Potential Treatment of Autism with Traditional Chinese Medicine

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In 2002 the Center for Disease Control estimated that autism affected about 1 in 150 children. By 2012 the CDC estimate had increased to 1 in 88. Now, according to the latest revision of the estimate recently released, autism affects 1 in 50 children.
Autism: The Facts

• Fastest growing developmental disability
• Annual growth 10-17%
• 1/10000 in 1960’s, now 1/50 in USA
• More children was diagnosed with Autism this year than with Cancer, diabetes and AIDS combined
• Boy: girl 4:1
• Autism cost nation over $35 billion per year
• CDC has called autism a national public health crisis
Intrusion of an experience for you and for many others

1200% increase in reported cases

Gene expression impacted by environment

Autism is a Whole-Body, Whole-System Condition

- Seizures (~30%+)
- Cognitive deficits
- Sensorimotor abnormalities
- Disordered sleep
- Immune impairments
- GI distress
- Food allergies
- Systemic metabolic disturbances
Autism: The Facts

How much do we know about the etiology of Autism? Identified etiology is only 10%!

Do we have clues for the rest of 90%?

Autism and Genes
Brain Pathology-Selective area/Neurotransmitters
GI dysfunction
Immune dysfunction
Impaired detoxification system
Toxic exposure/increased burden
Inflammation and oxidative stress
The immune response in autism: a new frontier for autism research.

Ashwood P, Wills S, Van de Water J.
UC Davis, Wet Lab Building, 50th Street, Sacramento, CA 95817.
(partial abstract)
There is potential that such aberrant immune activity during vulnerable and critical periods of neurodevelopment could participate in the generation of neurological dysfunction characteristic of ASD. This review will examine the status of the research linking the immune response with ASD.
Immune dysfunction in Autism

1. Allergy problem/Autoimmune dysfunction

Eczema as marker of Th2 shift
Allergic rhinitis, seasonal exacerbation
Asthma
Food allergy
Cerebral autoimmunity, antibodies detected, Myelin basic Ab, etc

2. Chronic low grade infections
Bacteria, strep. elevated urinary bacterial metabolites in 50% patients
PANDAS (pediatric autoimmune neuropsychiatric disorder associated with streptococcus) OCD
Fungal, dermatitis, candidiasis
Virus, MMR, HSV, EBV, HPV warts,
Mycoplasma, gulf war phenomenon
Lyme

3. Chronic inflammation
Cytokines elevation

4. Immunogenomic profile

IL-1beta almost 100% with mutation in autism
TH-1 cytokine—TNF-alpha, viral infection and cancer
TH-2 cytokines--- IL-4,6,10,13, allergy/atopy
Autism: New Research Frontier

• Autism represents an immunological and inflammatory disorder with definable biomarkers, mainly targeting GI and Brain
The Every Day of Some Autisms

*What we need:* Clinical labs that will detect and report pertinent gut pathogens
Gut dysfunction in Autism

Chronic diarrhea
Food allergy/sensitivity
Endoscopy: inflammation
Infection: bacteria, yeast, virus

Stool analysis: Maldigestion and Malabsorption

Leak bowel syndrome
GI enzyme deficiency, Secretin, DDP-IV
Urinary peptides
Nutritional deficiency
Low B6 50%
Low Magnesium almost 100%
Low zinc almost 100%
Low selenium, vitamin A, biotin, B1, B3, B5, B12, Vitamin C,
Immune dysfunction in Autism

There is potential that aberrant immune activity during vulnerable and critical period of neurodevelopment could participate in the generation of neurological dysfunction characteristic of ASD.

Immune dysfunction in Autism: A New Frontier for Autism Research

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   Eczema as marker of Th2 shift
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   Immunological profile

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   Fungal, dermatitis, candidiasis
   Virus, MMR, HSV, EBV, HPV warts
   Mycoplasma
   Lyme

3. Chronic inflammation

   Cytokines elevation
Changes of Plasma Cytokine Profiles in Subjects with High-Functioning Autism Spectrum Disorders

K. Suzuki et al., PLOS/one, 2011
Intestinal immune changes lead to increased intestinal permeability
Intestinal Lymphocyte Populations in Children with Regressive Autism: Evidence for Extensive Mucosal Immunopathology


PAUL ASHWOOD,¹,²,⁶ ANDREW ANTHONY,¹,³ ALICIA A. PELLICER,² FRANCO TORRENTE,²,⁴ JOHN A. WALKER-SMITH,² and ANDREW J. WAKEFIELD¹,⁵
PRBC testing often reveals deficiencies in zinc and selenium

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- Tells us where to begin with supplements
- Easy to follow over time
Immune dysregulation Especially in the GI tract and Brain
Neuroglial Activation particularly in cerebellum

Responses are primarily from Innate Immunity

Adaptive immunity markers like T cells or antibody reactions not found

Cytokines significantly elevated in brain and CSF of autistic patients

Pro-inflammatory: MCP-1, IL6 and IFNgamma

Anti-inflammatory: TGFbeta1
Brain cells in inflammation

- Excitatory chemicals created by activated glial cells
- Normal housekeeping functions of glial cells get neglected
- Chronic inflammation is irritating and promotes excitotoxicity
- Chronic inflammation can cause damage

Inflammation and Its Discontents: The Role of Cytokines in the Pathophysiology of Major Depression. Miller et al., BIOL PSYCHIATRY 2009;65:732–741
Neuropathology of Brain

1. Enlarged brain size in autistic children
   Autopsy data: 5-13 years old, fresh brain weight increase by 100-200g when compared with expected age and sex, 20% head circumferences over 97th percentile, mostly above average.

2. Overgrowth and enlargement of white matter
   Axon and myelination process (Herbert, MGH)

3. Evidence of inflammation and oxidative stress in autistic brain tissue from childhood and middle age
   (Ann Neurol 57:67-81,2005)

Brain Inflammation in Autism

Neuroglial Activation particularly in cerebellum

Responses are primarily from Innate Immunity

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Cytokines significantly elevated in brain and CSF of autistic patients

Pro-inflammatory: MCP-1, I-L6 and IFNγ

Anti-inflammatory: TGFβ1
Autism Treatments:

Traditional:
Behavioral and educational training
Medications

Biochemical and Alternative
Diet and nutritional supplement
Treatment for infection
Chelation
Immunomodulation: LDN, Actos
RNA therapy
TMS
Stem cell
Current Medications for Autism

There is no known cure for autism and not everyone with Autism has the same symptoms, and not all symptoms can be treated with the same drugs.

Most often, the prescription is intended to address specific symptoms such as anxiety, depression, mood swings (bipolar disorder), obsessions, compulsions, inattention, and hyperactivity.

SSRIs
Antipsychotics
Anticonvulsants
Stimulants.

Because these medications give only symptomatic relief, and there is a large individual differences, therefore clinical improvement is quite limited.
Osteoarthritis

• It is estimated that Osteoarthritis (OA) alone will reach 7 billion and the total market size for arthritis drug will reach 20 billion in 2010.

• Modern COX2 type anti-inflammatory drug, such as (Vioxx) was recalled by FDA in 2004 and currently there is no effective prescription drug for OA.
Traditional Chinese Medicine (HLXL) for Osteoarthritis

HLXL (Huo-Luo-Xiau-Lin Dan): A Traditional Chinese Remedy which consists of 11 herbs for treatment of arthritis

HLXL has been studied in the US for over 10 years and funded continuously by NIH (NCCAM-AT-P01-002605)

HLXL is under Phase II Trial (IND#70324) in the US
HLXL modulates the T cell proliferative and cytokine responses to Bhsp65 of arthritic LEW rats.

LNC of arthritic rats harvested on d 7 after initiation of the daily feeding of HLXL or water were tested for their T cell proliferative (A) and cytokine response (B-D) to antigenic re-stimulation with Bhsp65 in vitro. Ova served as the control antigen.
Effect of HLXL on IL-1β and TNF-α levels (pg/mg protein, Mean ± S.E.) 25 days post-CFA injection.

Tissue was obtained from four groups of rats: group N (no arthritis + vehicle treatment, n=4), group H4.6 (arthritis + HLXL treatment at 4.60g/kg/day, n=7), group H2.3 (arthritis + HLXL treatment at 2.30g/kg/day n=6), and group C (arthritis + vehicle treatment n= 6). Data showed that both IL-1β and TNF-α increased significantly in local tissue following development of arthritis. However, after HLXL treatment, local tissue IL-1β and TNF-α decreased significantly, *p<0.05 and **p<0.01, compared to the vehicle control (Group C).
Effect of HLXL on Arthritis in Rats
(Arthritic Scores: Mean ± S.E., n = 4/group)
HLXL: Mechanism of Actions

**Arthritis**

- **Pathogenic cytokines produced by the mononuclear cells (IL-1, TNF-α, IL-17)**
- **Disease-regulating cytokines (IL-10, IFN-γ*)**
- **Activation and proliferation of antigen (Bhsp-65)-reactive effector T cells**
- **Antibodies against the disease-related antigen, Bhsp65 (anti-Bhsp65)**
- **Cox2**
- **5-LPO**
- **Biochemical mediator of inflammation (Nitric oxide)**

**Induction**

- Green

**Inhibition**

- Pink
TCM for Treatment of Human Diseases

1. A large number of bioactive natural products with medium potencies vs highly potent single chemical entity

2. A multi-components and multi-targeted vs single targeted approach

3. Re-discovery the wisdom of traditional Chinese medicine
Summary

• Autism represents an immunological and inflammatory disorder with definable biomarkers, mainly targeting GI and Brain

• Application of clinical measures to address the abnormalities identified by the biomarkers would be a viable approach for treatment of Autism

• Evidence based TCM with immune-modulatory and anti-inflammatory activities such as HLXL may have the potential as an alternative treatment for Autism
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