopathology--PP; \*Gastrointestinal Diseases--epidemiology--EP ; Adolescent;  
Child; Child Development; Child, Preschool; Family; Gastrointestinal Diseases--  
classification--CL; Humans; Infant; Socioeconomic Factors

Record Date Created: 20060510

Record Date Completed: 20061025

## **Patterns of complementary and alternative medical therapy use in children diagnosed with autism spectrum disorders**

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Journal of Autism and Developmental Disorders ( J. Autism Dev. Disord. ) ( United States ) October 1, 2006 , 36/7 (901-909)

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DOI: 10.1007/s10803-006-0131-0

Item Identifier (DOI): 10.1007/s10803-006-0131-0

DOCUMENT TYPE: Journal ; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 33

Previous studies suggest that complementary and alternative medical (CAM) therapy use in children with chronic illnesses is higher than in children in the general population. In this study, we investigated patterns of CAM therapy use in children diagnosed with autism spectrum disorders (ASD, n = 50) as compared to a control population of children with no ASD (n = 50). Over half of the parents in the ASD group reported using, or had used at least one CAM therapy for their child (52%) as compared to 28% of the control group (P = 0.024). Seventy percent of therapies used in the ASD group were biologically based therapies comprised of special diets or supplements, and parents felt that 75% of the therapies used were beneficial. (c) Springer Science+Business Media, Inc. 2006.

DESCRIPTORS:

\* alternative medicine; \*autism acupuncture; adolescent; adult; aged; aromatherapy; article; ascorbic acid; attention disturbance; biological therapy; caffeine; calcium; case control study; casein; child; chiropractic; clinical article; controlled study; cyanocobalamin; diet supplementation; diet therapy; Echinacea extract; education; enzyme; essential fatty acid; female; fish oil; gastrointestinal symptom; glucose; gluten; health care utilization; herbal medicine; homeopathy; human; human relation; magnesium; male; manipulative medicine; massage; melatonin; music therapy; omega 3 fatty acid; parent; parental age ; physician; priority journal; psychotherapy; pyridoxine; relaxation training; seizure; selenium; sleep disorder; speech; spiritual healing; touch; vitamin D  
TERMS (UNCONTROLLED): doctor parent relation

## **Changes in cellular immune reactivity to cow rectangle fs milk protein (CMP) following dietary intervention in children with autism apectrum disorders (ASD) and positive gastrointestinal (GI) symptoms**

Author: Jyonouchi Harumi (Reprint); Zimmerman-Bier Barbie; Ruby Agnes; Geng Lee

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Journal: FASEB Journal 19 ( 4, Suppl. S, Part 1 ): p A501 MAR 4 2005 2005  
Conference/Meeting: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences San Diego, CA, USA March 31 -April 06, 2005; 20050331

Sponsor: Amer Assoc Anatomists

Amer Assoc Immunologists

Amer Physiol Soc

Amer Soc Biochem & Mol Biol

Amer Soc Investigat Pathol

Amer Soc Nutr Sci

Amer Soc Pharmacol & Expt Therapeut

Int Union Physiol Sci

ISSN: 0892-6638

Document Type: Meeting; Meeting Abstract

Record Type: Abstract

Language: English

Abstract: Our previous results indicate a high prevalence of non-allergic food hypersensitivity (NFH) to CMP in young ASD children with positive GI [GI (+)] symptoms (diarrhea, loose stool, and constipation). This study evaluated changes in cellular immune reactivity to CMP and its major components (B-lactoglobulin, casein, and alpha-lactoalbumin) after implementation of a dairy-free diet in 29 GI(+) ASD children (median: 4 yr). Wheat-free diet was also implemented in 8/29 ASD children due to > 2 standard deviation (SD)+control mean (CM) TNF-alpha/IL-12 production by peripheral blood mononuclear cells (PBMCs) with wheat protein. Following dietary intervention, we observed resolution of GI symptoms in 26/29 subjects as observed in control NFH children. Among them, 23 initially revealed > 2SD+CM TNF-alpha/IL-12 production with CMP/beta-lactoglobulin that declined 3-4 months after dietary intervention ( $p < 0.05$  for TNF-alpha and  $p < 0.005$  for IL-12 for CMP and beta-lactoglobulin), while 3 of them had > 2SD+CM IL-5 production with CMP/casein which became < 3.9 pg/ml after dietary intervention. In 3 subjects without significant reactivity to CMP, we found no changes in clinical features or immune reactivity following dietary intervention. These results indicate good association between changes in immune reactivity to CMP and clinical outcomes (resolution of GI symptoms) in young GI (+) ASD children. Funded by Jonty Foundation, St. Paul, MN.

**DESCRIPTORS:**

Major Concepts: Clinical Immunology--Human Medicine, Medical Sciences;

Gastroenterology-- Human Medicine, Medical Sciences; Psychiatry--Human

Medicine, Medical Sciences; Pediatrics--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child

Organisms: Parts Etc: peripheral blood mononuclear cell--immune system, blood and lymphatics

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: diarrhea--digestive system disease; constipation--digestive system disease; gastrointestinal symptom--digestive system disease; autism spectral disorder--behavioral and mental disorders; loose stool--digestive system disease

Mesh Terms: Diarrhea (MeSH); Constipation (MeSH)

Chemicals & Biochemicals: casein; TNF-alpha {tumor necrosis factor-alpha}; beta-lactoglobulin; IL-5 {interleukin-5}--production; cow's milk protein; alpha-lactoalbumin; IL-12 {interleukin-12}--production

Methods & Equipment: dietary intervention--clinical techniques

Miscellaneous Terms: Concept Codes: cellular immune reactivity; Meeting Abstract

## **Diet, immunity, and autistic spectrum disorders**

Author: Murch Simon (Reprint)

Author Address: Warwick Med Sch, Clin Sci Res Inst, Clifford Bridge Rd, Coventry CV2 2DX, W Midlands, UK\*\*UK

Author E-mail Address: s.murch@warwick.ac.uk

Journal: Journal of Pediatrics 146 ( 5 ): p 582-584 MAY 05 2005

ISSN: 0022-3476

Document Type: Article; Editorial

Record Type: Citation

Language: English

DESCRIPTORS:

Major Concepts: Clinical Chemistry--Allied Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences; Psychiatry--Human Medicine, Medical Sciences; Allergy--Clinical Immunology, Human Medicine, Medical Sciences; Pediatrics --Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child, female, male

Organisms: Parts Etc: immune system--immune system; monocyte--immune system, blood and lymphatics ; lymphocyte--immune system, blood and lymphatics; gastrointestinal system --digestive system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: food allergy--immune system disease, etiology; autistic spectrum disorders --behavioral and mental disorders, complications, diet therapy, immunology, genetics, therapy, diagnosis, etiology

Mesh Terms: Food Hypersensitivity (MeSH)

Chemicals & Biochemicals: immunoglobulin E; T-H-2 cytokines; T-H-1 cytokines

## **Gastrointestinal factors in autistic disorder: a critical review.**

Erickson Craig A; Stigler Kimberly A; Corkins Mark R; Posey David J; Fitzgerald Joseph F; McDougle Christopher J

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Journal of autism and developmental disorders ( United States ) Dec 2005 , 35 (6) p713-27 , ISSN: 0162-3257--Print Journal Code: 7904301

Contract/Grant No.: K23-MH068627-01; MH; NIMH NIH HHS United States; U10-MH66766-02; MH; NIMH NIH HHS United States

Publishing Model Print

Document type: Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Interest in the gastrointestinal (GI) factors of autistic disorder (autism) has developed from descriptions of symptoms such as constipation and diarrhea in autistic children and advanced towards more detailed studies of GI histopathology and treatment modalities. This review attempts to critically and comprehensively analyze the literature as it applies to all aspects of GI factors in autism, including discussion of symptoms, pathology, nutrition, and treatment. While much literature is available on this topic, a dearth of rigorous study was found to validate GI factors specific to children with autism. ( 81 Refs.)

Descriptors: \*Autistic Disorder--epidemiology--EP; \*Gastrointestinal Diseases --epidemiology--EP ; Child; Endoscopy--methods--MT; Gastrointestinal Diseases--physiopathology --PP; Gastrointestinal Diseases--therapy--TH; Humans

Record Date Created: 20060324

Record Date Completed: 20060425

## **Short report: Autistic gastrointestinal and eating symptoms treated with secretin: a subtype of autism.**

Pallanti Stefano; Lassi Stefano; La Malfa Giampaolo; Campigli Marco; Di Rubbo Roberto; Paolini Giulia; Cesarali Valentina

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Clinical practice and epidemiology in mental health - CP & EMH ( England ) Nov

15 2005 , 1 p24 , ISSN: 1745-0179--Electronic Journal Code: 101245735

Publishing Model Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Other Citation Owner: NLM

Record type: PubMed not MEDLINE

Pervasive Developmental Disorders (PDD) are chronic, lifelong disorders for which there is as yet no effective cure, and medical management remains a challenge for clinicians. The current report describes two patients affected by autistic disorder with associated gastrointestinal symptoms. They received multiple doses of intravenous secretin for a six-month period and were assessed with several specific outcome measures to evaluate drug effect. The administration of secretin led to some significant and lasting improvement in only one case.

Gastroesophageal reflux may contribute to some of the behavioural problems and explain the effect of secretin since its suppressive effect on gastric secretion is well known. It is also true that autistic children with gastroesophageal reflux and a higher IQ could constitute a subtype which responds to secretin administration and that could be labelled as a "gastrointestinal subtype".

Record Date Created: 20051212

Record Date Completed: 20060123

Date of Electronic Publication: 20051115

## **Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children.**

Parracho Helena M R T; Bingham Max O; Gibson Glenn R; McCartney Anne L  
Food Microbial Sciences Unit, School of Food Biosciences, The University of Reading, Whiteknights, PO Box 226, Reading RG6 6AP, UK.

Journal of medical microbiology ( England ) Oct 2005 , 54 (Pt 10) p987-91 ,

ISSN: 0022-2615--Print Journal Code: 0224131

Publishing Model Print

Document type: Comparative Study; Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Children with autistic spectrum disorders (ASDs) tend to suffer from severe gastrointestinal problems. Such symptoms may be due to a disruption of the indigenous gut flora promoting the overgrowth of potentially pathogenic micro-organisms. The faecal flora of patients with ASDs was studied and compared with those of two control groups (healthy siblings and unrelated healthy children).

Faecal bacterial populations were assessed through the use of a culture-independent technique, fluorescence in situ hybridization, using oligonucleotide probes targeting predominant components of the gut flora. The faecal flora of ASD patients contained a higher incidence of the *Clostridium histolyticum* group

(Clostridium clusters I and II) of bacteria than that of healthy children. However, the non-autistic sibling group had an intermediate level of the C. histolyticum group, which was not significantly different from either of the other subject groups. Members of the C. histolyticum group are recognized toxin-producers and may contribute towards gut dysfunction, with their metabolic products also exerting systemic effects. Strategies to reduce clostridial population levels harboured by ASD patients or to improve their gut microflora profile through dietary modulation may help to alleviate gut disorders common in such patients.

Tags: Female; Male

Descriptors: \*Autistic Disorder--microbiology--MI; \*Bacteria--isolation and purification --IP; \*Clostridium--isolation and purification--IP; \*Feces--microbiology --MI; \*Gastrointestinal Tract--microbiology--MI ; Child; Child, Preschool; Clostridium histolyticum--isolation and purification--IP; Humans; In Situ Hybridization, Fluorescence

Record Date Created: 20050913

Record Date Completed: 20051024

## **Tight junctions, leaky intestines, and pediatric diseases.**

Liu Z; Li N; Neu J

International Peace Maternity and Child Health Hospital, Shanghai, China.

Acta paediatrica (Oslo, Norway - 1992) ( Norway ) Apr 2005 , 94 (4) p386-93 , ISSN: 0803-5253--Print Journal Code: 9205968

Contract/Grant No.: R01HD38954; HD; NICHD NIH HHS United States

Publishing Model Print

Document type: Journal Article; Research Support, N.I.H., Extramural; Research Support, U.S. Gov't, P.H.S.; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

BACKGROUND: Tight junctions (TJs) represent the major barrier within the paracellular pathway between intestinal epithelial cells. Disruption of TJs leads to intestinal hyperpermeability (the so-called "leaky gut") and is implicated in the pathogenesis of several acute and chronic pediatric disease entities that are likely to have their origin during infancy. AIM: This review provides an overview of evidence for the role of TJ breakdown in diseases such as systemic inflammatory response syndrome (SIRS), inflammatory bowel disease, type 1 diabetes, allergies, asthma, and autism. CONCLUSION: A better basic understanding of this structure might lead to prevention or treatment of these diseases using nutritional or other means. ( 66 Refs.)

Descriptors: \*Intercellular Junctions--physiology--PH; \*Intestines--cytology--CY ; Celiac Disease--physiopathology--PP; Child; Diabetes Mellitus, Type 1 --physiopathology--PP; Epithelial Cells--physiology--PH; Humans; Hypersensitivity--physiopathology--PP; Inflammatory Bowel Diseases --physiopathology--PP; Intestines--physiopathology--PP

Record Date Created: 20050811

Record Date Completed: 20050826

## **The significance of ileo-colonic lymphoid nodular hyperplasia in children with autistic spectrum disorder.**

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Wakersa@aol.com

European journal of gastroenterology & hepatology ( England ) Aug 2005 , 17

(8) p827-36 , ISSN: 0954-691X--Print Journal Code: 9000874

Publishing Model Print; Comment in Eur J Gastroenterol Hepatol. 2005 Aug; 17(8)

821-2; Comment in PMID 16003130; Comment in Eur J Gastroenterol Hepatol.

2006 May; 18(5):569-71; author reply 571-3; Comment in PMID 16607159

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

**BACKGROUND:** Intestinal mucosal pathology, characterized by ileo-colonic lymphoid nodular hyperplasia (LNH) and mild acute and chronic inflammation of the colorectum, small bowel and stomach, has been reported in children with autistic spectrum disorder (ASD). **AIM:** To assess ileo-colonic LNH in ASD and control children and to test the hypothesis that there is an association between ileo-colonic LNH and ASD in children. **PATIENTS AND METHODS:** One hundred and forty-eight consecutive children with ASD (median age 6 years; range 2-16; 127 male) with gastrointestinal symptoms were investigated by ileo-colonoscopy. Macroscopic and histological features were scored and compared with 30 developmentally normal (non-inflammatory bowel disease, non-coeliac disease) controls (median age 7 years; range 1-11; 25 male) showing mild non-specific colitis in 16 cases (13 male) and normal colonic histology in 14 cases (12 male). Seventy-four ASD children and 23 controls also underwent upper gastrointestinal endoscopy. The influence on ileal LNH of dietary restriction, age at colonoscopy, and co-existent LNH elsewhere in the intestine, was examined. **RESULTS:** The prevalence of LNH was significantly greater in ASD children compared with controls in the ileum (129/144 (90%) vs. 8/27 (30%),  $P < 0.0001$ ) and colon (88/148 (59%) vs. 7/30 (23%),  $P = 0.0003$ ), whether or not controls had co-existent colonic inflammation. The severity of ileal LNH was significantly greater in ASD children compared with controls, with moderate to severe ileal LNH present in 98 of 144 (68%) ASD children versus 4 of 27 (15%) controls ( $P < 0.0001$ ). Severe ileal LNH was associated with co-existent colonic LNH in ASD children ( $P = 0.01$ ). The presence and severity of ileal LNH was not influenced by either diet or age at colonoscopy ( $P = 0.2$ ). Isolated ileal LNH without evidence of pathology elsewhere in the intestine was a rare event, occurring in less than 3% of children overall. On histopathological examination, hyperplastic lymphoid follicles are significantly more prevalent in the ileum of ASD children (84/138; 61%) compared with controls (2/23; 9%,  $P = 0.0001$ ). **CONCLUSION:** Ileo-colonic LNH is a characteristic pathological finding in children with ASD and gastrointestinal symptoms, and is associated with mucosal inflammation. Differences in age at colonoscopy and diet do not account for these changes. The data support the hypothesis that LNH is a significant pathological finding in ASD children.

Tags: Female; Male

Descriptors: \*Autistic Disorder--etiology--ET; \*Intestinal Diseases--complications--CO; \*Lymphatic Diseases--complications--CO ; Adolescent; Autistic Disorder--pathology--PA; Child; Child, Preschool; Cohort Studies; Colitis--complications--CO; Colitis--pathology--PA; Colonic Diseases--complications--CO; Colonic Diseases--pathology--PA; Diet ; Endoscopy, Gastrointestinal--methods--MT; Humans; Hyperplasia--pathology --PA; Ileal Diseases--complications--CO; Ileal Diseases--pathology--PA; Ileitis--complications--CO; Ileitis--pathology--PA; Intestinal Diseases --pathology--PA; Intestinal Mucosa--pathology--PA; Lymph Nodes--pathology --PA; Lymphatic Diseases--pathology--PA; Prospective Studies; Rectum --pathology--PA

Record Date Created: 20050708

Record Date Completed: 20051229

## **Evaluation of an association between gastrointestinal symptoms and cytokine production against common dietary proteins in children with autism spectrum disorders.**

Jyonouchi Harumi; Geng Lee; Ruby Agnes; Reddy Chitra; Zimmerman-Bier Barbie  
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Journal of pediatrics ( United States ) May 2005 , 146 (5) p605-10 , ISSN:  
0022-3476--Print Journal Code: 0375410

Publishing Model Print; Comment in J Pediatr. 2005 May;146(5) 582-4; Comment  
in PMID 15870657

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

**OBJECTIVE:** To evaluate an association between cytokine production with common dietary proteins as a marker of non-allergic food hypersensitivity (NFH) and gastrointestinal (GI) symptoms in young children with autism spectrum disorders (ASD). **STUDY DESIGN:** Peripheral blood mononuclear cells (PBMCs) were obtained from 109 ASD children with or without GI symptoms (GI [+] ASD, N = 75 and GI (-) ASD, N = 34], from children with NFH (N = 15), and control subjects (N = 19). Diarrhea and constipation were the major GI symptoms. We measured production of type 1 T-helper cells (Th1), type 2 T-helper cells (Th2), and regulatory cytokines by PBMCs stimulated with whole cow's milk protein (CMP), its major components (casein, beta-lactoglobulin, and alpha-lactalbumin), gliadin, and soy. **RESULTS:** PBMCs obtained from GI (+) ASD children produced more tumor necrosis factor-alpha (TNF-alpha)/interleukin-12 (IL-12) than those obtained from control subjects with CMP, beta-lactoglobulin, and alpha-lactalbumin, irrespective of objective GI symptoms. They also produced more TNF-alpha with gliadin, which was more frequently observed in the group with loose stools. PBMCs obtained from GI (-) ASD children produced more TNF-alpha/IL-12 with CMP than those from control subjects, but not with beta-lactoglobulin, alpha-lactalbumin, or gliadin. Cytokine production with casein and soy were unremarkable. **CONCLUSION:** A high prevalence of elevated TNF-alpha/IL-12 production by GI (+) ASD PBMCs with CMP and its major components indicates a role of NFH in GI symptoms observed in children with ASD.

Tags: Female; Male

Descriptors: \*Autistic Disorder--metabolism--ME; \*Cytokines--biosynthesis--BI; \*Milk Proteins--adverse effects--AE ; Autistic Disorder--complications--CO; Case-Control Studies; Child; Child, Preschool; Constipation--etiology--ET; Diarrhea--etiology--ET; Food Analysis; Humans; Infant; Milk Proteins--analysis--AN; Milk Proteins --immunology--IM

CAS Registry No.: 0 (Cytokines); 0 (Milk Proteins)

Record Date Created: 20050504

Record Date Completed: 20050607

## **Dysregulated innate immune responses in young children with autism spectrum disorders: their**

## relationship to gastrointestinal symptoms and dietary intervention.

Jyonouchi Harumi; Geng Lee; Ruby Agnes; Zimmerman-Bier Barbie  
Department of Pediatrics, New Jersey Medical School, UMDNJ, Newark, NJ 07101-1709, USA. jyanouha@umdnj.edu  
Neuropsychobiology ( Switzerland ) 2005 , 51 (2) p77-85 , ISSN: 0302-282X-  
-Print Journal Code: 7512895

Publishing Model Print

Document type: Clinical Trial; In Vitro; Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

**OBJECTIVE:** Our previous study indicated an association between cellular immune reactivity to common dietary proteins (DPs) and excessive proinflammatory cytokine production with endotoxin (lipopolysaccharide, LPS), a major stimulant of innate immunity in the gut mucosa, in a subset of autism spectrum disorder (ASD) children. However, it is unclear whether such abnormal LPS responses are intrinsic in these ASD children or the results of chronic gastrointestinal (GI) inflammation secondary to immune reactivity to DPs. This study further explored possible dysregulated production of proinflammatory and counter-regulatory cytokines with LPS in ASD children and its relationship to GI symptoms and the effects of dietary intervention measures. **METHODS:** This study includes ASD children (median age 4.8 years) on the unrestricted (n = 100) or elimination (n = 77) diet appropriate with their immune reactivity. Controls include children with non-allergic food hypersensitivity (NFH; median age 2.9 years) on the unrestricted (n = 14) or elimination (n = 16) diet, and typically developing children (median age 4.5 years, n = 13). The innate immune responses were assessed by measuring production of proinflammatory (TNF-alpha, IL-1beta, IL-6, and IL-12) and counter-regulatory (IL-1ra, IL-10, and sTNFRII) cytokines by peripheral blood mononuclear cells (PBMCs) with LPS. The results were also compared to T-cell responses with common DPs and control T-cell mitogens assessed by measuring T-cell cytokine production. **RESULTS:** ASD and NFH PBMCs produced higher levels of TNF-alpha with LPS than controls regardless of dietary interventions. However, only in PBMCs from ASD children with positive gastrointestinal (GI(+)) symptoms, did we find a positive association between TNF-alpha levels produced with LPS and those with cow's milk protein (CMP) and its major components regardless of dietary interventions. In the unrestricted diet group, GI(+) ASD PBMCs produced higher IL-12 than controls and less IL-10 than GI(-) ASD PBMCs with LPS. GI(+) ASD but not GI(-) ASD or NFH PBMCs produced less counter-regulatory cytokines with LPS in the unrestricted diet group than in the elimination diet group. There was no significant difference among the study groups with regard to cytokine production in responses to T-cell mitogens and other recall antigens. **Conclusion:** Our results revealed that there are findings limited to GI(+) ASD PBMCs in both the unrestricted and elimination diet groups. Thus our findings indicate intrinsic defects of innate immune responses in GI(+) ASD children but not in NFH or GI(-) ASD children, suggesting a possible link between GI and behavioral symptoms mediated by innate immune abnormalities. Copyright 2005 S. Karger AG, Basel.

**Descriptors:** \*Autistic Disorder--complications--CO; \*Autistic Disorder--immunology--IM; \*Diet; \*Gastrointestinal Diseases--etiology--ET; \*Gastrointestinal Diseases--immunology--IM; \*Immunity--physiology--PH ; Child; Child, Preschool; Cytokines--biosynthesis--BI; Dietary Proteins --pharmacology--PD; Enzyme-Linked Immunosorbent Assay; Food Hypersensitivity--

physiopathology--PP; Food Hypersensitivity--psychology --PX; Humans; Infant; Lactoglobulins--pharmacology--PD; Lipopolysaccharides --pharmacology--PD; Monocytes--drug effects--DE; Monocytes--metabolism--ME ; T-Lymphocytes--drug effects--DE; T-Lymphocytes--immunology--IM; T-Lymphocytes--metabolism--ME

CAS Registry No.: 0 (Cytokines); 0 (Dietary Proteins); 0 (Lactoglobulins); 0 (Lipopolysaccharides)

Record Date Created: 20050329

Record Date Completed: 20050429

## **Parental report of eating problems and gastrointestinal symptoms in children with pervasive developmental disorders**

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Children's Health Care ( Child. Health Care ) ( United States ) June 1, 2005 , 34/3 (217-234)

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DOCUMENT TYPE: Journal ; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 34

Parents of children of 89 children with pervasive developmental disorder were surveyed about their child's eating, gastrointestinal symptoms, and behavior problems. Results revealed potentially interesting relationships among self-injurious behavior, pica, feeding problems, and gastrointestinal symptoms in this population. Although over 60% of children were reported to have strong food preferences, only 6.7% of parents reported that their child had a feeding problem. Most children exhibited high rates of pica and self-injurious behavior that affected the family's quality of life. Some children experienced at least one symptom of gastrointestinal distress weekly, and bowel problems appeared to be related to some aspects of feeding. Although methodological issues limit these data, future research should focus on further relations among these factors in this population. Copyright (c) 2005, Lawrence Erlbaum Associates, Inc.

DESCRIPTORS:

\* autism; \*child; \*eating; \*gastrointestinal symptom automutilation; behavior disorder; feeding; food preference; intestine; parent; population; quality of life

## **Novel treatments for autistic spectrum disorders**

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Mental Retardation and Developmental Disabilities Research Reviews ( Ment. Retard. Dev. Disabil. Res. Rev. ) ( United States ) July 25, 2005 , 11/2 (131-142)

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DOI: 10.1002/mrdd.20062

Item Identifier (DOI): 10.1002/mrdd.20062

DOCUMENT TYPE: Journal ; Review RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 179

In no area of developmental pediatric practice is there more controversy regarding the choice of treatment than related to children with autistic spectrum disorders (ASD). Complementary and alternative medical therapies (CAM) are often elected because they are perceived as treating the cause of symptoms rather than the symptoms themselves. CAM used for autism can be divided by proposed mechanism: immune modulation, gastrointestinal, supplements that affect neurotransmitter function, and non-biologic intervention. Secretin as a therapy for autism is discussed as an example of how a clinical observation rapidly grew to a widespread treatment before well-designed studies demonstrated absence of effect. The plausibility for behavioral effect was not substantiated by clinical studies. CAM used for treatment of autism is examined in terms of rationale, evidence of efficacy, side effects, and additional commentary. Families and clinicians need access to well-designed clinical evidence to assist them in choice of therapies. (c) 2005 Wiley-Liss, Inc.

BRAND NAME/MANUFACTURER NAME: enzymaid; periactin

DESCRIPTORS:

\* autism; \*heart atrium septum defect; \*therapy child; clinical observation; clinical study; diethylaminoethyl dextran; immunomodulation; neurotransmitter; pediatrics; secretin; side effect

## **Glucosamine and plant lectins in autistic spectrum disorders: An initial report on six children with uncontrolled diarrhoea**

Author: Danczak E (Reprint)

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Journal: Journal of Nutritional & Environmental Medicine (Abingdon) 14 ( 4 ): p 327-330 DEC 04 2004

ISSN: 1359-0847

Document Type: Article

Record Type: Abstract

Language: English

Abstract: Purpose: To identify changes in bowel habits when there is exposure to glucosamine. Design: Case study. Materials and Methods: Six autistic children were exposed to glucosamine 500 mg twice daily without any change in diet. Results: Five of the children had relief of diarrhoea, the sixth had no change in bowel habit but ate bread containing gluten without any change in behaviour. Conclusion: Gluten contains a plant lectin that binds glucosamine. Glucosamine binds to potato lectin in the same manner and may protect the gut in responsive children.

This is reflected in a change in bowel habit, indicating a possible protective activity.

Registry Numbers: 3416-24-8: glucosamine

**DESCRIPTORS:**

Major Concepts: Behavior; Biochemistry and Molecular Biophysics; Nutrition; Gastroenterology--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Plantae-- Plantae; Solanaceae--Dicotyledones, Angiospermae, Spermatophyta, Plantae

Organisms: human (Hominidae)--child; plant (Plantae); potato (Solanaceae)

Organisms: Parts Etc: bowel--digestive system; gut--digestive system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates; Angiosperms; Dicots; Plants; Spermatophytes; Vascular Plants

Diseases: diarrhea--digestive system disease; autism--behavioral and mental disorders

Mesh Terms: Diarrhea (MeSH); Autistic Disorder (MeSH)

Chemicals & Biochemicals: lectin; gluten; glucosamine--metabolic-drug, dosage

Miscellaneous Terms: Concept Codes: protective activity; bowel habit

## **The Effects of the Elimination Diet on Cytokine Production Profile against Common Dietary Proteins (DPs) in Children with Autism Spectrum Disorders (ASD)**

Author: Jyonouchi Harumi (Reprint); Geng Lee; Ruby Agnes; Zimmerman-Bier Barbie

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Journal: FASEB Journal 18 ( 4-5 ): p Abst. 617.10 2004 2004

Medium: e-file

Conference/Meeting: FASEB Meeting on Experimental Biology: Translating the Genome Washington, District of Columbia, USA April 17-21, 2004; 20040417

Sponsor: FASEB

ISSN: 0892-6638 \_(ISSN print)

Document Type: Meeting; Meeting Abstract

Record Type: Abstract

Language: English

**Abstract:** A casein-free and gluten-free (cf/gf) diet is a popular intervention measure for ASD children with apparent favorable responses. This may be associated with increased TNF- $\alpha$  production with cow's milk protein (CMP) and gliadin by ASD peripheral blood mononuclear cells (PBMCs) (Neuropsychobiology 46: 76, 2002). We then evaluated production of IFN- $\gamma$ , TNF- $\alpha$ , IL-5, IL-10, and IL-12p40 with common DPs in 52 ASD children (Median 5.5 y) on the cf/gf diet (6 mo to 4 y): 47/52 had gastrointestinal (GI) symptoms before the diet and 43/47 (91.5%) of GI (+) ASD children positively responded to the diet. There were no changes in behavioral symptoms in 5/5 GI (-) ASD children with the diet. Control included 7 DP intolerance (DPI) children on the cf/gf diet. ASD and DPI PBMCs still produced higher amounts of TNF- $\alpha$  with CMPs and gliadin than normal PBMCs (N=12, median 5.4 y) ( $p < 0.05$ ) but not other cytokines. In GI (+) ASD and DPI PBMCs, TNF- $\alpha$  production with CMP is positively associated with IL-12 production ( $p < 0.05$ ). GI (+) ASD PBMCs produced not only higher TNF- $\alpha$  ( $p < 0.01$ ) but

also higher regulatory cytokines (IL-10, sTNRII, IL-1ra)( $p < 0.05$ ) with LPS, while no increase in regulatory cytokine production by PBMCs from ASD children on a regular diet. Thus elevated TNF- $\alpha$  production to DPs likely persists in some ASD children but there might be altered regulatory cytokine profile with the elimination diet. Funded by Jonty Foundation, St. Paul, MN.

**DESCRIPTORS:**

Major Concepts: Clinical Immunology--Human Medicine, Medical Sciences; Neurology--Human Medicine, Medical Sciences; Nutrition; Psychiatry--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child, patient

Organisms: Parts Etc: gastrointestinal tract--digestive system; peripheral blood mononuclear cell {PBMC}--blood and lymphatics, immune system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: autism spectrum disorders--behavioral and mental disorders, nervous system disease

Mesh Terms: Autistic Disorder (MeSH)

Chemicals & Biochemicals: IFN-gamma {interferon-gamma}; IL-10 {interleukin-10}; IL-12p40; IL-5 {interleukin-5}; TNF-alpha {tumor necrosis factor-alpha}; casein--dietary; cow milk protein; dietary proteins; gliadin; gluten-dietary

Methods & Equipment: casein-free gluten-free diet--clinical techniques, therapeutic and prophylactic techniques

## **Nutrition implications to medications and supplements administered to children with autism**

Author: Hires Brigette B (Reprint); Forsythe Hazel W

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Journal: FASEB Journal 18 ( 4-5 ): p Abst. 134.8 2004 2004

Medium: e-file

Conference/Meeting: FASEB Meeting on Experimental Biology: Translating the Genome Washington, District of Columbia, USA April 17-21, 2004; 20040417

Sponsor: FASEB

ISSN: 0892-6638 \_(ISSN print)

Document Type: Meeting; Meeting Abstract

Record Type: Abstract

Language: English

Abstract: Autism, a neurodevelopmental disorder, presents core symptoms of impairment in socialization, verbal and non-verbal communication, and restrictive, repetitive behaviors. The study proposed to quantify the amount and types of medications and supplements consumed by twenty-five children diagnosed with autism. Parents of these children completed a questionnaire for an on-going study investigating nutritional inadequacy. Responses to current medication and supplement intake were analyzed. Medication classifications included antianxiety, antipsychotic, anticonvulsant, antiyeast, antihypertensive, asthma, antimanic, antidepressive, and antiepileptic medications. Supplements included multivitamins, specific B-vitamin preparations, dimethylglycine, probiotics, essential fatty acids, lecithin, primrose oil, magnesium, calcium, and zinc. Implications for nutrient intake related to medication interactions centered

on decreased nutrient bioavailability, and gastrointestinal tract distress. Recommendations are that drug and nutrient interactions should be taken into account when formulating a therapeutic pharmacological and medical nutrition therapy plan for children with autism. The National Institutes of Health (NIH) training grant number T32 DK 07778 supports this research.

**DESCRIPTORS:**

Major Concepts: Nutrition; Pediatrics--Human Medicine, Medical Sciences; Psychiatry--Human Medicine, Medical Sciences  
Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia  
Organisms: human (Hominidae)--child, patient  
Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
Diseases: autism--behavioral and mental disorders  
Mesh Terms: Autistic Disorder (MeSH)  
Chemicals & Biochemicals: supplements  
Miscellaneous Terms: Concept Codes: medications; non-verbal communication; nutrition implications; repetitive behavior; restrictive behavior; verbal communication; Meeting Abstract

## **Cytokine Production Profile against Common Dietary Proteins (DPs) in Children with Autism Spectrum Disorders (ASD) on a regular diet: Relationship to Gastrointestinal (GI) Symptoms and Responses to LPS**

Author: Jyonouchi Harumi (Reprint); Geng Lee; Ruby Agnes; Reddy Chitra; Zimmerman-Bier Barbie

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Author E-mail Address: jyanouha@umdnj.edu

Journal: FASEB Journal 18 ( 4-5 ): p Abst. 617.9 2004 2004

Medium: e-file

Conference/Meeting: FASEB Meeting on Experimental Biology: Translating the Genome Washington, District of Columbia, USA April 17-21, 2004; 20040417

Sponsor: FASEB

ISSN: 0892-6638 \_(ISSN print)

Document Type: Meeting; Meeting Abstract

Record Type: Abstract

Language: English

**Abstract:** We have shown that peripheral blood mononuclear cells (PBMCs) from ASD children tend to produce large amounts of TNF- $\alpha$ ; with common DPs as in children with DP intolerance (DPI) (Neuropsychobiology 46: 76, 2002). We now evaluated production of TNF- $\alpha$ ; , IFN- $\gamma$ ; , IL-5, IL-10, & IL-12 with common DPs (cow's milk protein (CMP), soy, & gliadin) by PBMCs from GI (+) (N=52, median 5.2 y) and GI (-) (N=21, median 5.8 y) ASD children on a regular diet in comparison with production of IL-1 $\beta$ ; , IL-6, TNF- $\alpha$ ; , IL-12, IL-10, sTNFRII, IL-1 $\alpha$  with LPS. Controls included normal (N=12, median 5.4 y) and DPI children (prior to dietary intervention, N=12, median 2.5 y). GI (+) ASD PBMCs produced more TNF- $\alpha$ ; with CMPs and gliadin ( $p < 0.005$ ) as did DPI PBMCs. GI (-) ASD PBMCs also produced more TNF- $\alpha$ ; with CMP ( $p < 0.02$ ) but not with gliadin. Production of other cytokine did not differ in the study groups, but 7/21 GI (-) ASD PBMCs produced higher IL-5 with soy and/or CMP. GI (+) ASD PBMCs also produced the most TNF- $\alpha$ ; among the study

groups ( $p < 0.01$ ) along with higher IL-12 but production of other cytokines did not differ among the study groups. Thus GI (+) ASD PBMCs likely produce more TNF- $\alpha$ ; against common DPs in parallel to excessive production of TNF- $\alpha$ ; over counter-regulatory cytokines with LPS, a stimulant of innate immunity. In GI (-) ASD children, GI symptoms might be less appreciated. Funded by Jonty Foundation, St. Paul, MN. .

**DESCRIPTORS:**

Major Concepts: Clinical Chemistry--Allied Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences; Pediatrics--Human Medicine, Medical Sciences; Psychiatry--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: human (Hominidae)--child, patient

Organisms: Parts Etc: peripheral blood mononuclear cells--blood and lymphatics, immune system

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Diseases: autism spectrum disorders--behavioral and mental disorders

Mesh Terms: Autistic Disorder (MeSH)

Chemicals & Biochemicals: common dietary proteins; gliadin; interferon-gamma; interleukin-1-receptor antagonist; interleukin-10; interleukin-12; interleukin-5; interleukin-6; milk protein; soy; tumor necrosis factor receptor type II; tumor necrosis factor-alpha

Miscellaneous Terms: Concept Codes: cytokine production profile; gastrointestinal symptoms; lipopolysaccharide responses; regular diet; Meeting Abstract

## **Pilot study of a moderate dose multivitamin/mineral supplement for children with autistic spectrum disorder.**

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Journal of alternative and complementary medicine (New York, N.Y.) ( United States ) Dec 2004 , 10 (6) p1033-9 , ISSN: 1075-5535--Print Journal Code: 9508124

Publishing Model Print; Erratum in J Altern Complement Med. 2005 Aug;11(4) 749

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

**OBJECTIVE:** Determine the effect of a moderate dose multivitamin/mineral supplement on children with autistic spectrum disorder. **DESIGN:** Randomized, double-blind, placebo-controlled 3-month study. **SUBJECTS:** Twenty (20) children with autistic spectrum disorder, ages 3-8 years. **RESULTS:** A Global Impressions parental questionnaire found that the supplement group reported statistically significant improvements in sleep and gastrointestinal problems compared to the placebo group. An evaluation of vitamin B(6) levels prior to the study found that the autistic children had substantially elevated levels of B6 compared to a control group of typical children (75% higher,  $p < 0.000001$ ). Vitamin C levels were measured at the end of the study, and the placebo group had levels that were significantly below average for typical children, whereas the supplement group

had near-average levels. DISCUSSION: The finding of high vitamin B(6) levels is consistent with recent reports of low levels of pyridoxal-5-phosphate and low activity of pyridoxal kinase (i.e., pyridoxal is only poorly converted to pyridoxal-5-phosphate, the enzymatically active form). This may explain the functional need for high-dose vitamin B(6) supplementation in many children and adults with autism.

Tags: Female; Male

Descriptors: \*Autistic Disorder--drug therapy--DT; \*Child Behavior--drug effects--DE; \*Trace Elements--therapeutic use--TU; \*Vitamins--therapeutic use--TU ; Adult; Child; Child, Preschool; Dietary Supplements; Dose-Response Relationship, Drug; Double-Blind Method; Humans; Pilot Projects; Time Factors; Treatment Outcome; Vitamin B 6--therapeutic use--TU

CAS Registry No.: 0 (Trace Elements); 0 (Vitamins); 8059-24-3 (Vitamin B 6)

Record Date Created: 20050127

Record Date Completed: 20050519

## **Spontaneous mucosal lymphocyte cytokine profiles in children with autism and gastrointestinal symptoms: mucosal immune activation and reduced counter regulatory interleukin-10.**

Ashwood Paul; Anthony Andrew; Torrente Franco; Wakefield Andrew J  
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Journal of clinical immunology ( United States ) Nov 2004 , 24 (6) p664-73 ,  
ISSN: 0271-9142--Print Journal Code: 8102137

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

A lymphocytic enterocolitis has been reported in a cohort of children with autistic spectrum disorder (ASD) and gastrointestinal (GI) symptoms. This study tested the hypothesis that dysregulated intestinal mucosal immunity with enhanced pro-inflammatory cytokine production is present in these ASD children. Comparison was made with developmentally normal children with, and without, mucosal inflammation. Duodenal and colonic biopsies were obtained from 21 ASD children, and 65 developmentally normal paediatric controls, of which 38 had signs of histological inflammation. Detection of CD3+ lymphocyte staining for spontaneous intracellular TNFalpha, IL-2, IL-4, IFNgamma, and IL-10, was performed by multicolor flow cytometry. Duodenal and colonic mucosal CD3+ lymphocyte counts were elevated in ASD children compared with noninflamed controls ( $p < 0.03$ ). In the duodenum, the proportion of lamina propria (LP) and epithelial CD3(+)TNFalpha+ cells in ASD children was significantly greater compared with noninflamed controls ( $p < 0.002$ ) but not coeliac disease controls. In addition, LP and epithelial CD3(+)IL-2+ and CD3(+)IFNgamma+, and epithelial CD3(+)IL-4+ cells were more numerous in ASD children than in noninflamed controls ( $p < 0.04$ ). In contrast, CD3(+)IL-10+ cells were fewer in ASD children than in noninflamed controls ( $p < 0.05$ ). In the colon, LP CD3(+)TNFalpha+ and CD3(+)IFNgamma+ were more frequent in ASD children than in noninflamed controls ( $p < 0.01$ ). In contrast with Crohn's disease and non-Crohn's colitis, LP and epithelial CD3(+)IL-10+ cells were fewer in ASD children than in nondisease controls ( $p < 0.01$ ). There was a significantly greater proportion of CD3(+)TNFalpha+ cells in colonic

mucosa in those ASD children who had no dietary exclusion compared with those on a gluten and/or casein free diet ( $p < 0.05$ ). There is a consistent profile of CD3+ lymphocyte cytokines in the small and large intestinal mucosa of these ASD children, involving increased pro-inflammatory and decreased regulatory activities. The data provide further evidence of a diffuse mucosal immunopathology in some ASD children and the potential for benefit of dietary and immunomodulatory therapies.

Tags: Female; Male

Descriptors: \*Autistic Disorder--complications--CO; \*Cytokines--analysis--AN;

\*Gastrointestinal Diseases--immunology--IM; \*Interleukin-10--analysis--AN;

\*Intestinal Mucosa--immunology--IM; \*Lymphocytes--immunology--IM ;

Adolescent; Antigens, CD3; Autistic Disorder--immunology--IM; Autistic Disorder-

-pathology--PA; Case-Control Studies; Child; Child, Preschool; Diet; Enterocolitis;

Gastrointestinal Diseases--pathology--PA; Humans; Immunity; Inflammation;

Intestinal Mucosa--pathology--PA; Prospective Studies

CAS Registry No.: 0 (Antigens, CD3); 0 (Cytokines); 130068-27-8 (Interleukin-10)

Record Date Created: 20041228

Record Date Completed: 20050630

## **Intestinal lymphocyte populations in children with regressive autism: evidence for extensive mucosal immunopathology.**

Ashwood Paul; Anthony Andrew; Pellicer Alicia A; Torrente Franco; Walker-Smith John A; Wakefield Andrew J

The Inflammatory Bowel Disease Study Group, and Centre for Paediatric Gastroenterology, Royal Free and University College, Medical School, London, United Kingdom. pashwood@ucdavis.edu

Journal of clinical immunology ( United States ) Nov 2003 , 23 (6) p504-17 ,

ISSN: 0271-9142--Print Journal Code: 8102137

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Inflammatory intestinal pathology has been reported in children with regressive autism (affected children). Detailed analysis of intestinal biopsies in these children indicates a novel lymphocytic enterocolitis with autoimmune features; however, links with cognitive function remain unclear. To characterize further, the nature and extent of this disease we examined the mucosal infiltrate using flow cytometry. Duodenal, ileal, and colonic biopsies were obtained from 52 affected children, 25 histologically normal, and 54 histologically inflamed, developmentally normal controls. Epithelial and lamina propria lymphocyte populations were isolated and examined by multicolor flow cytometry. Adjacent biopsies were assessed by semiquantitative histopathology. At all sites, CD3(+) and CD3(+)CD8(+) IEL as well as CD3(+) LPL were significantly increased in affected children compared with developmentally normal noninflamed control groups ( $p < 0.01$ ) reaching levels similar to inflamed controls. In addition, two populations--CD3(+)CD4(+) IEL and LP CD19(+) B cells--were significantly increased in affected children compared with both noninflamed and inflamed control groups including IBD, at all sites examined ( $p < 0.01$ ). Histologically there was a prominent mucosal eosinophil infiltrate in affected children that was

significantly lower in those on a gluten- and casein-free diet, although lymphocyte populations were not influenced by diet. The data provide further evidence of a pan-enteric mucosal immunopathology in children with regressive autism that is apparently distinct from other inflammatory bowel diseases.

Descriptors: \*Autistic Disorder--pathology--PA; \*Inflammatory Bowel Diseases--pathology --PA; \*Intestinal Mucosa--pathology--PA; \*Intestine, Small--pathology--PA; \*Lymphocytes--immunology--IM ; Adolescent; Autistic Disorder--immunology--IM; Biopsy; Child; Flow Cytometry; Humans; Inflammatory Bowel Diseases--immunology--IM; Intestinal Mucosa--immunology--IM; Intestine, Small--immunology--IM; Lymphocyte Subsets--immunology--IM

Record Date Created: 20040319

Record Date Completed: 20041007

## **Use of complementary and alternative treatments for children with autistic spectrum disorders is increasing.**

Levy Susan E; Hyman Susan L

Division of Child Development and Rehabilitation, Children's Seashore House, Children's Hospital of Philadelphia, PA, USA.

Pediatric annals ( United States ) Oct 2003 , 32 (10) p685-91 , ISSN: 0090-4481--Print Journal Code: 0356657

Publishing Model Print

Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Interventions considered to be CAM are in constant flux. New treatments emerge, older treatments become less popular, and the cycle recurs. Data supporting new treatments should be scrutinized for scientific study design, clinical safety, and scientific validity. Many families approach the clinician armed with brochures, handouts, and printouts from Web sites that are dedicated to the care and support of parents and children with ASD. A recent web search using "autism and detoxification" resulted in almost 8,000 sites. The Defeat Autism Now! (DAN!) Project arose in 1995 from collaboration of members of the Autism Research Institute. The DAN! Project advocates a specific and extensive protocol for diagnosis and treatment and can be viewed at <http://www.autism.com/ari/#dan>. The scientific validation and support for many interventions is incomplete and disparate from the recommendation in the American Academy of Pediatrics Policy Statement. Families should be encouraged to discuss all proposed investigations or treatments they wish to try with their primary care provider so the practitioner can serve as the medical home (Sidebar, page 688). The clinician should communicate and collaborate with the family and educational professionals to encourage objective identification of what works. With increasing access to health information and societal pressure for families to actively participate in their health management, continued growth of interest in CAM can be anticipated. Clinicians must remember that parents may have different beliefs regarding the effectiveness of treatment and different tolerance for treatment risks. Practitioners must keep avenues of communication open, remain open-minded, and not assume a "don't ask, don't tell" posture in the context of providing a medical home to the increasing number of children diagnosed with autism.

Descriptors: \*Autistic Disorder--psychology--PX; \*Complementary Therapies--methods--MT; \*Mental Disorders--etiology--ET; \*Mental Disorders--therapy--TH ; Child, Preschool; Complementary Therapies--adverse effects--AE; Evidence-Based Medicine; Food Habits; Gastrointestinal Agents--therapeutic use--TU; Humans;

Infant; Pediatrics--methods--MT; Professional-Family Relations; Randomized Controlled Trials as Topic; Secretin--therapeutic use --TU; Treatment Failure CAS Registry No.: 0 (Gastrointestinal Agents); 1393-25-5 (Secretin)

Record Date Created: 20031110

Record Date Completed: 20040129

## **Constipation with acquired megarectum in children with autism.**

Afzal Nadeem; Murch Simon; Thirrupathy Kumran; Berger Leslie; Fagbemi Andrew; Heuschkel Robert

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Pediatrics ( United States ) Oct 2003 , 112 (4) p939-42 , ISSN: 1098-4275--Electronic Journal Code: 0376422

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

**OBJECTIVE:** Recent evidence suggests that autistic children may have significant gastrointestinal symptoms. Although constipation occurs in 2% to 5% of healthy children, its clinical diagnosis is often difficult in children with behavioral disorders. We thus aimed to assess the prevalence of fecal loading in autistic children with gastrointestinal symptoms and to identify possible predictors of constipation. **METHODS:** We studied abdominal radiographs of 103 autistic children (87 boys) who were referred for gastroenterological assessment, in comparison with 29 control radiographs from children who were referred to the emergency department, most with abdominal pain. Radiographs were scored independently, in blinded manner, by 4 pediatric gastroenterologists and a radiologist. The severity of constipation was determined using a validated index. Details of stool habit, abdominal pain, dietary history, and laxative use were obtained from case notes. **RESULTS:** The incidence of constipation in the control subjects with abdominal pain was higher than reported for normal children. Despite this, moderate or severe constipation was more frequent in the autistic group than in the control subjects (36% vs 10%). Analysis of rectosigmoid loading showed more striking differences (54.4% of autistic children had moderate/severe loading or acquired megarectum compared with 24.1% of control subjects). Multivariate regression analysis showed consumption of milk to be the strongest predictor of constipation in the autistic group, whereas stool frequency, gluten consumption, soiling, and abdominal pain were not predictive of constipation. **CONCLUSIONS:** Constipation is a frequent finding in children with gastrointestinal symptoms and autism, particularly in the rectosigmoid colon, often with acquired megarectum. The absence of any correlation between the clinical history and the degree of fecal impaction in autistic children confirms the importance of an abdominal radiograph in the assessment of their degree of constipation.

Tags: Female; Male

Descriptors: \*Autistic Disorder--complications--CO; \*Constipation--epidemiology--EP; \*Rectum--pathology--PA ; Abdominal Pain--epidemiology--EP; Abdominal Pain--etiology--ET; Adolescent ; Child; Child, Preschool; Constipation--complications--CO; Constipation --radiography--RA; Dilatation, Pathologic--epidemiology--EP; Dilatation, Pathologic--etiology--ET; Dilatation, Pathologic--radiography--RA; Fecal Impaction--epidemiology--EP; Fecal Impaction--etiology--

ET; Fecal Impaction--radiography--RA; Humans; Prevalence; Rectum--radiography--RA; Retrospective Studies; Severity of Illness Index; Single-Blind Method

Record Date Created: 20031002

Record Date Completed: 20031017

## **Intestinal pathophysiology in autism.**

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jfwhite@physio.emory.edu

Experimental biology and medicine (Maywood, N.J.) ( United States ) Jun 2003 , 228 (6) p639-49 , ISSN: 1535-3702--Print Journal Code: 100973463

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Autism is a life-long developmental disorder affecting as many as 1 in 500 children. The causes for this profound disorder are largely unknown. Recent research has uncovered pathology in the gastrointestinal tract of autistic children. The pathology, reported to extend from the esophagus to the colon, is described here along with other studies pointing to a connection between diet and the severity of symptoms expressed in autism. The evidence that there is impaired intestinal permeability in autism is reviewed, and various theories are discussed by which a leaky gut could develop. Lastly, some possible ways in which impaired gastrointestinal function might influence brain function are discussed. ( 98 Refs.)

Descriptors: \*Autistic Disorder--complications--CO; \*Gastrointestinal Diseases--etiology --ET; \*Intestines--physiopathology--PP ; Antigens--immunology--IM; Autistic Disorder--physiopathology--PP; Brain --metabolism--ME; Brain--physiopathology--PP; Child; Child, Preschool; Diet; Humans; Immunohistochemistry; Immunotherapy, Active--adverse effects --AE; Intestinal Absorption--physiology--PH; Intestines--immunology--IM; Intestines--metabolism--ME

CAS Registry No.: 0 (Antigens)

Record Date Created: 20030529

Record Date Completed: 20030709

## **Correlates of specific childhood feeding problems.**

Field D; Garland M; Williams K

Hershey Medical Center, Hershey, PA 17033, USA.

Journal of paediatrics and child health ( Australia ) May-Jun 2003 , 39 (4) p299-304 , ISSN: 1034-4810--Print Journal Code: 9005421

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

OBJECTIVE: The correlates of specific childhood feeding problems are described to further examine possible predisposing factors for feeding problems. We report our experience with 349 participants evaluated by an interdisciplinary feeding

team. METHODS: A review of records was conducted and each participant was identified as having one or more of five functionally defined feeding problems: food refusal, food selectivity by type, food selectivity by texture, oral motor delays, or dysphagia. The prevalence of predisposing factors for these feeding problems was examined. Predisposing factors included developmental disabilities, gastrointestinal problems, cardiopulmonary problems, neurological problems, renal disease and anatomical anomalies. RESULTS: The frequencies of predisposing factors varied by feeding problem. Differences were found in the prevalence of the five feeding problems among children with three different developmental disabilities: autism, Down syndrome and cerebral palsy. Gastro-oesophageal reflux was the most prevalent condition found among all children in the sample and was the factor most often associated with food refusal. Neurological conditions and anatomical anomalies were highly associated with skill deficits, such as oral motor delays and dysphagia. CONCLUSIONS: Specific medical conditions and developmental disabilities are often associated with certain feeding problems. Information concerning predisposing factors of feeding problems can help providers employ appropriate primary, secondary and tertiary prevention measures to decrease the frequency or severity of some feeding problems.

Tags: Female; Male

Descriptors: \*Developmental Disabilities--complications--CO; \*Eating Disorders--etiology --ET; \*Gastrointestinal Diseases--complications--CO; \*Mouth Abnormalities --complications--CO ; Child; Child, Preschool; Eating Disorders--classification--CL; Eating Disorders--epidemiology--EP; Gastrointestinal Diseases--epidemiology--EP; Humans; Infant; Medical Records; Prevalence

Record Date Created: 20030520

Record Date Completed: 20030916

## **Diet in autism and associated disorders.**

Garvey Josephine

Royal Free Hospital, London.

journal of family health care ( England ) 2002 , 12 (2) p34-8 , ISSN: 1474-9114--Print Journal Code: 101142028

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: NURSING

A dietitian discusses the theory that peptides with opioid activity may cause or trigger autism. The use of an exclusion diet to treat autism is explained, weighing the potential benefits against some of the practical difficulties of keeping to a strict exclusion diet. The use of nutritional supplements is described. An abnormal gut flora has also been implicated in autism and the use of probiotics and prebiotics in improving the integrity of the gut mucosa is also discussed. ( 25 Refs.)

Descriptors: \*Autistic Disorder--diet therapy--DH; \*Autistic Disorder--etiology--ET; \*Dietary Proteins--adverse effects--AE ; Autistic Disorder--physiopathology--PP; Child; Dairy Products; Dietary Proteins--metabolism--ME; Dietary Supplements; Glutens; Humans

CAS Registry No.: 0 (Dietary Proteins); 8002-80-0 (Glutens)

Record Date Created: 20021105

Record Date Completed: 20021122

## **Innate immunity associated with inflammatory responses and cytokine production against common dietary proteins in patients with autism spectrum disorder.**

Jyonouchi Harumi; Sun Sining; Itokazu Nanae

Department of Pediatrics, University of Minnesota, Minneapolis, Minn, USA.

Neuropsychobiology ( Switzerland ) 2002 , 46 (2) p76-84 , ISSN: 0302-282X-

-Print Journal Code: 7512895

Publishing Model Print

Document type: Clinical Trial; Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

**OBJECTIVES:** Children with autism spectrum disorder (ASD) frequently reveal various gastrointestinal (GI) symptoms that may resolve with an elimination diet along with apparent improvement of some of the behavioral symptoms. Evidence suggests that ASD may be accompanied by aberrant (inflammatory) innate immune responses. This may predispose ASD children to sensitization to common dietary proteins (DP), leading to GI inflammation and aggravation of some behavioral symptoms. **METHODS:** We measured IFN-gamma, IL-5, and TNF-alpha production against representative DPs [gliadin, cow's milk protein (CMP), and soy] by peripheral blood mononuclear cells (PBMCs) from ASD and control children [those with DP intolerance (DPI), ASD siblings, and healthy unrelated children]. We evaluated the results in association with proinflammatory and counter-regulatory cytokine production with endotoxin (LPS), a microbial product of intestinal flora and a surrogate stimulant for innate immune responses.

**RESULTS:** ASD PBMCs produced elevated IFN-gamma and TNF-alpha, but not IL-5 with common DPs at high frequency as observed in DPI PBMCs. ASD PBMCs revealed increased proinflammatory cytokine responses with LPS at high frequency with positive correlation between proinflammatory cytokine production with LPS and IFN-gamma and TNF-alpha production against DPs. Such correlation was less evident in DPI PBMCs. **CONCLUSION:** Immune reactivity to DPs may be associated with apparent DPI and GI inflammation in ASD children that may be partly associated with aberrant innate immune response against endotoxin, a product of the gut bacteria. Copyright 2002 S. Karger AG, Basel

Tags: Female; Male

Descriptors: \*Autistic Disorder--immunology--IM; \*Autistic Disorder--metabolism--ME; \*Cytokines--biosynthesis--BI; \*Dietary Proteins--adverse effects--AE; \*Dietary Proteins--immunology--IM; \*Food Hypersensitivity--immunology--IM; \*Inflammation--immunology--IM ; Adolescent; Child; Child, Preschool; Enzyme-Linked Immunosorbent Assay; Gliadin--adverse effects--AE; Gliadin--immunology--IM; Humans; Infant; Interferon-gamma--biosynthesis--BI; Interleukin-5--biosynthesis--BI; Intestinal Mucosa--immunology--IM; Lipopolysaccharides--pharmacology--PD; Milk Proteins--adverse effects--AE; Milk Proteins--immunology--IM; Monocytes--immunology--IM; Soybean Proteins--adverse effects--AE; Soybean Proteins--immunology--IM; T-Lymphocytes--immunology--IM; T-Lymphocytes --metabolism--ME; Tumor Necrosis Factor-alpha--biosynthesis--BI

CAS Registry No.: 0 (Cytokines); 0 (Dietary Proteins); 0 (Interleukin-5); 0 (Lipopolysaccharides); 0 (Milk Proteins); 0 (Soybean Proteins); 0 (Tumor Necrosis Factor-alpha); 82115-62-6 (Interferon-gamma); 9007-90-3 (Gliadin)

Record Date Created: 20021014

Record Date Completed: 20021125

## **Relation of childhood gastrointestinal disorders to autism: nested case-control study using data from the UK General Practice Research Database.**

Black Corri; Kaye James A; Jick Hershel  
Boston Collaborative Drug Surveillance Program, Boston University School of Medicine, MA 02421, USA. cxb2@ph.abdn.ac.uk  
BMJ (Clinical research ed.) ( England ) Aug 24 2002 , 325 (7361) p419-21 ,  
ISSN: 1468-5833--Electronic Journal Code: 8900488  
Publishing Model Print  
Document type: Journal Article; Research Support, Non-U.S. Gov't  
Languages: ENGLISH  
Main Citation Owner: NLM  
Other Citation Owner: NLM  
Record type: MEDLINE; Completed  
Subfile: AIM; INDEX MEDICUS  
OBJECTIVES: To assess whether children with autism are more likely to have a history of gastrointestinal disorders than children without autism. DESIGN: Nested case-control study. SETTING: UK General Practice Research Database. SUBJECTS: Children born after 1 January 1988 and registered with the General Practice Research Database within 6 months of birth. OUTCOME MEASURES: Chronic inflammation of the gastrointestinal tract, coeliac disease, food intolerance, and recurrent gastrointestinal symptoms recorded by the general practitioner. RESULTS: 9 of 96 (9%) children with a diagnosis of autism (cases) and 41 of 449 (9%) children without autism (matched controls) had a history of gastrointestinal disorders before the index date (the date of first recorded diagnosis of autism in the cases and the same date for controls). The estimated odds ratio for a history of gastrointestinal disorders among children with autism compared with children without autism was 1.0 (95% confidence interval 0.5 to 2.2). CONCLUSIONS: No evidence was found that children with autism were more likely than children without autism to have had defined gastrointestinal disorders at any time before their diagnosis of autism.  
Tags: Female; Male  
Descriptors: \*Autistic Disorder--etiology--ET; \*Gastrointestinal Diseases--complications --CO ; Case-Control Studies; Celiac Disease--complications--CO; Child; Child, Preschool; Chronic Disease; Food Hypersensitivity--complications--CO; Gastroenteritis--complications--CO; Humans; Odds Ratio; Recurrence  
Record Date Created: 20020823  
Record Date Completed: 20020926

## **An audit of referrals of children with autistic spectrum disorder to the dietetic service.**

Bowers L  
Llanfrechfa Grange Hospital, Gwent Healthcare NHS Trust, Cwmbran, UK.  
sue.cullen@gwent.wales.nhs.uk  
Journal of human nutrition and dietetics - the official journal of the British Dietetic Association ( England ) Apr 2002 , 15 (2) p141-4 , ISSN: 0952-3871--Print  
Journal Code: 8904840  
Publishing Model Print  
Document type: Journal Article  
Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Autistic spectrum disorder (ASD) is a developing area for dietetic referrals. There is little published data on current dietetic practice. Some children with ASD are referred for gluten/casein free diet. The theory is that abnormal metabolites in the urine may be a result of incomplete breakdown of gluten and casein in the gut. There are some published open studies that support the efficiency of such a diet [Knivsberg et al. (1995) Scand. J. Educ. Res.39: 223; Lucarelli et al. (1995) Panminerva Med.37: 137; Whiteley et al. (1999) Int. J. Res. Practice 3: 45] and also that there are many anecdotal reports that the diet helps some children.

**AIMS AND OBJECTIVES:** This study aimed to audit the types of referral made to the dietetic service to identify key dietetic issues and to describe factors which may influence outcome/disease management.

**METHODS:** Dietetic records were used to audit the referrals to the dietetic service over a 3-month period. Seven-day diet histories were assessed using computer food composition tables and topics of interest recorded against a draft protocol agreed within the profession.

**RESULTS:** Requests for gluten-free and casein-free dietetic advice, and/or the management of food selectivity and dysfunctional feeding behaviour constituted the majority of referrals. In many cases, child's environment was rarely simple.

**CONCLUSIONS:** Despite the limitations of this small study, the findings suggest that the management of these referrals is highly complex. A dietitian's input should ensure that the nutritional adequacy of the diet is maintained or restored.

**Descriptors:** \*Autistic Disorder--diet therapy--DH; \*Caseins--administration and dosage --AD; \*Dietary Services--utilization--UT; \*Glutens--administration and dosage--AD; \*Referral and Consultation--statistics and numerical data--SN ;

Autistic Disorder--metabolism--ME; Caseins--metabolism--ME; Child; Diet Records; Food Analysis; Glutens--metabolism--ME; Humans; Medical Audit;

Nutritional Requirements; Treatment Outcome; Utilization Review

CAS Registry No.: 0 (Caseins); 8002-80-0 (Glutens)

Record Date Created: 20020425

Record Date Completed: 20020802

## **Review article: the concept of entero-colonic encephalopathy, autism and opioid receptor ligands.**

Wakefield A J; Puleston J M; Montgomery S M; Anthony A; O'Leary J J; Murch S H  
Inflammatory Bowel Disease Study Group, Centre for Gastroenterology,  
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Alimentary pharmacology & therapeutics ( England ) Apr 2002 , 16 (4) p663-74 , ISSN: 0269-2813--Print Journal Code: 8707234

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxibib

There is growing awareness that primary gastrointestinal pathology may play an important role in the inception and clinical expression of some childhood developmental disorders, including autism. In addition to frequent gastrointestinal symptoms, children with autism often manifest complex biochemical and immunological abnormalities. The gut-brain axis is central to certain encephalopathies of extra-cranial origin, hepatic encephalopathy being the best characterized. Commonalities in the clinical characteristics of hepatic

encephalopathy and a form of autism associated with developmental regression in an apparently previously normal child, accompanied by immune-mediated gastrointestinal pathology, have led to the proposal that there may be analogous mechanisms of toxic encephalopathy in patients with liver failure and some children with autism. Aberrations in opioid biochemistry are common to these two conditions, and there is evidence that opioid peptides may mediate certain aspects of the respective syndromes. The generation of plausible and testable hypotheses in this area may help to identify new treatment options in encephalopathies of extra-cranial origin. Therapeutic targets for this autistic phenotype may include: modification of diet and entero-colonic microbial milieu in order to reduce toxin substrates, improve nutritional status and modify mucosal immunity; anti-inflammatory/immunomodulatory therapy; and specific treatment of dysmotility, focusing, for example, on the pharmacology of local opioid activity in the gut. ( 121 Refs.)

Descriptors: \*Autistic Disorder--etiology--ET; \*Celiac Disease--complications--CO; \*Hepatic Encephalopathy--complications--CO; \*Neuroimmunomodulation; \*Receptors, Opioid--metabolism--ME ; Autistic Disorder--immunology--IM; Autistic Disorder--metabolism--ME; Blood-Brain Barrier--immunology--IM; Celiac Disease--immunology--IM; Celiac Disease--metabolism--ME; Child; Hepatic Encephalopathy--immunology --IM; Hepatic Encephalopathy--metabolism--ME; Humans; Immunity, Mucosal --immunology--IM; Intestinal Absorption--immunology--IM; Ligands; Opioid Peptides--immunology--IM; Opioid Peptides--metabolism--ME; Receptors, Opioid--immunology--IM  
CAS Registry No.: 0 (Ligands); 0 (Opioid Peptides); 0 (Receptors, Opioid)  
Record Date Created: 20020403  
Record Date Completed: 20020906

## **Autism, an extreme challenge to integrative medicine. Part II: Medical management**

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Alternative Medicine Review ( Altern. Med. Rev. ) ( United States ) December 1, 2002 , 7/6 (472-499)

PUBLISHER: Thorne Research Inc.

CODEN: ALMRF ISSN: 1089-5159

DOCUMENT TYPE: Journal ; Review RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 130

Autism and allied autistic spectrum disorders (ASD) present myriad behavioral, clinical, and biochemical abnormalities. Parental participation, advanced testing protocols, and eclectic treatment strategies have driven progress toward cure. Behavioral modification and structured education are beneficial but insufficient. Dietary restrictions, including removal of milk and other casein dairy products, wheat and other gluten sources, sugar, chocolate, preservatives, and food coloring are beneficial and prerequisite to benefit from other interventions. Individualized IgG or IgE testing can identify other troublesome foods but not non-immune mediated food sensitivities. Gastrointestinal improvement rests on controlling Candida and other parasites, and using probiotic bacteria and nutrients to correct dysbiosis and decrease gut permeability. Detoxification of mercury and other heavy metals by DMSA/DMPS chelation can have marked benefit. Documented sulfoxidation-sulfation inadequacies call for sulfur-sulphydryl

repletion and other liver p450 support. Many nutrient supplements are beneficial and well tolerated, including dimethylglycine (DMG) and a combination of pyridoxine (vitamin B6) and magnesium, both of which benefit roughly half of ASD cases. Vitamins A, B3, C, and folic acid; the minerals calcium and zinc; cod liver oil; and digestive enzymes, all offer benefit. Secretin, a triggering factor for digestion, is presently under investigation. Immune therapies (pentoxifyllin, intravenous immunoglobulin, transfer factor, and colostrum) benefit selected cases. Long-chain omega-3 fatty acids offer great promise. Current pharmaceuticals fail to benefit the primary symptoms and can have marked adverse effects. Individualized, indepth clinical and laboratory assessments and integrative parent-physician-scientist cooperation are the keys to successful ASD management.

**DESCRIPTORS:**

\* autism; \*integrative medicine adolescent; adverse drug reaction; aggression; agitation; akathisia; anxiety disorder; appetite disorder; ascorbic acid; atypical antipsychotic agent; autonomic dysfunction; bacterium; behavior disorder; behavior modification; body weight disorder; cacao; calcium; Candida; cardiovascular disease; casein; chelation; child; clinical article; clinical feature; clozapine; cod liver oil; colostrum; cooperation; cytochrome P450; dairy product; detoxification; diet restriction; diet supplementation; digestion; dimethylglycine; dopamine receptor blocking agent; drowsiness; drug tolerability; dyskinesia; dystonia; education; enzyme; fatigue; female; folic acid; food; food analysis; food composition; food dye; gastrointestinal absorption; gastrointestinal tract function; gluten; haloperidol; headache; heart atrium septum defect; heavy metal; human; hypotension; immunoglobulin; immunoglobulin E; immunoglobulin G; immunotherapy; individualization; intestine; laboratory; laboratory diagnosis; lethargy; liver; liver disease; magnesium; male; mercury; milk; mineral; nausea; nicotinamide; nutrient; omega 3 fatty acid; parasite; parasitosis; parent; parkinsonism; pentoxifylline; permeability; physician; preservative; probiotic agent; pyridoxine; restlessness; retinol; risperidone; scientist; secretin; sedation; sleep disorder; sulfation; sulfoxidation; sulfur; symptomatology; tardive dyskinesia; teamwork; thiol derivative; transfer factor; vitamin; vomiting; weight gain; wheat; zinc

## **Measles, mumps, and rubella vaccination and bowel problems or developmental regression in children with autism: Population study**

Taylor B.; Miller E.; Lingam R.; Andrews N.; Simmons A.; Stowe J.  
Centre for Community Child Health, Royal Free and Univ. Coll. Med. Sch., Univ. Coll. London Royal Free Campus, London NW3 2PF, United Kingdom  
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British Medical Journal ( Br. Med. J. ) ( United Kingdom ) February 16, 2002 , 324/7334 (393-396)

PUBLISHER: BMJ Publishing Group

CODEN: BMJOA ISSN: 0959-8146

DOCUMENT TYPE: Journal ; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 14

Objectives: To investigate whether measles, mumps, and rubella (MMR) vaccination is associated with bowel problems and developmental regression in

children with autism, looking for evidence of a "new variant" form of autism. Design: Population study with case note review linked to independently recorded vaccine data. Setting: Five health districts in north east London. Participants: 278 children with core autism and 195 with atypical autism, mainly identified from computerised disability registers and born between 1979 and 1998. Main outcome measures: Recorded bowel problems lasting at least three months, age of reported regression of the child's development where it was a feature, and relation of these to MMR vaccination. Results: The proportion of children with developmental regression (25% overall) or bowel symptoms (17%) did not change significantly (P value for trend 0.50 and 0.47, respectively) during the 20 years from 1979, a period which included the introduction of MMR vaccination in October 1988. No significant difference was found in rates of bowel problems or regression in children who received the MMR vaccine before their parents became concerned about their development (where MMR might have caused or triggered the autism with regression or bowel problem), compared with those who received it only after such concern and those who had not received the MMR vaccine. A possible association between non-specific bowel problems and regression in children with autism was seen but this was unrelated to MMR vaccination. Conclusions: These findings provide no support for an MMR associated "new variant" form of autism with developmental regression and bowel problems, and further evidence against involvement of MMR vaccine in the initiation of autism.

**DESCRIPTORS:**

\* autism; \*child; \*intestine; \*measles; \*mumps; \*population research; \*rubella; \*vaccination child development; childhood disease; constipation; developmental disorder; diarrhea; disability; disease association; disease course; disease exacerbation; disease severity; drug safety; enteropathy; food allergy; health; human; major clinical study; measles mumps rubella vaccine; measles vaccination; mental deficiency; parent; priority journal; register; regression analysis; speech disorder; statistical significance; United Kingdom; vaccine

## **Metabolic approaches to the treatment of autism spectrum disorders.**

Page T

Department of Neurosciences, University of California, San Diego, USA.

Journal of autism and developmental disorders ( UNITED STATES ) Oct 2000 , 30 (5) p463-9 , ISSN: 0162-3257--Print Journal Code: 7904301

Publishing Model Print; Comment in J Autism Dev Disord. 2000 Oct;30(5) 471-3; Comment in PMID 11098886

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Although the exact prevalence of metabolic abnormalities in autism spectrum disorders is unknown, several metabolic defects have been associated with autistic symptoms. These include phenylketonuria, histidinemia, adenylosuccinate lyase deficiency, dihydropyrimidine dehydrogenase deficiency, 5'-nucleotidase superactivity, and phosphoribosylpyrophosphate synthetase deficiency. When the metabolic consequences of an enzyme defect are well defined (e.g., phenylketonuria, 5'-nucleotidase superactivity), treatment with diet, drugs, or nutritional supplements may bring about a dramatic reduction in autistic symptoms. This review evaluates evidence for metabolic etiologies in autism spectrum disorders, as well as for the efficacy of dietary and vitamin treatments.

The relationship between gastrointestinal abnormalities and autism spectrum disorders is also considered.

Descriptors: \*Autistic Disorder--metabolism--ME ; Autistic Disorder--drug therapy--DT; Autistic Disorder--genetics--GE; Child, Preschool; Humans; Vitamins--therapeutic use--TU

CAS Registry No.: 0 (Vitamins)

Record Date Created: 20010405

Record Date Completed: 20010628

## **Sulphur metabolism in autism**

Waring R.H.; Klovrcza L.V.

School of Biosciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom

CORRESP. AUTHOR/AFFIL: Waring R.H.: School of Biosciences, University of Birmingham, Birmingham B15 2TT, United Kingdom

Journal of Nutritional and Environmental Medicine ( J. Nutr. Environ. Med. ) ( United Kingdom ) April 26, 2000 , 10/1 (25-32)

PUBLISHER: Carfax Publishing Company

CODEN: JNEMF ISSN: 1359-0847

DOI: 10.1080/13590840050000861

Item Identifier (DOI): 10.1080/13590840050000861

DOCUMENT TYPE: Journal ; Review RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 43

Purpose: Previous studies in autistic children have shown that they have reduced levels of plasma sulphate as compared with age-matched control children and the aim of this study was to see if this reflected increased urinary sulphate loss.

Design: Outpatient-based survey of autistic children and matched controls.

Materials and methods: The children in the study were elected on the basis of ICD-10 criteria and a diagnosis of autism. Use of a behavioural questionnaire allowed children with autism to be divided into 3 subsets. Urinary excretion of sulphate, sulphite, thiosulphate and thiocyanate was measured in 232 autistic children and compared with values from 68 age-matched controls. Results:

Autistic children excreted higher levels of sulphate, sulphite and thiosulphate, but reduced levels of thiocyanate. Conclusions: The significance of these altered parameters is discussed with respect to catecholamine metabolism, mucin formation, gastrointestinal hormone activation and sulphur anion metabolism.

DESCRIPTORS:

\* amine; \*autism; \*diet; \*gastrin; \*gastrointestinal tract; \*metabolism; \* phenol derivative; \*protein; \*secretin; \*sulfate; \*sulfur anion; blood level; catecholamine; catecholamine metabolism; child; controlled study; diagnosis; disease classification; gastrointestinal hormone; human; infantile autism; major clinical study; mucin; normal human ; outpatient; plasma; priority journal; questionnaire; sulfite; thiocyanate ; thiosulfate; urinary excretion

## **Abnormal intestinal permeability in children with autism.**

D'Eufemia P; Celli M; Finocchiaro R; Pacifico L; Viozzi L; Zaccagnini M; Cardi E; Giardini O

Institute of Pediatrics, La Sapienza University of Rome, Italy.

Acta paediatrica (Oslo, Norway - 1992) ( NORWAY ) Sep 1996 , 85 (9) p1076-9 , ISSN: 0803-5253--Print Journal Code: 9205968

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We determined the occurrence of gut mucosal damage using the intestinal permeability test in 21 autistic children who had no clinical and laboratory findings consistent with known intestinal disorders. An altered intestinal permeability was found in 9 of the 21 (43%) autistic patients, but in none of the 40 controls. Compared to the controls, these nine patients showed a similar mean mannitol recovery, but a significantly higher mean lactulose recovery (1.64% +/- 1.43 vs 0.38% +/- 0.14;  $P < 0.001$ ). We speculate that an altered intestinal permeability could represent a possible mechanism for the increased passage through the gut mucosa of peptides derived from foods with subsequent behavioural abnormalities.

Tags: Female; Male

Descriptors: \*Autistic Disorder--physiopathology--PP; \*Gastrointestinal Diseases - -etiology--ET; \*Intestinal Absorption ; Adolescent; Autistic Disorder--complications--CO; Biological Transport; Case-Control Studies; Child; Child, Preschool; Humans; Intestinal Mucosa; Lactulose--pharmacokinetics--PK; Mannitol--pharmacokinetics--PK

CAS Registry No.: 4618-18-2 (Lactulose); 69-65-8 (Mannitol)

Record Date Created: 19970107

Record Date Completed: 19970107

## **Behavioral medicine treatment of ruminative vomiting and associated weight loss in an adolescent with autism**

Author: Luiselli James K (Reprint); Medeiros Joann; Jasinowski Carol; Smith Ann; Cameron Michael J

Author Address: Psychol. and Educ. Resource Associates, 40 Bronson Way, Concord, MA 01742, USA\*\*USA

Journal: Journal of Autism and Developmental Disorders 24 ( 5 ): p 619-629  
1994 1994

ISSN: 0162-3257

Document Type: Article

Record Type: Abstract

Language: English

Abstract: Treated persistent ruminative vomiting of a 15-year-old boy with autism using a multicomponent behavioral medicine program within a residential facility. Preceding intervention the boy had lost 15 pounds associated with high-rate ruminating. The treatment program included a combination of dietary, nutritional, and behavioral procedures that emphasized food restrictions, satiation, and setting condition manipulations. Ruminative vomiting was reduced to near-zero levels and weight gain was achieved following treatment implementation. These therapeutic gains were sustained during a maintenance programming phase and at 1- through 4-month follow-up assessments. Issues related to functional assessment and treatment formulation in behavioral medicine intervention for ruminative vomiting are discussed.

DESCRIPTORS:

Major Concepts: Behavior; Gastroenterology--Human Medicine, Medical Sciences; Pediatrics-- Human Medicine, Medical Sciences; Physiology; Psychiatry--Human Medicine, Medical Sciences

Biosystematic Names: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

Organisms: Hominidae (Hominidae)

Common Taxonomic Terms: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

Miscellaneous Terms: Concept Codes: FOOD RESTRICTION; MENTAL RETARDATION; SATIATION; THERAPEUTIC INTERVENTION

## **Response of intestinal mucosa to gluten challenge in autistic subjects.**

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Eight autistic patients with steatorrhea, hypocalciuria, and alleged behavioural improvements on gluten restriction, were fed ordinary diets plus 20 g gluten/day for 4 weeks. None of the patients had any significant change in body-weight or bowel habit as a result of gluten challenge, nor were any histological abnormalities detected on jejunal biopsy. The data suggest that the steatorrhea and hypocalciuria seen in some autistic subjects cannot be accounted for by the presence of coeliac disease. Furthermore, these patients should not be confined to gluten-free diets, unless rigorous behavioural studies demonstrate a statistically significant improvement in behaviour as a result of the diet, or deterioration during challenge.

Descriptors: \*Autistic Disorder--complications--CO; \*Glutens--toxicity--TO; \*Intestinal Mucosa--pathology--PA; \*Jejunum--pathology--PA ; Autistic Disorder--diet therapy--DH; Autistic Disorder--pathology--PA; Calcium--urine--UR; Calcium Metabolism Disorders--etiology--ET; Celiac Disease--complications--CO; Celiac Disease--diagnosis--DI; Child; Glutens --administration and dosage--AD; Humans  
CAS Registry No.: 7440-70-2 (Calcium); 8002-80-0 (Glutens)

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