Autism and paleodiets

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I would like to respond to Moira's post which indicated improvement in symptoms in an Autistic child following adoption of a paleodiet.

Autism in children is a neuro-developmental disorder characterized by few or no language and imaginative skills, repetitive-rocking and self-injurious behavior, and abnormal responses to sensations, people, events and objects. The cause of the syndrome is unknown, but there is increasing evidence that it may be auto-immune in nature. Reed Warren's group (1) found that 58% of autistic children maintained antibodies to myelin basic protein (a protein found in the myelin sheaths of nerves and suspected of being the target protein = [self antigen] for T-lymphocytes in the autoimmune disease, Multiple Sclerosis). Additional support for the concept that Autism may be autoimmune in nature comes from work showing that 46% of autistic children maintain major histocompatibility complex (MHC) alleles associated with the disease (2). The function of the MHC is to = present self and foreign peptides to circulating T-lymphocytes at the surface = of all cells throughout the body. Thus, if foreign peptides are = presented by the MHC, circulatingT-lymphocytes can mount an immune response on the cell or cells which present, via the MHC, that foreign peptide and destroy them.

The MHC not only presents foreign peptides, but it also presents peptides derived from the proteins of genes comprising the MHC itself. The susceptiblity genes for autism are: DRB1*0404, DRB1*401 and DRB1*0101 (2). In a particular portion of these genes (the third hypervariable region [HVR-3]), there is a common amino acid sequence shared by all three genes. This amino acid sequence is either QKRAA (glutamine-lysine-arginine-arginine-alanine-alanine) or QRRAA. Thus, either the QKRAA amino acid motif or the QRRAA amino acid motif can be presented to circulating T-lymphocytes. This particular shared epitope increases the susceptibility to a number of autoimmune = diseases, including rheumatoid arthritis (3).

The QKRAA or QRRAA amino acid motif also occurs quite frequently in pathogens which reside in the human gastro-intestinal tract = including Escherichia coli, Proteus mirabilis, lactobacillus lactis, Brucella = ovis and many other anaerobic gut bacteria (3). The QKRAA or QRRAA sequences are found specifically in a particular type of protein contained in gut bacteria, called DnaJ proteins. DnaJ proteins normally have a bacterial partner/ligand protein called heat shock proteins (HSP70). It is the QKRAA or QRRAA amino acid sequence of DnaJ which allows it to bind HSP70.=20

When the MHC presents endogenously derived DRB1 alleles which contain the QKRAA or QRRAA amino acid motif, then circulating HSP70 proteins (which normally bind DnaJ proteins) can bind the body's own = MHC presented QKRAA or QRRAA sequences. Circulating CD4+ T-lymphocytes

recognize this HSP70/QRRAA sequence as foreign and mount an immune response on all cells presenting this (HSP70) amino acid motif.

We believe that myelin basic protein contains an amino acid sequence that is homologous to an A.A. sequence found in HSP70, and it is this three way mimicry between DRB1 peptides, bacterial peptides and self peptides which causes self tolerance to be broken.

So, how does a paleodiet have anything to do with this process? Paleodiets are characterized by their lack of cereal grains, legumes, dairy products, and yeast containing foods. Both cereal grains and legumes contain glycoproteins called lectins which bind intestinal epithelial cells and change the permeability characteristics of these intestinal cells (4,5). Not only do these lectins cause an increase = of
the translocation of gut bacteria to the peripheracy, they cause an increased overgrowth of gut bacteria as well as a change in the gut flora (4,5). Further, cereal and legume derived lectins (WGA, PHA respectively) cause increased expression of intracellular adhesion molecules (ICAM) in lymphocytes (6) which allow bacterial/immune complexes to move from gut to the affected tissue. Additionally, cereal and legume lectins increase lymphocytic expression of common inflammatory cytokines such as tumor necrosis factor alpha (TNFa), interleukin 1 (IL-1) and IL-6 which are known promoters of autoimmune disease.

The cell walls of cereals and legumes contain a storage protein, GRP 180, which also can act as a ligand to self presented MHC peptides (7). Further, peptides contained in dairy proteins (bovine serum albumins - BSA, among many) also may contain peptide sequences which = can
interact with endogenously presented peptides (8). Cereal, legume, dairy and yeast free diets potentially have therapeutic benefit in many autoimmune related disorders via their ability to reduce gut permeability and decrease the exogenous antigenic load both from pathogenic bacteria and from potentially self mimicking dietary peptides.

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