Written Public Comments

IACC Full Committee Meeting

January 29, 2013

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Brad Trahan

December 18, 2012

Subject: Public comment from a dad in Minn

Autism, is the fastest growing disability our nation faces today! However, it is also a disability, while complex, that parents and caregivers throughout our nation struggle with day in and day out for any type of relief! Our nation needs to see a sense of urgency as it relates to many services affecting individuals and families affected by this diagnosis.

One area that the IACC should make sure is on its radar is "Autism in the Judicial System"! Our individuals, no matter where they fall on the spectrum, will be in our judicial system either as; victims, defendants, witnesses, and of the subject matter of trusts & guardianship.

If we do not take time to educate our judicial system about autism, how can we ever expect any of them to make fair decisions that impact our individuals and society in serious matters? Judges, Attorney's, Social Services, Public Safety and more!

Thank you for your review and your work!

Regards,
Brad Trahan
Founder
RT Autism Awareness Foundation, Inc.
Chair - 2012 Minnesota Task Force
Parent - Son with severe autism

Nasra Mirreh

December 18, 2012

Here in Georgia (GA) we have comprehensive supports (COMP) and new option waiver (NOW) waivers through the Department of Behavioral Health & Developmental Disabilities. The Comp waiver supports individuals who are in need of 24 hours care. The NOW supports short term and long term care. Many of our kids are on the NOW waiver waiting list. The waiting list is long and for instance my son is on the waiting list for 5 years. Lock of funding is the main hold up. The low income families like the community we serve the refugee communities which have economic, language and cultural barriers are having the most difficulties and are undeserved. We also need support for special need summer camps and special need after school programs here in GA. The local Universities provide interns to our agency and can offer speech and occupational therapy (OT) services to the kids. We have the ideas and cultural appropriate programs to serve these diverse communities, but have no support from the Federal or from the State of Georgia. All the families we serve are on GA Medicaid, and Medicaid pays one hour per week of speech or occupational therapy outside of the School Systems. The School Systems provide 1-2 hours per week of speech or occupational therapy to these kids. It has been recommended 30-35 hours per a week of intervention therapies. As you see there is a great deal of disparities. We need your support and recommending to the IACC to support the local communities and encourage community engagement, more outreach and education on what risk factors are.

Sincerely,
Nasra Mirreh
Executive Director
Refugee Family Assistance Program
www.refugeefamilyassistanceprogram.org

Gail Elbek

December 22, 2012

Subject: Sandy Hook Tragedy Compares To Withholding Autism Tragedy

Yes Sandy Hook is a terrible tragedy, and equally tragic is IACC withholding massive published studies proving a cause of severe and irreversible neurological disorders to include the cause of autism! Why? Gail Elbek

1. Soy Estrogenic Endocrine Disruptors Cause Adverse Brain Functions:
2005, As weak estrogen agonists/antagonists with a range of other enzymatic activities, the (soy) isoflavonoids provide a useful model to investigate the actions of endocrine disruptors. Isoflavonoids act in vivo through both ER (Estrogen Receptor) –alpha and ER-beta. Their neurobehavioral actions are largely anti-estrogenic, either antagonizing or producing an action in opposition to that of estradiol. Small, physiologically relevant exposure levels can alter estrogen-dependent gene expression in the brain and affects complex behavior in a wide range of species.
www.ncbi.nlm.nih.gov/pubmed?term=Phytoestrogen action in the adult and developing brain

2008, Endocrine disrupting chemicals (EDCs) exert hormone-like activity and exposure to these compounds may induce both short- and long-term deleterious effects. The EDCs examined included estradiol, androgen, soy phytoestrogens, and atrazine. Effects on behavior and hypothalamic neuroendocrine systems were examined. All EDCs impaired reproduction. Several hypothalamic neural systems proved to be EDC responsive, including arginine vasotocin, catecholamines, and gonadotropin releasing hormone system. Exposure to EDCs during embryonic development has consequences beyond impaired function of the reproductive axis. Behavioral alterations reveal both direct and indirect effects of exposure to EDC. www.ncbi.nlm.nih.gov/pubmed/18006066

2008, Genistein, a phytoestrogen found abundantly in soy products stimulates brain protein synthesis rates. In the cerebral cortex, the cerebellum and the hypothalamus, results suggest that dietary genistein elevates the rate of protein synthesis in the brain. Estrogen receptors of the brain are at least partly related to the rate of brain protein synthesis caused by genistein.
www.ncbi.nlm.nih.gov/pubmed/18681983

2002, Small doses of soy genistein or daidzein can alter estrogen-dependent gene expression in brain and complex behavior www.ncbi.nlm.nih.gov/pubmed/11836071

2001, Males fed the soy phytoestrogen diet had significantly higher phytoestrogen concentrations in a number of brain regions, (frontal cortex, amygdale & cerebellum); in frontal cortex, expression of calbindin (a neuroprotective calcium-binding protein) decreased, while COX-2 (an inducible inflammatory factor prevalent in Alzheimer's disease) increased. Dietary phytoestrogens significantly sex-reversed the normal sexually dimorphic expression of the visual spatial memory (VSM). In females VSM was enhanced in males VSM was inhibited by the same phytoestrogen diet. Findings suggest that dietary soy derived phytoestrogens can influence learning and memory and alter the expression of proteins involved in neuro-protection and inflammation in rats.
www.ncbi.nlm.nih.gov/pubmed/11801187

1993, Estrogen exposure during critical periods of development promotes androgenization of the brain

which is reflected in altered morphology, behavior, and cyclic hormone secretion in females. There is dose-response characteristics of neonatal exposure to the isoflavonoid phytoestrogen genistein on pituitary sensitivity to gonadotropin release in the sexually dimorphic nucleus of the preoptic area in female rats. Results confirm that low doses of genistein have nonandrogenizing, pituitary-sensitizing effects, while higher doses of genistein mimic the more typical effects of estrogens. Morphologic and physiologic endpoints more completely defines the reproductive consequences of environmental (soy isoflavone genistein) estrogen exposure during critical periods of central nervous system development. www.ncbi.nlm.nih.gov/pubmed/8448414

2005, Genistein-induced neuronal differentiation is associate with activation of extracellular signal-regulated kinases and upregulation of p21 and N-cadherin.
http://onlinelibrary.wiley.com/doi/10.1002/jcb.20626/abstract

2010, Serious malformation and a higher abnormal frequency of the central nervous system were induced by the combination of Bisphenol A (BPA) and Genistein. Our findings suggest that genistein is embryotoxic and teratogenic to humans. BPA alone may not be a potential teratogen, but these two estrogenic chemicals have a synergistic effect on emybryonic development when present together during the critical period of major organ formation. Pregnant women should not take soy supplements. www.ncbi.nlm.nih.gov/pubmed/20505512

2003, Significant alterations in MBH-POA (medial basal hypothalamic preoptic area) and amygdale 5a-reductasee activities were detected in animals receiving the phytoestrogen-containing versus the phytoestrogen-free diets. www.ncbi.nlm.nih.gov/pubmed/10352124

2002, Neurobehavioral effects of dietary soy phytoestrogens. These studies used a commercially available diet rich in phytoestrogens via a diet free of phytoestrogens. Results indicate that consumption of dietary phytoestrogens resulting in very high plasma isoflavone levels (many cases over a short interval of consumption) can significantly alter sexually dimorphic brain regions, anxiety, learning and memory. www.ncbi.nlm.nih.gov/pubmed/11836067

2007, AVPV (essential part of neural pathways mediating hormonal feedback) neurons containing estrogen receptor-beta in adult male rats are influence by soy isoflavones. These findings provide direct evidence that consumption of soy isoflavones influence the loss of ERbeta-containing neurons in male anteroventral periventricular nucleus AVPV. www.biomedcentral.com/1471-2202/8/13

2009, Autism is probably attributable to a combination of a common genetic background and a possible prenatal exposure or alteration in fetal environment during pregnancy.
www.ncbi.nlm.nih.gov/pubmed/19581261

2. Soy Damage Caused to Multiple Brain Neurotransmitter Systems: Both excitatory and inhibitory receptors-

***Soy Inhibits GABA:
2007, Autism is a complex neurodevelopmental disorder. It is in agreement with the evidence of lower levels of GABA-A receptors in autistic brains, and joined by other variants could explain the autistic phenotype and its heterogeneity. www.ncbi.nlm.nih.gov/pubmed/17598645

2007, Neurotoxic Effects of soy genistein and daidzein could be due to their inhibition of the GABA (A)

receptor resulting in further enhancement of excitation by glutamate and leading to cellular damage. (Gamma-aminobutyric Acid (GABA). Inhibition of GABA can cause: anxiety disorders, panic attacks, seizure disorders, headaches, Parkinson's Cognitive impairment, depression, bipolar, infertility, lowers insulin levels). www.ncbi.nlm.nih.gov/pubmed?term=Genistein and daidzein induce neurotoxicity at high concentrations in primary rat neuronal cultures

2007, Genistein and daidzein induce neurotoxicity at high concentrations in primary rat neuronal cultures. Soy isoflavones possess estrogen-like activity. Specifically genistein and daidzein are toxic to primary neuronal culture at high concentrations, indicating a significant cellular damage. Both genistein and daidzein increases intracellular calcium level (CA2)i, significantly. The toxic effect of soy genistein and daidzein could be due to their inhibition of the GABA(A) receptor resulting in further enhancement of excitation by glutamate and leading to cellular damage. www.ncbi.nlm.nih.gov/pubmed/17245525

***Soy Significantly Increases VASOPRESSIN

2003, Soya isoflavone content of rat diet can increase anxiety and stress hormone release in the male rat. Rats fed the soy isoflavone diet spent significantly less time in active social interaction. The soy isoflavone group had significantly elevated stress induced corticosteroid concentrations. Stress-induced plasma vasopressin concentrations were also significantly elevated in the soy group compared to soy-free rats. Major changes in behavioral measures of anxiety and in stress hormones can result from soy isoflavone content in rat diet. These changes are as striking as those seen following drug administration. www.ncbi.nlm.nih.gov/pubmed/12618915

2003, Dietary exposure to genistein increases vasopressin. Vasopressin was significantly elevated in the 1250ppm genistein group, consistent with known actions of estradiol. These data are consistent with known actions of estradiol and may explain our finding in a previous study that estrogenic endocrine disruptors such as genistein increased sodium preference in rats exposed to genistein in their diet. www.ncbi.nlm.nih.gov/pubmed/12660364

2005, Soy contains phytoestrogens, which are nonsteroidal polyphenolic compounds with the ability to bind and activate nuclear estrogen receptors. Soy isoflavones act as transcriptional activators of estrogen receptors (ERs) in vitro. These effects are generally greater in the presence of ER-b, but significant activation through ERa is also observed. In the brain, soy diets and isolated phytoestrogens can also mimic estrogen-transcriptional actions. Soy isoflavones increases brain-derived neurotropic factor, and choline acetyl transferase mRNA levels in the frontal cortex, and increase vasopressin levels in the hypothalamus. Phytoestrogens genistein, daidzein and equol are all found in the brains of rat on high soy diets. http://ajpregu.physiology.org/content/289/1/R103/full

1979, Results: Androgen inhibition and estrogen stimulation of vasopressin levels. www.ncbi.nlm.nih.gov/pubmed/511789 as related to: 2012, Estrogenic agents, soy isoflavones inhibit testosterone (androgen) production. www.ncbi.nlm.nih.gov/pubmed/22155228

2004, Impaired vasopressin system is a strong candidates for involvement in autism susceptibility. www.ncbi.nlm.nih.gov/pubmed/15098001

2010, Syrian hamsters on the phytoestrogen-rich diet also had lower vasopressin receptor expression in the lateral septum but higher vasopressin expression in the lateral hypothalamus indicating that altered behavior might result from changes within vasopressin signaling pathways. Similarly, male rats on genistein and daidzein displayed increased anxiety and elevated stress-induced plasma vasopressin and

corticosterone levels. Male monkeys fed soy protein isolate containing 1.88mg isoflavones/g protein over 18 months demonstrated higher frequencies of intense aggressive and submissive behaviors as well as decreased time spent in physical contact with other monkeys. Phytoestrogens have widespread effects in the adult human brain which have been previously reviewed in detail elsewhere. Genistein stimulates ER (estrogen receptor) -beta mRNA expression in the PVN, (paraventricular nucleus), an effect opposite to that of 17b estradiol. PVN is primary site of oxytocin production. ER-alpha is required for the up-regulation of oxytocin. Consumption of prepared phytoestrogen supplement attenuated estrogen-dependent upregulation of oxytocin in the rat ventromedial nucleus
www.ncbi.nlm.nih.gov/pmc/articles/PMC3074428/

***Soy Manipulates OXYTOCIN:
2011, Phytoestrogens have widespread effects in the adult human brain which have been previously reviewed in detail elsewhere. Genistein stimulates ER (estrogen receptor) -beta mRNA expression in the PVN, (paraventricular nucleus), an effect opposite to that of 17b estradiol. PVN is primary site of oxytocin production. ER-alpha is required for the up-regulation of oxytocin. Consumption of prepared phytoestrogen supplement attenuated estrogen-dependent upregulation of oxytocin in the rat ventromedial nucleus. www.ncbi.nlm.nih.gov/pmc/articles/PMC3074428/

2001, Soy isoflavones antagonize reproductive behavior and estrogen receptor alpha and beta dependent gene expression in the brain. Soy diminishes the up-regulation of oxytocin receptor in the hypothalamus. There is significant decrease in receptive behavior probably due to anti-estrogenic soy effects in the brain. www.ncbi.nlm.nih.gov/pubmed/11416015

2003, Genistein increased oxytocin, oxytocin receptor, and ERalpha mRNA.
www.ncbi.nlm.nih.gov/pubmed/12504828

***Soy's Adverse Effects on CHOLINE Or Catecholamine Neurotransmitter System:
1985, Pregnant rat dams were fed a 5 or 2% soy lecithin preparation. Results indicate that dietary soy lecithin preparation enrichment during development leads to behavioral and neurochemical abnormalities in the exposed offspring.
Onlinelibrary.wiley.com/doi/10.1002/dev.420180105/abstract

1986, Previous work has shown that exposure of developing rats to soy lecithin preparations (SLP) influences macromolecular constituents of immature brain cells and causes abnormal behavior patterns. Both catecholamines were profoundly disturbed in an age-dependent, regionally-selective manner. Transmitter uptake capabilities were also affected by developmental exposure to SLP, as was tyrosine hydroxylase activity. The altered transmitter utilization rate reflected a change in impulse activity in the affected neuron populations, with promotion of activity in the midbrain + brainstem and reduced activity in the cerebral cortex. These data indicate that dietary supplementation with SLP throughout perinatal development alters synaptic characteristics in a manner consistent with disturbances in neural function. www.ncbi.nlm.nih.gov/pubmed/2876756

1986, Results suggest that soy lecithin preparation exposure has a major effect on cholinergic synaptic development and reactivity, followed by secondary changes in other neurotransmitter pathways.
www.ncbi.nlm.nih.gov/pubmed/3455608

1999, Soy phytoestrogens may function as estrogen agonists in regulating (increasing) choline acetyltransferase and nerve growth factor mRNA's in the frontal cortex and hippocampus in the brain of female rats. www.ncbi.nlm.nih.gov/pubmed/10352122

2005, Soy contains phytoestrogens, which are nonsteroidal polyphenolic compounds with the ability to bind and activate nuclear estrogen receptors. Soy isoflavones act as transcriptional activators of estrogen receptors (ERs) in vitro. These effects are generally greater in the presence of ER-b, but significant activation through ERa is also observed. In the brain, soy diets and isolated phytoestrogens can also mimic estrogen-transcriptional actions. Soy isoflavones increases brain-derived neurotropic factor, and choline acetyl transferase mRNA levels in the frontal cortex, and increase vasopressin levels in the hypothalamus. Phytoestrogens genistein, daidzein and equol are all found in the brains of rat on high soy diets. http://ajpregu.physiology.org/content/289/1/R103/full

(Choline acetyltranserase forms the Choline Neurotransmitter System). Cholinergic systems are implicated in numerous neurologic functions, and excess cholinergic neuron differentiation can lead to aberrant brain development. www.ncbi.nlm.nih.gov/pubmed/17211134

2008, Soy phytoestrogens stimulate catecholamine synthesis via estrogen receptors, but in high concentrations, phytoestrogens inhibit catecholamine secretion induced in adrenal cells, and brain neurons. www.ncbi.nlm.nih.gov/pubmed/18591472

***Soy Causes Dysfunctional DOPAMINE:
2001, Genistein inhibits protein tyrosine kinases that regulate dopamine function interfering with cellular signaling cascades that regulate neurotransmitter transporters in humans. These data provide several lines of evidence showing that PTK (Protein Tyrosine Kinases) inhibition rapidly reduces human dopamine transporter activity that controls levels of dopamine. This PTK's represent cellular signaling cascades that acutely regulate neurotransmitter transports. www.ncbi.nlm.nih.gov/pubmed/11181926

1995, Tyrosine kinases are abundant in the adult CNS. Soy genistein inhibits tyrosine kinases suggesting a changing role in neurotransmitter release caused by kinase-regulation of dopamine. Genistein increases endogenous dopamine release. www.ncbi.nlm.nih.gov/pubmed/7595495
Soy genistein significantly potentiated dopamine release in males. Genistein exposure may act similarly to estradiol (potent estrogen) in augmenting dopamine release.
www.ncbi.nlm.nih.gov/pubmed/11836070

2003, Endogenous estrogen may play an important role in regulating the activity of dopamine neurons in mid-limbic systems, and that soy isoflavones exert an estrogen-like effect on the dopaminergic systems in the amygdale. www.ncbi.nlm.nih.gov/pubmed/14566409

***Manganese: Soy Causes Toxic Manganese Levels, Another Soy-Cause of Dysfunctional Dopamine System:
2004, Manganese is an essential mineral nutrient found at high levels in plants such as soy. Excessive Manganese exposure increases the risk of adverse neurological effects. Well meaning but inadequately informed parents may perceive plant-based beverages such as soy beverages as an alternative to infant formula. Soy beverages should not be fed to infants because they are nutritionally inadequate and contain manganese at levels which may present an increased risk of adverse neurological effects. www.jacn.org/content/23/2/124.full (IACC Note: URL is not valid.)

2006, Manganese can cause a neurotoxic syndrome due to its interactions with monoamine systems, especially dopamine. Perturbations of the dopamine system are known to underlie a number of neurobehavioral problems, including ADHD. Manganese in soy-based infant formula can contain up to 80 times the Manganese concentrations of breast milk. Ingestion of soy formula in infancy could influence overabsorption of manganese and neurobehavioural consequences. We conclude that, during infancy the ingestion of high levels of manganese, as found in soy-based infant formula, is associated with a variety of behavioral deficits.
http://toxnet.nlm.nih.gov/cgibin/sis/search/f?./temp/~5nPFQZ:3:BODY

2002, Neonatal exposure to high levels of manganese has been indirectly implicated as a causal agent in ADHD, since Manganese toxicity and ADHD both involve dysfunction in brain dopamine systems. Results support neonatal manganese exposure is related to brain dopamine levels and neurocognitive deficit in the rodent. www.ncbi.nlm.nih.gov/pubmed?term=Effects of neonatal dietary manganese exposure on brain dopamine levels and neurocognitive functions

2008, Newborn babies are fed infant formula high in the toxic metal manganese. Two University of California campuses affirm that manganese in infant formula may damage the infant brain and trigger aberrant behavior. David Goodman affirms that the soy infant formula currently on shelves permits an estimated manganese dose about 120 times the amount found in mother-s milk. Excess manganese is stored in body organs, about 8% in the brain, in proximity to dopamine-bearing neurons responsible in part for neurological development. Infants given soy formula may be at risk for brain and behavioral disorders. www.soyonlineservice.com.nz/articles/goodman.htm (IACC Note: URL is not valid.)

***Soy is Tyrosine Kinase Inhibitor Related To Brain Dysfunction:
2002, NIH confirms that genistein is the active form of the soy isoflavone, genistin. It has both phytoestrogens, and has protein tyrosine kinase inhibiting properties that are involved in central nervous system regulation of neurotransmission inhibition by genistein. (Neurotransmission inhibition is a cause of multiple brain disorders to include autism. In this study, the NIH is looking for benefits, not the adverse developmental brain effects caused by soy isoflavone and tyrosine inhibition of neurotransmitters systems). http://clinicaltrials.gov/ct2/show/NCT00042380
Kinase enzymes that specifically phosphorylate tyrosine amino acids are termed tyrosine kinases. Receptor tyrosine kinases (RTK)s are the high-affinity cell surface receptors for many polypeptide growth factors, cytokines, and hormones. Of the 90 unique tyrosine kinase genes identified in the human genome, 58 encode receptor tyrosine kinase proteins. Receptor tyrosine kinases have been shown to be key regulators of normal cellular processes. Soy is a well-known inhibitor of tyrosine kinases.

1997, The phosphorylation of proteins on tyrosine residues is now recognized as having a critical role in regulating the function of mature cells. The brain exhibits one of the highest levels of tyrosine kinase activity in the adult animal and the synaptic reason is particularly rich in tyrosine kinases and tyrosine phosphorylated proteins. Involved in the regulation of synaptic function. Tyrosine phosphorylation is involved in the modification of synaptic activity. Changes in the activities of tyrosine kinases and or protein tyrosine phosphatases which are associated with synaptic structures leads to both short-term and long-lasting changes in synaptic and neuronal function. www.ncbi.nlm.nih.gov/pubmed/9364450

1991, Long-term potentiation (related to learning and long-term memory) in the hippocampus is blocked by tyrosine kinase inhibitors such as genistein. Tyrosine kinases participate in a kinase network with serine and threonine kinases. www.ncbi.nlm.nih.gov/pubmed/1656271

1993, We report that genistein, a specific tyrosine kinase inhibitor, decreases tyrosine kinase activity and the content of phosphotyrosine proteins in cultured primary cortical neurons. Genistein inhibits protein synthesis by >80% in a dose-dependent manner and concurrently decreases ternary complex formation by 60%. Genistein depresses tyrosine kinase activity and concomitantly stimulates PKC activity. Protein tyrosine kinase participates in the initiation of protein synthesis in neurons. www.ncbi.nlm.nih.gov/pubmed/8228995

(PKC, Protein kinase is a group of calcium and phospholipid-dependent enzymes, which plays a pivotal role in cell signaling systems. Recently accumulated evidence indicates that alterations in PKC activity play a significant role in the pathophysiology of bipolar disorder. More importantly, alterations in platelet PKC was shown in bipolar patients during the manic state of the illness. In comparison to patients with major depressive disorder, schizophrenia, or healthy controls, PKC activity was significantly increased in manic patients, suggesting that changes in PKC may be an illness-specific marker. The alterations of PKC activity in bipolar disorder may be related to changes in these other intracellular signaling mechanisms. Alternatively, the changes of PKC activity may be the core pathology of the illness).

2001, Tyrosine kinase inhibitors, soy genistein, inhibits the glutamate-induced proliferation of astrocytes (which are important for many brain functions).
http://ncbi.nlm.nih.gov/pubmed/11733703

2003, Genistein inhibits glutamate release and Ca(2+) influx from hippocampal synaptosomes. Genistein, a broad range inhibitor of tyrosine kinases did inhibit the intracellular CA(2+) and decrease glutamate release evoked by a drug stimulus in a dose-dependent manner.
www.ncbi.nlm.nih.gov/pubmed/12421598

1998, Modulation of Ca2+ channel activity by protein kinases constitutes one of the major mechanisms regulating neuronal functions. PTK inhibitors on whole–cell Ba2+ currents (1Ba) were analyzed. Genistein and daidzein suppressed IBa. We estimated that specific PTK inhibition by genistein reduced 1Ba by 30%. Results suggest that the activity of neuronal Ca2+ channels can be modulated by protein tyrosine kinases in the nervous system that are mediated by Ca2+ channel modulation.
www.ncbi.nlm.nih.gov/pubmed/9560456

1998, Genistein and daidzein inhibited L-type Ca2+ current in young rat ventricular cells. We investigated the developmental differences in the effects of genistein, an inhibitor of tyrosine kinases on Ca2+ in neonatal and adult rats. Genistein inhibits the basal L-type Ca2+ in rat ventricular cells and the inhibition of L-type Ca2+ by genistein is greater in immature cells than in adult cells.
www.ncbi.nlm.nih.gov/pubmed/9592031

2005, Ca2+ and cAMP are important second messengers that regulate multiple cellular processes. Findings indicate highly coordinated interplay between Ca2+ and cAMP signaling in electrically excitable endocrine cells. www.jbc.org/cgi/content/abstract/280/35/31294 (Evidence of cascading brain-damaging effects).

2002, A role for tyrosine kinase in expression of long-term potentiation (LTP). Tyrosine phosphorylation of proteins occurs in both the presynaptic and postsynaptic areas. We report that LTP was associated with increased calcium influx and glutamate release. LTP is also associated with an increase in

phosphorylation of the alpha-subunit of calcium channels and ERK in synaptosomes prepared from dentate gyrus and these effects were inhibited when LTP was blocked by the tyrosine kinase inhibitor genistein. LTP was accompanied by increased protein synthesis and increased phosphorylation of CREB in entorhinal cortex, effects that were also blocked by genistein.
www.ncbi.nlm.nih.gov/pubmed/12099488

(Long-term potentiation (LTP) is a long-lasting enhancement in signal transmission between two neurons that results from stimulating them synchronously. It is one of several phenomena underlying synaptic plasticity, the ability of chemical synapses to change their strength. Memories are thought to be encoded by modification of synaptic strength. LTP is widely considered one of the major cellular mechanisms that underlies learning and memory. Soy inhibition of tyrosine kinase results in multiple cascading brain-modifying effects proven to disturb normal brain development and functions. Another example: Nerve growth factor triggers a sequence of tyrosine kinase-dependent phosphorylation steps that modulate glutamate (important excitatory neurotransmitter important for learning and memory release) and calcium influx having an impact on expression of long-term potentiation in dentate gyrus, of which failure is due to soy inhibition of tyrosine kinase. Because of the hippocampus' well established role in LTP, some have suggested that the cognitive decline seen in individuals with AD may result from impaired LTP).

***Soy Affects SEROTONIN:
2003, Soy and social stress affect serotonin neurotransmission in primates. Prescribed estrogens and soy phytoestrogen increased serotonin reuptake transporter that was accompanied by increased serotonin synthesis and neuronal firing. www.ncbi.nlm.nih.gov/pubmed/12746737

2003, Conjugated equine estrogen (estrogen drug), and soy phytoestrogen increased serotonin. Increase in serotonin was accompanied by increased 5-HT synthesis and neuronal firing.
www.ncbi.nlm.nih.gov/pubmed/12746737

***Soy Modifies BDNF-
1999, Both estradiol and soy phytoestrogens significantly increased the mRNA levels of BDNF (brain-derived neurotrophic factor) compared to controls in the frontal cortex of female rats.
www.ncbi.nlm.nih.gov/pubmed/10081916

2005, Estrogenic effects of soy isoflavones on neurons have been observed in various studies. Soy contains numerous phytochemicals including isoflavones, phytic acid, trypsin inhibitors, saponins. Soy isoflavones are referred to as phytoestrogens because they bind to the estrogen receptors and affect estrogen-mediated processes. Soy isoflavones can exert both agonistic and antagonistic estrogenic effects, and have inhibitory effects on tyrosine kinase, topoisomerase and angiogenesis.
Soy can affect synthesis of acetylcholine, and neurotrophic factors such as BDNF and nerve growth factor in the brain of the female rat. Frontal cortex choline acetyltransferase mRNA levels and BDNF were significantly higher in rats receiving soy isoflavones.

DNA fragmentation was detected in homogenates of brain tissue from rats receiving either dose (2mg/day or 2mg/day) genistein.

Daidzein augments nitric oxide (neurotransmitter of the vasodilator nerve) synthesis in the basilar artery and increases contraction activity in the basilar arteries of male rats. Genistein can modulate the dopaminergic system. The pups of rats that consumed isoflavone containing genistein showed

significant increases in amphetamine-stimulated dopamine release in males. Genistein also inhibits dopamine uptake into mouse striatal homogenates. Genistein dose dependently suppresses dopamine transport.

Soy isoflavones affect ChAT (choline acetyltransferase) expression and activity. ChAT mRNA levels in soy isoflavones-treated rats were significantly higher in the frontal cortex.

Genistein decreases the expression of GABAa receptors in the plasma membrane of rat cerebellar granule cell bodies and dendrites, and inhibits GAMA-activated currents in HEK293 cells.
It has also been reported that glycine receptors are inhibited by genistein.

Soy isoflavones can affect the viability of neurons and cognitive function by acting as an estrogenic agonist and they can also utilize differential distribution and regulation of ERa and ERb in the brain. ERa is involved in mediating sexual and aggressive behavior, whereas, ERb modulates emotional and cognitive behavior.

Protein tyrosine phosphorylation is involved in various responses in the brain including neuroregeneration, synaptic plasticity and neuronal injury. Genistein is known to inhibit tyrosine kinase which is generally considered to be detrimental to a neuron. It was also reported that high concentrations of genistein induced neuronal apoptosis in primary cortical neurons, blocked tyrosine kinase activity and contributed to H2O2-induced apoptosis in human neuroblastoma cells. Tyrosine-kinases are highly expressed ins several brain regions including the hippocampus, and are reported to be involved in the induction of long-term potentiation in the hippocampus, which is crucial to learning and memory. Long-term potentiation is also reportedly associated with increased calcium influx and glutamate release. Protein tyrosine physphorylation contributes to synaptic plasticity. Three families of tyrosine kinases are implicated in memory. Because genistein is a tyrosine kinase inhibitor it can inhibit long term potentiation, which will also suppress calcium channels and extracellular-signal-related kinase in synaptosomes prepared from dentate gyrus. Genistein inhibits protein synthesis and phosphorylation of cAMP response element binding protein in entorhinal cortex. Inhibitory activity of long-term potentiation by genistein is associated with the inhibition of high-threshold voltage-activated calcium currents (VGCC). Genistein inhibits the Ca2+ dependent glutamate release by partially inhibiting p-/Q-type VGCC and by inhibiting N-type and unidentified BGCCs, in rat hippocampal synaptosomes.
It is reasonable to assume that rats consuming soy isoflavones have impaired spatial memory. Large amounts of genistein are needed to inhibit tyrosione kinases in the brain and suppress cognitive function in vivo. Thus soy isoflavones, especially genistein as a tyrosine kinases inhibitor can induce impairment of memory processing and cognitive function when concentration of genistein in vivo is excessive. Soy isoflavones can affect brain function by ER-mediated processes and by inhibiting tyrosine kinase. Genistein (one of soy isoflavones) can have negative influences on cognitive function when it is present at a high level due to its action as a tyrosine kinase inhibitor which enables it to block long-term potentiation and cognitive function.
(Study title, "Soy isoflavones and cognitive function" by YB Lee et al. Journal of Nutritional Biochemistry, Vol 16, Issue 11, Page: 641-49).

3. Soy Inhibits Mitochondrial Functions:
2002, Genistein is an isoflavone soy derivative that binds to estrogen receptors with selective estrogen receptor modulated (SERM) properties. FDA recommendations of soy for cholesterol reduction prompted investigation into the potentially estrogen role of dietary soy phytochemicals in the brain. 50nM genistein significantly reduces neuronal apoptosis in an estrogen receptor-dependent manner,

while the importance of apoptosis in the brain has been recognized with regard to the developing brain as well as degeneration in response to disease or stroke. We developed a model to test for apoptotic toxicity in primary cortical neurons caused by 17 beta estradiol and genistein and found; brain cell apoptosis confirmed loss of mitochondrial function, DNA laddering, nuclear condensation and fragmentation, and caspase activation were confirmed. Both 17beta estradiol and genistein reduced the number of apoptotic neurons and reduced the number of neurons containing active caspase-3. Results demonstrate that genistein and 17beta-estradiol have comparable anti-apoptotic properties in primary cortical neurons and these properties are mediated through estrogen receptors.
www.ncbi.nlm.nih.gov/pubmed/12441188

2000, Inhibition of mitochondrial proton FOF1-ATPase/ATP synthesis by (soy) phytochemicals. In conclusion the ATP synthase is a target for dietary phytochemicals, (genistein) with potential for cytotoxicity. www.ncbi.nlm.nih.gov/pmc/articles/PMC1572158/
(ATP, adenosine triphosphate, provides the energy for many cellular processes, including active transport of molecules across cell membranes, motility, and metabolism).

2005, Mitochondria are important targets of estrogen action. Another class of compounds, phytoestrogens which are found in our diet can also inhibit the activity of Complex 1 (NADH dehydrogenase). Phytoestrogens, genistein (found in soy beans) can inhibit the ATPase activity in rat brain mitochondria. www.ncbi.nlm.nih.gov/pmc/articles/PMC548143/

(NADH Dehydrogenase: Enzyme located in the mitochondrial transport chain involved in respiratory complexes. Mutations in subunits of Complex I can cause mitochondrial diseases, including Leigh syndrome (rare neurometabolic disorder that usually affects infants between 3 months and 2 years old, but sometimes teenagers and adults. Mutations in mitochondrial DNA cause degradation of motor skills and eventually death. The disease is characterized by movement disorders, loss of heal control and motor skills, continuous crying in infants, and seizures). Complex I defects may play a role in the etiology of Parkinson's disease. Complex I was significantly decreased in patients with bipolar disorder. Complex I deficiency showed decreased oxygen consumption rates and slower growth rates. Exposure to pesticides (besides soy, is another endocrine disruptor) can also inhibit Complex I and cause disease symptoms to include liver dysfunction. Alteration in Complex I leads to decreased mitochondrial electron transfer activities and decreased ATP synthesis).

2005, Genistein produced mitochondrial depolarization as an early step in the induction of apoptosis. We identified the mitochondria permeability transition pore (PTP) as a potential target of genistein activity. There results indicate that the induction of apoptosis by pharmacological concentrations of genistein occurs via mitochondrial damage with the involvement of the PTP.
www.ncbi.nlm.nih.gov/pubmed/15749635

2002, Further analyses showed that genistein induces mitochondrial permeability transition by the generation of reactive oxygen species due to its interaction with respiratory chain at the level of mitochondrial complex III. Addition of genistein to isolated rat liver mitochondria induces swelling, loss of membrane potential and release of accumulated Ca2+. www.ncbi.nlm.nih.gov/pubmed/12460676

4. Soy Suppresses MET:
2006, Low concentrations of genistein was associated with down-regulation of MET. Genistein suppresses MET expression. www.ncbi.nlm.nih.gov/pubmed/16619504

5. Soy Effects on Cortisol Production:
1999, Phytoestrogens alter adrenocortical function: Genistein and daidzein suppress glucocorticoid and stimulate androgen production. Phytoestrogens influence a variety of biological processes. In human fetal and postnatal adrenal cortical cells, genistein and daidzein decreased ACTH-stimulated cortisol production to basal levels. In the adult adrenocortical cell line, H295, genistein daidzein and 17B estradiol decreased cAMP-stimulated cortisol synthesis in a similar fashion. Genistein and daidzein in postnatal adrenocortical cells, DHEA and DHEA-S were markedly increased. In H295 cells, basal and cAMP-stimulated DHEA production were similarly increased by the phytoestrogens and 17B estradiol. Genistein and daidzein specifically inhibited the activity of 21-hydroxylase (P450c21 steroidal enzyme). Consumption of foods containing phytoestrogens alter adrenocortical function.
www.ncbi.nlm.nih.gov/pubmed/10404819

2002, Inhibitory effects of soy phytochemicals on cortisol production was examined in human adrenal H295R cells. Daidzein induced reduction of cortisol. Daidzein and genistein strongly and significantly inhibited steroidogenic enzymes 2beta-HSD. Daidzein and genistein significantly inhibited P450c21 steroidogenic enzyme activity. Daidzein is a competitive inhibitor of 3beta-HSD II and P450c21 steroidal enzymes. www.ncbi.nlm.nih.gov/pubmed/1198020

6. Soy-Cause of Vitamin D Deficiency:
2004, Content analysis of soybean milk showed very low calcium, phosphate, magnesium and vitamin D levels compared to cow's-based infant formulas. This case highlights the unsuitability of soybean milk as the sole provider of infant nutrition and demonstrates the false perception that soybean milk is a healthy food for infants. It is necessary to be cautious about health claims for soybean milk….www.ncbi.nlm.nih.gov/pubmed/15009584

7. Soy Modulation of Calbindin D28k-modulates calcium channel activity and neuronal firing.
2001, Males fed the soy phytoestrogen diet had significantly higher phytoestrogen concentrations in a number of brain regions, (frontal cortex, amygdale & cerebellum); in frontal cortex, expression of calbindin decreased while COX-2 (an inducible inflammatory factor prevalent in Alzheimers' disease) increased. Dietary phytoestrogens significantly sex-reversed the normal sexually dimorphic expression of the visual spatial memory (VSM). In females VSM was enhanced, in males VSM was inhibited by the same phytoestrogen diet. Findings suggest that dietary soy derived phytoestrogens can influence learning and memory and alter the expression of proteins involved in neuro-protection and inflammation in rats. www.ncbi.nlm.nih.gov/pubmed/11801187

1999, In animals fed a phytoestrogen containing diet, males displayed significantly higher calbindin-D28k levels compared to females. Females exhibited significantly lower calbinin-D28 levels. Phytoestrogen content in diets apparently influence MBH-POA (medial basal hypothalamic preoptic area) calbindin levels prenatally. Altered calbindin-D28 levels modify sexually dimorphic brain structure during neural development by buffering ca2+ that is associated with programmed cell death.
www.ncbi.nlm.nih.gov/pubmed/10320769

2006, Soybean isoflavones changes calbindin D-28k (CB) immunoreactivity in the hippocampus in female rats as well as male rats, correlating between calcium levels and phytoestrogens. In the dentate gyrus, CB immunoreatvity in females and males was significantly lower than controls.
www.ncbi.nlm.nih.gov/pubmed/1681163

2000, Phytoestrogens are plant estrogenic-like molecules. Calcium binding proteins are associated with protecting against neurodegenerative diseases. In male rats on a phytoestrogen containing diet, plasma phytoestrogen levels were 78-fold higher than the control group, and the medial basal hypothalamic and preoptic area (mbh-poa) phytoestrogen content was 8-fold higher, demonstrating the passage of phytoestrogens into the brain. Independent brain site, i.e., mbh-poa, or amygdale, the abundance of calbindin from male phytoestrogen fed rats was significantly lower than controls. In the amygdale a similar pattern of expression was seen to that of the calbindin results. Consumption of phytoestrogens via a soy diet for a relatively short interval can (1). Significantly elevate plasma and brain phytoestrogen levels, and (2). Decrease brain calcium-binding proteins. www.ncbi.nlm.nih.gov/pubmed/10720621

2000, Brigham Young Neuroscience Center researcher found that consumption of phytoestrogens via a soy diet for a relatively short interval can significantly elevate phytoestrogens levels in the brain and decrease brain calcium binding proteins. www.rense.com/general3/soy.htm

8. Iron & Zinc Deficiency Caused by Soy's Phytic Acid Content:

2000, Another way that soybeans may affect brain function is because of the phytic acid content. Also known as phytates, they block the uptake of essential minerals in the intestinal tract: calcium, magnesium, iron and especially zinc. Both phytates and soy protein reduce iron absorption. Researchers testing soy formula found that it caused negative zinc balance in every infant to whom it was given, even when the diets were additionally supplemented with zinc. There is a strong correlation between soy phytate content in formula and poor growth. www.rense.com/general3/soy.htm

1988, Results suggest that the low bioavailability of zinc from soy formula is a function of its phytate concentration. www.ncbi.nlm.nih.gov/pubmed/3189220

2002, Phyto-containing legumes and movement toward plant-based diets reduces dietary iron and zinc absorption. Monitoring methods are needed to detect and prevent possible iron and zinc deficiency with plant-based diets.
www.ncbi.nlm.nih.gov/pubmed/12030275

2011, In the isoflavone-treated group, statistically significant decreased concentrations of zinc. The exposure of rats to genistein and daidzein during intrauterine life until sexual maturity influenced the mineral metabolism of the organism by significant decreases of zinc concentration in serum. Estradiol levels of rats receiving phytoestrogen were significantly higher than control group.
www.ncbi.nlm.nih.gov/pubmed/21167684

2007, Zinc and iron bioavailability was lower for GMO soybeans possibly due to its higher content of antinutrient factors, especially soybean levels of phytate. www.ncbi.nlm.nih.gov/pubmed/18034754

2011, Levels of estradiol of rats receiving phytoestrogens were significantly higher than control group. Estradiol is a dangerously potent endogenous estrogen. Soy treated group showed statistically significant decreased concentrations of zinc in blood serum. (Study evidence links low zinc levels to brain disorders including autism). www.ncbi.nlm.nih.gov/pubmed/21167684

1999, Soy infant formulas may also contain phytate, which may negatively affect trace element absorption. Zinc absorption was significantly higher in low-phytate soy formula than from regular soy

formulas. Reducing phytate content in soy formula had beneficial effect on zinc and copper absorption. www.ncbi.nlm.nih.gov/pubmed/10075335

2001, Dialysability of all the minerals (calcium, phosphorus, magnesium, iron and zinc) analyzed from soy-protein based formulas showed significant differences. www.ncbi.nlm.nih.gov/pubmed/11702418

2004, Even in low doses, phytic acid is a potent inhibitor of iron absorption, and low absorption of iron is a major factor in the etiology of iron deficiency in infants. www.ncbi.nlm.nih.gov/pubmed/15743020

9. Copper: Soy-Cause of Excess Copper.
2003, Survival (rat) time in the soy protein isolate (SPI as in soy infant formulas) group was shorter than in control group. Copper concentrations in the livers of rats in the SPI diet groups were approximately 80% higher than in rats fed the control diet. Results indicate that SPI enhances copper uptake into the liver cells and promotes liver cell damage in rats. Recommendations to individuals suffering from Wilson's (too much copper builds up in the liver, brain and/or eyes causing serious illness, eventually causing death) disease to avoid consuming soy protein may be warranted.
www.ncbi.nlm.nih.gov/pubmed?term=soy protein isoflavone enhances hepatic copper accumulation and cell damage in LEC rats

10. Soy Causes SELENIUM Overdose:
2008, Soy products typically contain a significant amount of selenium and the soy phytoestrogens may also influence selenium status. Selenium in a soy supplement was determined to be bioavailable. Isoflavones in the soy supplement may have interfered with the bioefficacy of selenium.
https://kb.osu.edu/dspace/handle/1811/580?mode=full

2002, Effect of the application of selenium fertilizer on selenium content of soybean and its products. Significant differences were found in that soybean cultivars exhibited different accumulation of selenium. Selenium enriched protein derived from selenium enriched soybean increases selenium intake. www.ncbi.nlm.nih.gov/pubmed/12835506

2009, Selenium and arsenic levels in soybeans from different production regions of the United States. Whole soybeans were analyzed for total arsenic and selenium content. Arsenic levels were .1ppm or less. Selenium levels in soybeans varied from .07 - .90 ppm in the major production areas across the USA. www.osti.gov/energycitations/product.biblio.jsp?osti_id-6511424 (IACC Note: URL is not valid.)

1998, Selenium absorption from the soy isolate source was very high indicating that the selenium present is well absorbed from this soybean plant source.
www.ncbi.nlm.nih.gov/pubmed/3772518

11. Soy Contains Neuoro-Toxic Heavy Metals: having a devastating influence on mental, emotional, and physical health and well-being.
2000, Soy infant formulas contain other neurotoxins: aluminum, cadmium and fluoride. Studies found aluminum concentrations in soy-based formulas were 100-fold greater compared to human breast milk. Cadmium content was 8-15 times higher. Fluoride content of soy-based formulas ranged from 1.08 to 2.86 parts per million. www.rense.com/general3/soy.htm

2003, Our own concern is the high amounts of fluoride and aluminum in soy formula. Infants fed soy formula there was an increase of 200% in autoimmune thyroid disease compared to breast-fed infants.

A study concluded aluminum content in soy formula for 1-3 month old infants could result in intake of 363 micrograms/kg/day. Soy based formulas contains about 6-15 times more cadmium than milk based formulas, as well as high amounts of fluoride. Fluoride and phytates in soy formula will induce zinc deficiency. www.wwestonaprice.org/soy/notmilk.html (IACC Note: URL is not valid.)

2006, There was significant difference in the fluoride content of infant formulas from distinct batchers in most brands. Milk formula varied in fluoride concentrations; 0.014 to 0.045, and soy formula was 0.253 to 0.702 mg F/L. www.ncbi.nlm.nih.gov/pubmed/17119712
(Fluoride toxicity can cause a variety of symptoms: abdominal pain, vomiting, hypocalcemia, headache, muscle weakness, or spasm, seizures etc.).

1987, Soy-based or milk-free formula contained about 8-15 times more cadmium than milk-based formulas. Canadian and U.S. ready-to-use formulas contained 900 and 230 ng/g fluoride attributed to the level of fluoride in the processing water used by the manufacturers.
www.ncbi.nlm.nih.gov/pubmed/3624190

1999, Soy formulas contained approximately 6 times more cadmium that cow's milk formulas, and diets with a cereal content had 4-21 times higher mean levels. Compared to breast-fed infants the exposure of dietary cadmium from weaning diets can be up to 12 times higher in children fed infant formulas.
www.ncbi.nlm.nih.gov/pubmed/10789373
(Toxic overexposure of cadmium occurs art very low levels. Toxic heavy metal cadmium is a known carcinogen. Cadmium is a bio-accumulating substance which means that the body absorbs and holds it and isn't able to expel it at a rate fast enough to be safe).

12. Soy Cause of Adverse Visual Spatial Memory, Allterations in Sexually Dimorphic Brain Regions:
2001, Visual spatial memory is inhibited in males (rat) by dietary soy phytoestrogens. Furthermore, males fed the phytoestrogen diets had significantly higher phytoestrogen concentrations in a number of brain regions (frontal cortex, amygdale, and cerebellum): in frontal cortex the expression of CALB (neuroprotective calcium-binding protein) decreased, while COX-2, an inducible inflammatory factor prevalent in Alzheimer's disease increased. Results suggest that dietary phytoestrogen significantly sex-reversed the normal sexually dimorphic expression of visual spatial memory. These findings suggest that dietary soy derived phytoestrogens can influence learning and memory and alter the expression of proteins involved in neural protection and inflammation in rats.
www.ncbi.nlm.nih.gov/pubmed/11801187

2003, Phytoestrogens, derived from plants (especially soy products) are molecules structurally and functionally similar to estradiol. In summary, consumption of dietary phytoestrogens (estrogen mimics) can alter hormone-sensitive hypothalamic brain volumes in rodents during adulthood.
www.ncbi.nlm.nih.gov/pubmed/12943716

2004, Results indicate that long-term consumption of a diet rich in soy isoflavones can have marked influences on patterns of aggressive and social behavior. Frequencies of intense aggressive and submissive behavior were elevated relative to monkeys fed the control diet. Time spent by these monkeys in physical contact with other monkeys was reduced by 68%.
www.ncbi.nlm.nih.gov/pubmed/15053944

2004, Dietary soy isoflavones alter regulatory behaviors, metabolic hormones and neuroendocrine function in male rats. This study demonstrates that consumption of a soy-based diet, significantly alters

several parameters involved in maintaining body homeostatic balance, energy expenditure, feeding behavior, hormonal, metabolic and neuroendocrine function in male rats.
www.ncbi.nlm.nih.gov/pubmed/15617573

2009, Administration of soy phytoestrogen genistein and 17B-estradiol induced rapid cAMP response element-binding protein (CREB) phosphorylation in the rat hypothalamus. Genistein induced a dose-dependent increase in CREB phosphorylation in the medial preoptic area and anteroventral periventricular nucleus. These results demonstrate that genistein induces estrogen-like rapid action on CREB phosphorylation in the neonatal central nervous system in vivo.
www.ncbi.nlm.nih.gov/pubmed/19840237

2002, Soy isoflavone supplements containing a mixture of soy phytoestrogens inhibited estrogen-dependent female sexual behavior and was estrogen for both ER alpha and ER beta dependent gene expression in the hypothalamus. However, at 55ppm genistein had differential activity through ER alpha and ER beta in the hypothalamus. Genistein increased ER beta mRNA expression in the paraventricular nucleus of the hypothalamus by 24%....
www.ncbi.nlm.nih.gov/pubmed/12021182

2001, We show that genistein, a potent plant-derived isoflavone displaying estrogenic activity at low nanomolar concentrations, is toxic to rat primary cortical neurons…. Findings provide evidence for a delayed and prolonged activation of p42/44 mitogen-activated protein kinase (MAPK) and raise caution about potential side effects in the nervous system with genistein use.
www.ncbi.nlm.nih.gov/pubmed/11561064

2001, Ingestion of soy containing isoflavones was correlated with the suppression of tau. Tau is an important protein in early brain development and plays an important role in growth of axons. (Axons make contact with other cells, usually other neurons but sometimes muscle or gland cells at junctions called synapses). www.ncbi.nlm.nih.gov/pubmed/10352122

1999, “FDA Scientists Against Soy”: Docket # 98P-0683. Scientists Drs. Doerge and Sheehan report, “We oppose this health claim because there is abundant evidence that some of the isoflavones found in soy, including genistein and equol, a metabolize of daidzein, demonstrate toxicity in estrogen sensitive tissues and in the thyroid. This is true for a number of species including humans. Thus during pregnancy in humans, (soy) isoflavones per se could be a risk factor for abnormal brain and reproductive tract development. Development is recognized as the most sensitive life stage for estrogen toxicity because of the indisputable evidence of a very wide variety of frank malformations and serious functional deficits in experimental animals and humans. Our conclusions are that no dose is without risk; the extent of risk is simply a function of dose. Taken together, the findings presented here are self-consistent and demonstrate that genistein and other isoflavones can have adverse effects in a variety of species, including humans. ….the public will be put at potential risk from soy isoflavones in soy protein, isolate without adequate warnings and information.” www.alkalizeforhealth.net/Lsoy2.htm

2003, Sexually dimorphic brain volumes (sexually dimorphic nucleus of the hypothalamus preoptic area SDN-POA, and anteroventral periventricular AVPV nucleus: male characteristics/female characteristics and behaviors) are influenced by estrogens. In summary, consumption of dietary phytoestrogens (estrogen mimics) can alter hormone-sensitive hypothalamic brain regions in rodents.
www.ncbi.nlm.nih.gov/pubmed/12943716

2005, Evidence from rodents shows that certain phytoestrogens act as estrogen receptors in the brain. We sought to determine the estrogenic profile of food-borne phytoestrogens in neuronal cell lines. At sub-micromolar concentrations genistein, daidzein stimulated ERalpha and ERbeta-dependent transcription in neuronal cells co-transfected with ERs and estrogen-response element containing promoters. In neuronblastoma cells expressing endogenous ERs, genistein mimicked estrogen regulation of progesterone receptor mRNA levels. Results demonstrate that food-borne phytoestrogens particularly those found in soy act as estrogen-response elements in neurons. www.ncbi.nlm.nih.gov/pubmed/15713532

2000, Dr. Bernard A. Schwetz FDA Director of National Center for Toxicological Research: Adverse effects on reproductive tissues have been primary focus of attention, but effects from endocrine disruptors on other organ systems and processes, such as carcinogenesis have also been reported. Chemicals with estrogenic activity can affect the development and function of neural tissues through several different mechanisms. Experimental approaches to detect neurotoxic effects of estrogenic chemicals include neurobehavioral, neuropathological, and neurochemical endpoints. Genistein, a naturally occurring estrogen mimic is found in soy beans and soy products on which multigenerational studies are in progress. These studies will compare toxicity in neural, immune and reproductive systems and evaluate potential carcinogenicity. At dose levels that decreased maternal and offspring body weight, there were subtle alterations in some sexually dimorphic behaviors… Moderate doses of genistein also decreased the volume of sexually dimorphic nucleus of the hypothalamus in male offspring. Overall toxicity profile of chemicals to which humans are exposed is very important in order that the FDA may conduct sound risk assessments. www.ncbi.nlm.nih.gov/pubmed/11233764

2002, Neurobehavioral effects of soy phytoestrogens; The soy phytoestrogen diet fed to adult male and female rats produced anxioloytic effects. Results indicate that consumption of dietary phytoestrogens resulting in very high plasma isoflavone levels can significantly alter sexually dimorphic brain regions, anxiety, learning, and memory. The findings of these studies identify the biological actions of phytoestrogens. www.ncbi.nlm.nih.gov/pubmed/11836067

2001, Soy phytoestrogens influence estradiol estrogenic induced mechanism results in modified brain functions: www.ncbi.nlm.nih.gov/pubmed/11602649

2005, Soy isoflavonoids provide a useful model to investigate the actions of endocrine disruptor. Isoflavonoids act in vivo through both ERalpha and ERbeta. Their neurobehavioural actions are largely anti-estrogenic. Small physiologically relevant exposure levels of soy isoflavonoids can alter estrogen-dependent gene expression in the brain and affect complex behavior in a wide range of species. www.ncbi.nlm.nih.gov/pubmed/15720476

2004, Results indicate that long-term consumption of a diet rich in soy isoflavones can have marked influences on patterns of increased aggressive behavior and decreased social behavior. www.ncbi.nlm.nih.gov/pubmed/15053944

2004 Isoflavones genistein and daidzein have similar molecular weights and structural characteristics to that of 17-beta estradiol, exert estrogenic and antiestrogenic properties. Major source of endocrine disrupting substances soy derived isoflavones are most abundant and most studied are known endocrine disruptors. Exert estrogenic and antiestrogenic properties….equol act in turn to inhibit the action of testosterone/androgen. Influence of soy on learning and memory and anxiety behaviors is

identified, and insulin levels affected by dietary isoflavones are discussed.
www.ncbi.nlm.nih.gov/pubmed/15454683

2003, Soya isoflavone content of rat diet can increase anxiety and stress hormone release in the male rat causing major changes in behavioral anxiety and stress hormones.
www.ncbi.nlm.nih.gov/pubmed/12618915

2004, Phytoestrogens: implications in neurovascular research: Differences in dietary phytoestrogen consumption result in large variations in somatic phytoestrogen content. These molecules affect estrogen and estrogen receptor function in several ways, having both agonist and antagonist effects on estrogen receptors. Similar to estrogens, dietary phytoestrogens appear to affect certain aspects of vascular, neuroendocrine and cognitive function. This article reviews health effects of estrogen, isoflavones and their hormonal mechanism of action, brain penetration by isoflavones.
www.ncbi.nlm.nih.gov/pubmed/16181093

2010, Endocrine disruptors, chemicals that disturb the actions of endogenous hormone have been implicated in birth defects associated with hormone-dependent development. Phytoestrogens are a class of endocrine disruptors found in plants. ….soy phytoestrogens. Effects of genistein on reproductive development and spatial learning required exposure throughout the pre-and postnatal periods.
www.ncbi.nlm.nih.gov/pubmed/20053350

Evidence for genistein cytotoxicity in rat brain www.ncbi.nlm.nih.gov/pubmed/15147835

1999, Environmental chemicals, (soy is in fact classified as environmental chemical) which mimic the actions of estrogen have the potential to affect any estrogen responsive tissue. Inappropriate exposure to environmental estrogens at critically sensitive stages of development could potentially perturb the organizational activities of estrogen on selected neuronal populations in the CNS.
http://joe.endocrinology-journals.org/content/160/3/R1.abstract

2007, Effects of soy milk and isoflavone supplements on cognitive performance in healthy women- In contrast to predictions, soy did not improve attention, visual long-term memory, short-term memory. Also soy milk group showed a decline in verbal working memory compared to soy supplement and control groups. www.ncbi.nlm.nih.gov/pubmed/17435957

2009, Genistein is a phytoestrogen found at high levels in soybeans. In vitro and in vivo studies showed that high concentrations of genistein caused toxic effects. Zebrafish embryos were exposed to genistein. Genistein–treated embryos showed decreased heart rates, retarded hatching times, decreased body length, and increased mortality in a dose-dependent manner. Genistein treatment increased malformation of survived embryos such as pericardial edema and spinal kyphosis were observed. Assay results showed apoptotic DNA fragments in brain. This study also confirmed the estrogenic potential of genistein in the brain…. This study demonstrated that high concentrations of genistein caused teratogenic effects on zebrafish embryos and confirmed the estrogenic potential of genistein. www.

2003, Estrogens exhibit complex effect on brain structure function and behavior. Body weights are significantly decreased in Phytoestrogen fed animals, and had significantly higher plasma adrenocorticotrophin and hippocampal glucocorticoid receptor levels. Lifelong consumption of dietary

phytoestrogens alters the hypothalamic-pituitary-adrenal axis in male rats. www.ncbi.nlm.nih.gov/pubmed/127273197 (IACC Note: URL is not valid.)

2012, Phytoestrogens are promoted as safe, natural alternatives to estrogen therapies, yet their safety is poorly understood. Once daily treatment of female rats with soy phytoestrogen genistein resulted in subtle deficits in performance on cognitive tasks. Genistein treatment in concentrations similar to those achieved in humans, impaired the delayed spatial alternation task very similar to that observed with 17B-estradiol. www.ncbi.nlm.nih.gov/pubmed/21945133

2002, Neurobehavioral effects of dietary soy phytoestrogens; These studies used a commercially available diet rich in phytoestrogens (Phyto-rich) verses a diet relatively free of phytoestrogens (Phyto-free). The phyto-rich diet fed to adult male and female rats produced anxiolytic effects. When learning and memory parameters were examined the visual-spatial memory (VSM), the diet treatments significantly changed the typical sexually dimorphic pattern of VSM. Phyto-rich females executed the VSM task in a manner similar to that of phyto-free fed males. Phyto-rich males VSM was comparable to Phyto-free fed females. Results indicate that consumption of dietary phytoestrogens resulting in high plasma isoflavone levels (in many cases over a relative short interval of consumption) can significantly alter sexually dimorphic brain region, anxiety, learning, and memory. These findings identify biological actions of phytoestrogens on the brain and behavior. www.ncbi.nlm.nih.gov/pubmed/11836067

2001, NCTR/FDA report: Soy phytoestrogen genistein, the principal isoflavone in soybeans has adverse effects on animal reproduction. Since adult physiology and behavior are sensitive to perturbation by developmental estrogens, exposure to genistein during development may produce behavioral alterations. Results indicate that developmental genistein treatment, at levels that decrease maternal and offspring body weight, causes subtle alterations in some sexually dimorphic behaviors. www.ncbi.nlm.nih.gov/pubmed/10828262

2006, Neonatal (soy) genistein or BPA alters sexual differentiation de-masculinized males and de-feminized females. Endocrine active compounds…phytoestrogen genistein. Acute exposure to Endocrine Active Compounds alter AVPV Development www.ncbi.nlm.nih.gov/pubmed/16427766

2007, Soy de-masculinizes male, de-feminizes females…(Soy) Genistein exposure during critical developmental periods could disrupt brain differentiation. www.ncbi.nlm.nih.gov/pubmed/17109964

2003, Soy de-feminizes female brain: www.ncbi.nlm.nih.gov/pubmed/13129486

2010, Maternal exposure to daidzein alters behavioral and estrogen receptor alpha expression in adult female offspring. Females exposed to daidzein showed significantly less ERalpha expression in bed nucleus of the stria terminals and medial amygdale in the brains of female mice. Findings show that maternal exposure to daidzein has a masculinization effect on memory and social behavior, suggesting a potential role of ER alpha distribution in the brain. www.ncbi.nlm.nih.gov/pubmed/20505512

1996. Reversal of sex roles in genetic female mice by disruption of estrogen receptor gene. Deficiency of normal estrogen receptor gene function led to behavioral change in female mice, aggression was increased. Disruption of ER gene led to a pattern of hormonal and neural changes which caused female to lose their normal female-typical behavior and to behave more like males. www.ncbi.nlm.nih.gov/pubmed/8990081

2005, De-masculinize male mice: John Hopkins School of Medicine: Exposure to endocrine disrupting chemicals adversely affects reproductive development and behavior in males. Aggressive behaviors were decreased whereas defensive behaviors were increased in males that received the low-does genistein diet. Exposure to genistein during critical periods of sex differentiation results in concurrent and persistent de-masculinization in male mice. Given the popularity of soy infant formulas the influence isoflavone exposure on reproductive and behavioral health in boys and men should be considered. www.ncbi.nlm.nih.gov/pubmed/15708785

2003, Johns Hopkins, AB Wisniewski et al, Perinatal (soy) genistein exposure results in transient and lasting alterations in masculinization of the reproductive system. Exposure to genistein during gestation and lactation demasculinizes the reproductive system in rats. www.ncbi.nlm.nih.gov/pubmed/12629420

2011, Genistein impairs early testosterone production via estrogen receptor alpha. It is well known that genistein, an isoflavone found in soybeans and soy products, mimics the actions of estrogens and that fetal testis is responsive to estrogens. Genistein inhibits testosterone secretion by fetal Leydig cells in mice during early fetal development within the "masculinization programming window." Results suggest that fetal exposure to phytoestrogens can affect the development and function of the male reproductive system. www.ncbi.nlm.nih.gov/pubmed/21624456

2001, FDA, National Center For Toxicological Research (NCTR) report: Effects of dietary exposure to the weak estrogen, (soy) genistein have been assessed using a number of techniques with validated gender related outcome measures. Findings indicate dose-related alterations of the volume of the sexually dimorphic nucleus of the medial preoptic area were observed in genistein-exposed male rats. Observations indicate that dose-related effects of developmental and chronic dietary exposure to genistein can be observed in the rodent. Additional studies are necessary to further predict the effect(s) of genistein on human gender-based development. www.ncbi.nlm.nih.gov/pubmed/11488560

1993- The results confirm that low doses of genistein have non-androgenizing, pituitary-sensitizing effects while higher doses of genistein mimc the more typical effects of estrogens….defining the reproductive consequences of environmental estrogen exposure during critical periods of central nervous system development.
www.ncbi.nlm.nih.gov/pubmed/8448414

2007, Genistein is a phytoestrogen, abundant in soybeans that can bind estrogen receptors and sex hormone binding proteins, exerting both estrogenic and antiestrogenic activity. Results demonstrate that genistein acts similarly to estradiol. In this avian model embryonic exposure to phytoestrogens may have life-long effects on sexual differentiation of brain structures and behaviors.
www.ncbi.nlm.nih.gov/pubmed/17274996

2007, Isoflavones, the most abundant phytoestrogens in soy food are structurally similar to 17beta-estradiol. It is known that 17beta-estradiol induces cell death in anteroventral periventricular nucleus (AVPV) in rat brain. There is evidence that consumption of soy isoflavones reduces the volume of AVPV, (controls sex typical physiology and behaviors). These findings proved direct evidence that consumption of soy isoflavones, influences the loss of ERbeta-containing neurons in male AVPV.
www.ncbi.nlm.nih.gov/pubmed/17266774

2003, Sexually dimorphic brain volumes (sexually dimorphic nucleus of the hypothalamus preoptic area

SDN-POA, and anteroventral periventricular AVPV nucleus: male characteristics/female characteristics and behaviors) are influenced by estrogens. In summary, consumption of dietary phytoestrogens (estrogen mimics) can alter hormone-sensitive hypothalamic brain regions in rodents. www.ncbi.nlm.nih.gov/pubmed/12943716

2001, Males fed the soy phytoestrogen diet had significantly higher phytoestrogen concentrations in a number of brain regions, (frontal cortex, amygdale & cerebellum) and in frontal cortex. Dietary phytoestrogens significantly sex-reversed the normal sexually dimorphic expression of the visual spatial memory (VSM). In females VSM was enhanced, in males VSM was inhibited by the same phytoestrogen diet. www.ncbi.nlm.nih.gov/pubmed/11801187

13. Adverse Brain Effects Caused By Soy Tofu:

2003, Soy-induced neuro-degeneration. A positive correlation between tofu consumption and brain atrophy in men. Has been shown that the soy phytoestrogen genistein inhibits neuroprotetive functions in cell cultures, recent in-vivo findings strengthen the case for possible soy –induced neurodegeneration. Genistein has been shown to suppress both DNA synthesis and the effects of brain derived neurotrophic factor (BDNF) in the hippocampus and cerebral cortex. Seems reasonable that some individuals may chose to avoid soy until proven safe …avoidance of soy also seems reasonable and should not be discouraged as alarmist. www.ncbi.nlm.nih.gov/pubmed/15142435

1996, Tofu and other soybean foods contain isoflavones bearing structural resemblance to steroidal hormones and have significant estrogen agonistic or antagonistic activities related to estrogen receptors and/or with enzymes involved in estrogen metabolism. There is evidence that estrogens modulate neural and synaptic plasticity during aging. We found an association of consistently high levels of tofu consumption in mid-life with low cognitive test scores and with Alzheimer's disease in late life. www.jacn.org/content/19/2/242.full (IACC Note: URL is not valid.)

2000, Poor cognitive test performance, enlargement of ventricles and low brain weight were each significantly and independently associated with higher midlife tofu consumption, indicative of cognitive impairment and brain atrophy in late life.
www.ncbi.nlm.nih.gov/pubmed/10763906

2008 High tofu intake is associated with worse memory in elderly Indonesian men and women. Honolulu study also reported increased risk for cognitive impairment and other dementia markers with high tofu (soybean curd) intake. www.ncbi.nlm.nih.gov/pubmed/18583909

2009, The natural selective estrogen receptor modulator DT56a or Femarelle, (derived from tofu + flaxseed) is derived from the soybean. DT56a exerts an estrogen-like effect on selective areas related to mood, cognition, and homeostasis control, presenting a specific pattern of interaction with brain function. www.ncbi.nlm.nih.gov/pubmed/19295450

2000, The Trouble With Tofu- Soy and the Brain: Men who consumed soy tofu at least twice weekly had more cognitive impairment. Consumption of phytoestrogens via a soy diet for a relatively short interval can significantly elevate phytoestrogen levels in the brain and decrease brain calcium-binding proteins. Soy's ability to interfere with enzymes and amino acids may have direct consequence for the brain. High amounts of protein tyrosine kinases are found in the hippocampus a brain region involved with learning and memory. Soy is a tyrosine kinases inhibitor.
www.rense.com/general3/soy.htm

14. Alzheimer's Disease:

2001, Males fed the soy phytoestrogen diet had significantly higher phytoestrogen concentrations in a number of brain regions, (frontal cortex, amygdale & cerebellum); in frontal cortex, expression of calibindin decreased, while COX-2 (an inducible inflammatory factor prevalent in Alzheimers' disease) increased. Findings suggest that dietary soy derived phytoestrogens can influence learning and memory and alter the expression of proteins involved in neuro-protection and inflammation in rats. www.ncbi.nlm.nih.gov/pubmed/11801187

15. Evidence That Maternal Soy Diet Transfers Soy-Estrogenic Endocrine Disruptors to Fetus:

2001, FDA NIEHS, The developing fetus is uniquely sensitive to perturbations with estrogenic chemicals. DES is the classic example. Phytoestrogen use in nutritional and pharmaceutical applications for infants and children is increasing. We investigated the carcinogenic potential of genistein, a naturally occurring plant estrogen in soy. At 18 months (mice study) the incidence of uterine adenocarcinoma was 35% for genistein and 31% for DES. Data suggest that genistein is carcinogenic if exposure occurs during critical periods of differentiation. Use of soy –bead infant formulas in the absence of medical necessity and the marketing of soy products that appeal to children should be closely examined. www.ncbi.nlm.nih.gov/pubmed/11389053

2009, Autism is probably attributable to a combination of a common genetic background and a possible prenatal exposure or alteration in fetal environment during pregnancy. www.ncbi.nlm.nih.gov/pubmed/19581261 (Maternal consumption of soy phyto-toxic hormone disruptor exposure is repeatedly proven to alter fetal environment).

2001, FDA NIEHS scientists report; Genistein, the principal soy isoflavone has estrogenic activity and is widely consumed by humans. These studies show that genistein aglycone crosses the rat placenta and can reach fetal brain from maternal serum genistein levels that are relevant to those observed in humans. www.ncbi.nlm.nih.gov/pubmed/11297868

2011, The increasing incidence of hypospadias is partly attributed to increased gestational exposure to endocrine disruptors. Gestational exposure to soy genistein altered the urethral expression of 277 genes. Among the most affected were hormonally regulated genes. Genistein affected tyrosine kinase receptors. Gestational exposure to genistein contributes to hypospadias by altering pathways of tissue morphogenesis, cell proliferation and cell survival. www.ncbi.nlm.nih.gov/pubmed/21421236

2006, Toxicological Sciences: Diets high in soy –based products are well known for their estrogenic activity. Genistein the predominant phytoestrogen present in soy , is known to interact with estrogen receptors alpha and beta and elicits reproductive effects in developing rodents. It is critical to understand the delivery of free and conjugated genistein across the placenta to the fetus following maternal genistein exposure. Genistein level sin placental tissue was high…. Fetal concentrations of unconjugated genistein following administration of 40mg/kg were above the EC50 for ER beta activation. High placental concentrations of genistein indicate the placenta is a potential target organ for genistein action during gestation.
www.ncbi.nlm.nih.gov/pubmed?term=Kinetics of genistein and conjugated metabolites in pregnat Sprague-Dawley rats following single and repeated genistein administration

2002, Early exposure to genistein exerts long-lasting effects on the endocrine and immune systems.

Data illustrate that exposure to soy genistein during pregnancy and lactation exerts long-lasting effects on the endocrine and immune systems in adulthood. www.ncbi.nlm.nih.gov/pubmed/12520091

2006, Daidzein and genistein (soy hormone disruptors) are found in higher concentrations than BPA in fetal amniotic fluid www.ncbi.nlm.nih.gov/pubmed/16112541

2002, Fetal soy exposure; evidence of soy phytoestrogens found in amniotic fluid. www.ncbi.nlm.nih.gov/pubmed/11888703

2005, Phytoestrogens transfer between mother and fetus…..placental transfer…the effects of fetal exposure to phytoestrogens should be studied further. (Japan 2005) www.ncbi.nlm.nih.gov/pubmed/16194669

2009 Taiwan study: Genistein has cytotoxic effects on embryo development. Fetal and infant damage. www.ncbi.nlm.nih.gov/pubmed/19490995
2002, Since dietary phytoestrogens account for a significant proportion of human exposure to potential endocrine modulators, and since the placenta does not represent a barrier to daidzein or related soy estrogenic isoflavones, the consequences of these exposures early in life should be examined and monitored carefully. www.ncbi.nlm.nih.gov/pubmed/11875621

2011, Fetal exposure to phytoestrogens can affect the development and function of the male reproductive system www.ncbi.nlm.nih.gov/pubmed/21624456

2011, NIH web site: Effects of genistein in maternal diet on reproductive development and spatial learning in male rats.. exposure to pregnant females is toxic to multiple organs and reproductive behavior in male offspring…. Also alters learning and memory. Sex based differences in behavior….. sensitive to endo disruption… www.ncbi.nlm.nih.gov/pmc/articles/PMC2834867/

2010, Soy phyto-estrogens and male reproductive function. Caution…soy formula should be avoided www.ncbi.nlm.nih.gov/pubmed/19919579

2007, Exposure to soy phytoestrogens in perinatal period affects androgen secretion by testicular leydig cells in adult rat. Phytoestrogens have ability to regulate Leydig cells. www.ncbi.nlm.nih.gov/pubmed/17569756

2000, Maternal vegetarian diet associated with hypospadias.....soy phytoestrogens have a deleterious effect on the developing male reproductive system. www.ncbi.nlm.nih.gov/pubmed/10619956

2011, Endocrine disruptors and soy genistein damage to male urethral development www.ncbi.nlm.nih.gov/pubmed/21421236

2001, Neonatal exposure to genistein reduces expression of estrogen receptor alpha and androge4n receptor in testes of adult mice and affects male reproductive organs at molecular levels in adulthood. www.ncbi.nlm.nih.gov/pubmed/11873863

2007 Concern has been raised of potential adverse effects due to the estrogenic and other activities of isoflavones. To assess the teratogenic and fetal toxic potential of genistein several rat studies were conducted. Treatment related anomalies were observed at concentrations of > or =10microg and 100

microg/mL, all embryos were malformed. Adverse effects in the pups were observed. On basis of definitive Prenatal development study the NOAEL for maternal toxicity and adverse effects on embryonic development was considered to be 100mg/kg/day when administered orally by dietary admix. www.ncbi.nlm.nih.gov/pubmed/17433519

2004, In utero (fetal) exposure to genistein: There is pronounced ductal hyperplasia, lactational changes, and fibrosis were observed in mammary glands from genistein group. Postnatal exposure to pharmacological levels of genistein induces profound morphological changes in the mammary glands of adult female rats. There is also potential of genistein to modulate toxicological effects of other toxicant mixtures. Effects of in utero exposure to environmental toxicants and potential interaction with postnatal genistein there is enlargement of the thoracic mammary glands observed in female rat offspring at 200 days of age. www.ncbi.nlm.nih.gov/pubmed/14514955

2011, Developmental exposure to estrogenic compounds can disrupt sexual differentiation in adult reproductive function in many animals including humans. Phytoestrogens in the diet comprise a significant source of estrogenic exposure to humans, particularly infants who are fed soy-based infant formula. Studies clearly demonstrate that environmentally relevant doses of genistein have significant negative impacts on ovarian differentiation, estrous cyclicity, and fertility in the rodent model. Additional studies of reproductive function in human populations exposed to phytoestrogens during development are warranted. www.ncbi.nlm.nih.gov/pubmed/20955782

2006, Dietary component, such as fat or phytochemicals in plant foods, can have an opposite effect on breast cancer risk if exposed in utero through a pregnant mother or at puberty. Dietary exposure during pregnancy often has similar effects on breast cancer risk among mothers and their female offspring. There is extensive programming of the mammary gland during fetal life and subsequent reprogramming at puberty and pregnancy. Thus, dietary exposure during pregnancy and puberty may play an important role in determining later risk by inducing epigenetic changed that modify vulnerability to breast cancer. www.ncbi.nlm.nih.gov/pubmed/17261753

2011, Isoflavones are non-nutritive components of soy responsible for estrogenic responses. There is evidence of potential adverse effects e.g., stimulation of estrogen-dependent mammary tumors and aberrant peri-natal development. Studies of the major soy isoflavone genistein were conducted in pregnant and lactating rats to quantify placental and lactational transfer to plasma and brain to better understand biological effects observed in multi-generational studies. The information derived from these studies also makes it possible to predict internal exposures of children to genistein from soy infant formula. www.ncbi.nlm.nih.gov/pubmed/21034763

2002, Frequency of feedings with soy-based milk formulas in early life was significantly higher in children with autoimmune thyroid disease. Inappropriate thyroid hormone levels can also have a devastating effect on the developing human brain especially during the first 12 weeks of pregnancy when the fetus depends on the mother's thyroid hormones for brain development. www.rense.com/general3/soy.htm

2010, Serious malformation and a higher abnormal frequency of the central nervous system were induced by the combination of BPA and Genistein. Our findings suggest that genistein is embryotoxic and teratogenic to humans. BPA alone may not be a potential teratogen, but these two estrogenic chemicals have a synergistic effect on emybryonic development when present together during the critical period of major organ formation. Pregnant women should not take soy supplements. www.ncbi.nlm.nih.gov/pubmed/20505512

2004, In utero and lactational exposure to estrogenic agents has been shown to influence morphological and functional development of reproductive tissues. Experiments demonstrate that developmental exposure to dietary isoflavones, at levels comparable to the ranges of human exposure, modify expression of the estrogen-regulated progesterone receptor (PR) in the uterus of sexually mature rats weeks after exposure ended. Since the PR is essential for regulating key female reproductive processes, such as uterine proliferation, implantation, and maintenance of pregnancy, its increased expression suggests that soy phytoestrogen exposure during reproductive development may have long-term reproductive consequences. www.ncbi.nlm.nih.gov/pubmed/14709783

16. Lactational Transfer Of Soy Toxins to Nursing Infants:

2005, Although circulating isoflavone levels are highest among infants consuming soy formula, the fraction of bioavailable isoflavones may be higher in breast-fed infants with mothers who regularly consume soy. Both phytoestrogens and synthetic endocrine disruptors have been found to impair similar reproductive and neuroendocrine endpoints, including sexual differentiation and maturation, fertility, malformation of the genital tract, and sexual behavior suggesting that they have similar mechanisms of action. Indeed both can act as either estrogen agonists or antagonists, depending upon dose, timing of exposure, tissue type, gender, and species. (From, Endocrine Disruptors, Effects on male and Female Reproductive Systems, Second Edition, by Rajesh K. Naz).

2007, Institute of Food Safety, China. Effects of lactational exposure to soy isoflavones on ovary development in neonate rats. Lactational exposure to soy isoflavones induced adverse effects on ovary development in neonate rats, which mechanisms may, at least, particularly involve the modification of mRNA transcription for estrogen receptor and progesterone receptor.
www.ncbi.nlm.nih.gov/pubmed/18095567

2008, Lactational exposure to soy could result in estrogen-like actions on female reproductive system
www.ncbi.nlm.nih.gov/pubmed/18047477

2008, Genistein passed from the lactating mother to the suckling offspring at levels sufficient to activate gene expression in the reproductive and nonreproductive tissues of mouse pups. In the liver, Estrogen Receptor-alpha and ER-beta messengers RNA and two target genes, CYP17 and the progesterone receptor were modulated by soy genistein. ER-alpha protein level followed an opposite regulation by genistein and estradiol. www.ncbi.nlm.nih.gov/pubmed/18281260

2010, Teratogenic effects and fetal toxicity of environmental estrogenic endocrine disruptors have become a great concern in recent years. Combination bisphenal A (BPA) and Genistein on rat embryos are investigated. Both BPA and Genistein produced concentration-dependent inhibition of embryonic development. Analyses reveal a significant synergistic interaction between BPA and Genistein for most end points, as indicated by enhanced developmental toxicity of BPA after coexposure with Genistein. Serious malformations and higher abnormal frequency of the central nervous system were induced by the combination BPA and Genistein. Findings suggest that Genistein may be embryotoxic and teratogenic to humans. These two estrogenic chemicals have a synergistic effect on embryonic development. Pregnant women should not take soy supplements.
www.ncbi.nlm.nih.gov/pubmed/20299547

17. Soy Infant Formulas Cause Severe Adverse Effects:

1998, Exposure to estrogenic compound may pose a developmental hazard to infants. Phytoestrogen content of soy infant formulas were 87+/-3 and 49+/-2 microg/g. The phytoestrogen content of cereals varied with brain, with genistein ranging from 3 to 287 microg/g and daidzein from 2-276microg/g. Supplementing the diet of 4-month old infants with a single daily serving of cereal can increase their isoflavone intake by over 25% depending on the brain chosen. This rate of soy isoflavone intake is much greater than that shown in adult humans to alter reproductive hormones. Available evidence suggests that infants can digest and absorb dietary phytoestrogens in active forms and neonates are generally more susceptible than adults to perturbations of the sex steroid milieu, it would desirable to study the effects of soy isoflavone on steroid-dependent developmental processes in human babies. www.ncbi.nlm.nih.gov/pubmed/9402332

2001, FDA NIEHS, The developing fetus is uniquely sensitive to perturbations with estrogenic chemicals. DES is the classic example. Phytoestrogen use in nutritional and pharmaceutical applications for infants and children is increasing. We investigated the carcinogenic potential of genistein, a naturally occurring plant estrogen in soy. At 18 months (mice study) the incidence of uterine adenocarcinoma was 35% for genistein and 31% for DES. Data suggest that genistein is carcinogenic if exposure occurs during critical periods of differentiation. Use of soy –bead infant formulas in the absence of medical necessity and the marketing of soy products that appeal to children should be closely examined. www.ncbi.nlm.nih.gov/pubmed/11389053

2007, FDA, NIEHS report; Soy genistein causes deleterious effects on the developing female reproductive system in adulthood. Altered ovarian differentiation, disrupted ovarian function and estrous cyclicity caused by neonatal exposure, reduced fertility altered mammary gland and behavioral endpoints. Further trangenerational effects were observed in neonatal treatment with genistein at environmentally relevant doses caused adverse consequences on female mice development which is manifested in adulthood. Feeding genistein found in soy formula are similar to those obtained from injecting genistein in mice. www.ncbi.nlm.nih.gov/pubmed/17604387

2011, Compared with girls fed non-soy-based infant formula, soy-fed girls were at 25% higher risk of early menarche throughout the course of follow-up. ….observable manifestation of mild endocrine-disrupting effects of soy isoflavone exposure. www.ncbi.nlm.nih.gov/pubmed/22324503

2010, Soy-based infant formula contain high levels of the estrogenic isoflavone genistein leading to "concern" that neonatal genistein exposure could cause acute and/or long-term adverse effects on reproductive and other organs. Neonatal genistein treatment caused increased relative uterine weight, down-regulation of progesterone receptor in uterine epithelia, genistein was also seen in the neonatal ovary, and thymus, which had an increase in the incidence of multioocyte follicles (MOF) and decrease in thymic weight. Increased MOF's persisted into adulthood in neonatally treated genistein females. www.ncbi.nlm.nih.gov/pubmed/20357267

2009, French Warn: soy products, in any amount should not be eaten by children under 3 years of age, or women who have breast cancer or at risk of the disease. Israeli Health Ministry: Issued public warning on soy, suggesting soy consumption be limited in young children and avoided if possible in infants. Germany reports: there is a lack of evidence to confirm the safety of soy isoflavone supplements. www.tyroid.about.com/cs/soyinfo/a/soy_4.htm

2009, FDA NIEHS, Developmental exposure to environmental estrogens is associated with adverse consequences later in life. Exposure to genistein, the gylcosylated for of the phytoestrogen genistein

found in soy products is of "concern" because U.S. infants are fed soy formula. Exposure to genistein during neonatal life adversely affects the female reproductive system.
www.ncbi.nlm.nih.gov/pubmed/20049207

2008, One of eight infants during the first 6 months of life given soy formula may be at risk for brain and behavioral disorders not evident until adolescence, a charge denied by the soy industry.
www.soyonlineservice.co.nz/articles/goodman.htm (IACC Note: URL is not valid.)

2010, Soy As An Endocrine Disruptor: Cause For Caution: Endocrine disrupting compounds (EDCs_ alter the function of the endocrine system and consequently cause adverse health effects. Phytoestrogens, natural plant compounds abundantly found in soy and soy products, behave as weak estrogen mimics or as anti-estrogen. They are considered to be EDCs. Supporting evidence that consumption of phytoestrogens is beneficial is indirect and inconsistent. Lifetime exposure to estrogenic substances, especially during critical periods of development, has been associated with formation of malignancies and several anomalies of the reproductive systems. Phytoestrogen consumption in infants, through soy-based formulas is of particular concern. Possible adverse effects should not be taken lightly.
www.ncbi.nlm.nih.gov/pubmed/21175082

2001 Studies show that soybean-based formulas contain large quantities of phytoestrogens, particularly isoflavones. Because of experimental data suggesting a possible deleterious effect of phytoestrogens on the neuro-endocrine maturation, the reduction of soy content in formulas must be considered.
www.ncbi.nlm.nih.gov/pubmed/11760676

2010 Uterine fibroids are the most common pelvic tumors in U.S. women as well as the most common cause for hysterectomy. The results showed an association between early fibroid diagnosis and having been fed soy formula during infancy.
www.ncbi.nlm.nih.gov/pmc/articles/PMC2854791/

2009 Bulletin of Academy of National Medicine. Infant Nutrition Nutritional quality during the first weeks of life can influence health during both infancy and adulthood. Exclusive long-term breast feeding is strongly recommended….Soy-based formulas are not recommended for healthy infants.
www.ncbi.nlm.nih.gov/pubmed/19718896

2010 Soy isoflavones, genistein and daidzein are widely consumed with evidence for potential adverse effects. Study results show that soy protein isolate is an efficient isoflavone delivery vehicle capable of providing significant proportions of the total dose into the circulation in the active aglycone form for distribution to hormone receptor-bearing tissues and subsequent pharmacological effects that determine possible health risks. www.ncbi.nlm.nih.gov/pubmed/20225898

2011, Compared with girls fed non-soy-based infant formula or milk formula, early soy-fed girls were at 25% higher risk of menarche. Results also suggest that girls fed soy products in early infancy may have an increase risk of menarche specifically in early adolescence and may be the manifestation of mild endocrine disrupting effects o f soy isoflavone exposure. This soy formula association with menarche warrants more in-depth evaluation. www.ncbi.nlm.nih.gov/pubmed/22324503

2003, Soy infant formula and phytoestrogens: Soy infant formula contains high levels of the isoflavones, genistein and daidzein which are referred to as phytoestrogens, and are structurally similar to estrogen. Infants consuming soy have high levels of circulating isoflavones, grater than the levels of isoflavones

which have been shown to produce physiological effects in adult women consuming a high soy diet. Most would argue for a "precautionary approach to be taken where there are potential developmental effects from the consumption of pharmacologically active compounds." www.ncbi.nlm.nih.gov/pubmed/12919490

2010- Acute and Chronic Effects of soy…raise concerns that high genistein are estrogenic and impact development of human infants fed soy formula. www.ncbi.nlm.nih.gov/pubmed/20357267

2001, NIEHS report: Dietary (soy) genistein produced effects in multiple estrogen-sensitive tissues in males and females consistent with estrogenic activity….within exposure ranges in humans. www.ncbi.nlm.nih.gov/pubmed/11738518

2002, Early soy exposure causes long lasting adverse effects later in life: www.ncbi.nlm.nih.gov/pmc/articles/PMC2039948/

2006, Estrogen regulates thymic development and immune function. Genistein administration to mice that produced serum genistein concentrations similar to those reported in human infants consuming soy formula and had demonstrable effects. Genistein had similar effects on many estradiol target genes, affecting genes involved in transcription, apoptosis, cell cycle and thymic development and function. www.ncbi.nlm.nih.gov/pubmed/16484547
2010 NIEHS study: Acute and Chronic effects of soy genistein in neonatal mice… Immediate and long-term effects raise concerns that genistein are estrogenic and impact development of human infants fed soy formula. Increase uterine weight down-regulation of progesterone receptor in uterus, neonatal ovary and thymus decrease thymic weight…genistein are estrogenic and impact human infants fed soy formula. www.ncbi.nlm.nih.gov/pubmed/20357267

2010, Soy-based infant formula contain high levels of the estrogenic isoflavone genistein leading to "concern" that neonatal genistein exposure could cause acute and/or long-term adverse effects on reproductive and other organs. Neonatal genistein treatment caused increased relative uterine weight, down-regulation of progesterone receptor in uterine epithelia, genistein was also seen in the neonatal ovary, and thymus, which had an increase in the incidence of multioocyte follicles (MOF) and decrease in thymic weight. Increased MOF's persisted into adulthood in neonatally treated genistein females. www.ncbi.nlm.nih.gov/pubmed/20357267

2005, In summary, neonatal treatment with genistein caused abnormal estrous cycles, altered ovarian function, early reproductive senescence, and subfertility/infertility at environmentally relevant doses. www.bioreprod.org/cgi/content/abstract/73/4/798 (IACC Note: URL is not valid.)

2004, Trypsin inhibitors interfere with protein digestion, cause pancreatic disorders and act as a growth inhibitor. All of this is found in soy infant formula. Hemaglutinin, a clot-causing agent that is dangerous for those with heart disease. The phytic acid content in soybeans is highest of all grains or legumes. Phytic acid can cause mineral deficiencies in iron, copper, zinc, calcium, and magnesium. Zinc is essential for growth of the nervous system and is called the intelligence mineral. Soy is known goitrogen that may cause hypothyroidism, by causing damage to enzymes that produce thyroid hormones. Iodine is blocked with is essential for proper thyroid function. Aluminum content in soy is about 10 times higher than milk, and can directly damage the infant's brain, as the blood-brain barrier has not been formed. In 1913 the USDA classified soy not as a food but as an industrial product. Why has a product

that has only been given GRAS standards for industrial use become a major component of 60% of our supermarket foods? Have we made corporate profits and conveniences more important than health? www.htnetwork/org/articles/soycontroversy.html (IACC Note: URL is not valid.)

2005, Total isoflavone content in soy infant formula varies widely, but in general is quite high with as much as 122ug genistein and 77ug daidzein per gram of formula. This translates to a daily intake of approximately 6-9 mg/kg body weight per day, which is 4-7 times higher than the amounts regularly consumed by adults meeting the FDA guidelines for soy consumption. Infants fed soy formula have circulating phytoestrogen concentrations of approximately 13,000 to 22,000times higher than endogenous estrogens, or levels high enough to produce many of the physiological effects discussed in this chapter. Although circulating isoflavone levels are highest among infants consuming soy formula, the fraction of bioavailable isoflavones may be higher in breast-fed infants with mothers who regularly consume soy. Both phytoestrogens and synthetic endocrine disruptors have been found to impair similar reproductive and neuroendocrine endpoints, including sexual differentiation and maturation, fertility, malformation of the genital tract, and sexual behavior suggesting that they have similar mechanisms of action. Indeed both can act as either estrogen agonists or antagonists, depending upon dose, timing of exposure, tissue type, gender, and species. (Exert from, "Endocrine Disruptors, Effects on Male and Female Reproductive Systems," Second Edition, by Rajesh K. Naz).

2010, Soy isoflavone, genistein and daidzein, are widely consumed in soy-based foods, evidence for potential adverse effects has been obtained from experimental animal studies. These results show that soy protein isolate (used in soy infant formula) is an efficient isoflavone delivery vehicle capable of providing significant proportions of the total dose into the circulation in the active aglycone form for distribution to receptor-bearing tissues and subsequent pharmacological effects that determine possible health risks. www.ncbi.nlm.nih.gov/pubmed/20225898

New Zealand speaks out against soy formula as serious risks are caused by soy endocrine disruptors. www.kidalog.net/soyformula.html

18. BPA and Soy Combination = Toxic Cocktail:
2011, Bisphenol A (BPA) and Genistein, the predominant component of soy products are both known environmental estrogens. We investigated the developmental toxicity of BPA and Genistein and their combined effects. Genistein as a teratogen was solid… The combined effect of BPA and Genistein was generally additive action…
www.ncbi.nlm.nih.gov/pubmed/21034807

1997, In addition to exposure to man-made chemicals (pesticides, polychlorinated biphenyls, phenolic compounds, phthalate esters, and organochlorine), the consumption of plant-derived estrogens in foodstuffs poses a potential risk to human health as phytoestrogens are more potent estrogens and their intake by some infants is likely to be considerable. www.ncbi.nlm.nih.gov/pubmed/9414467

2010, Serious malformation and a higher abnormal frequency of the central nervous system were induced by the combination of BPA and Genistein. Our findings suggest that genistein is embryotoxic and teratogenic to humans. BPA alone may not be a potential teratogen, but these two estrogenic chemicals have a synergistic effect on emybryonic development when present together during the critical period of major organ formation. Pregnant women should not take soy supplements.
www.ncbi.nlm.nih.gov/pubmed/20505512

2007, NIEH study: We further demonstrated that neonatal exposure to the endocrine active compounds (EAC's) genistein and Bisphenol-A (BPA) can affect sexually dimorphic brain morphology and neuronal phenotypes in adulthood with regional and cellular specificity. Developmental EAC exposure has been shown to affect a variety of sexually dimorphic behaviors including reproductive behavior. Maladaptive behavior could translate to decreased fitness of entire populations.
www.ncbi.nlm.nih.gov/pubmed/17822772

19. Soy = Toxic HORMONE DISRUPTOR:
1999, NIH report, Phytoestrogens such as soy isoflavones, and organochlorine compounds (pesticides and polychlorinated biphenyls) are two broad classes of putative endocrine disruptors- chemicals that may have the capability to alter a woman's hormonal milieu. The U.S. public is exposed to dietary sources of phytoestrogens… In addition, residues of organochlorine compounds can be detected in a large proportion of the population. Although phytoestrogens and organochlorine compounds are suspected of being important environmental determinants of hormone-related neoplasia, there are few epidemiological studies testing these hypotheses. http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~0jBvA2:1

1998, We investigated the estrogenic activity of environmental chemicals and phytoestrogens in competition binding assays with ER alpha or ER beta protein. All environmental estrogenic chemicals compete with 17b-estradiol for binding to both ER subtypes. Phytoestrogens, including soy genistein stimulate the transcriptional activity of both ER subtypes at concentrations of 1-10nM. The estrogenic potency of phytoestrogens is significant, especially for ER-beta, and they may trigger many of the biological responses that are evoked by the physiological estrogens.
www.ncbi.nlm.nih.gov/pubmed/975150

2005, Male reproductive abnormalities and falling sperm counts prompt interest into threats to global fertility. Little is known about the effects of dietary estrogens on male reproductive health. These non-steroidal estrogens are potent endocrine disruptors that modulate normal physiological functions. Phytoestrogens have become major component in food diet over the last few decades. Soy formula is another common source of phytoestrogen. This use is of particular concern since most vulnerable periods for estrogenic insult are pre-and neonatal periods when irreversible damage can be inflicted on the developing germinal epithelium. www.ncbi.nlm.nih.gov/pubmed/16234205

2008, NIH, National Toxicology Program reports: (Soy) Genistein is a naturally occurring isoflavone that interacts with estrogen receptors and multiple other molecular targets. "Concerns" have been raised regarding potential adverse effects of genistein, particularly with regard to reproductive toxicity and the induction of potentiation of carcinogenesis due primarily to its weak estrogenic activity. There is also minimal transfer of genistein to rat pups via the dams'milk. In soy group there were significant effects on the onset of aberrant estrous cycles. Pituitary gland weights were significantly increased. There was a significant positive trend in the incidences of mammary gland adenoma or adenocarcinoma. There were positive trends in the incidences of adenoma or carcinoma in the pars distalis of the pituitary gland of females in males a significant positive trend occurred in incidences of combined adenoma or carcinoma of the pancreatic islets. There was some evidence of carcinogenic activity of genistein in female rats based on increased incidences of mammary gland adenoma or adenocarcinoma and pituitary gland neoplasms. The effects of genistein on common hormonally related spontaneous neoplasms of female rats are consistent with an estrogenic mechanism of toxicity.
www.ncbi.nlm.nih.gov/pubmed/18685716

2011, The increasing incidence of hypospadias is partly attributed to increased gestational exposure to endocrine disruptors. Gestational exposure to genistein altered the urethral expression of 277 genes. Among the most affected were hormonally regulated genes. Genistein affected tyrosine kinase receptors. Gestational exposure to genistein contributes to hypospadias by altering pathways of tissue morphogenesis, cell proliferation and cell survival. www.ncbi.nlm.nih.gov/pubmed/21421236

2005, Soy isoflavonoids are plant phytoestrogens are increasingly advocated as a natural alternative to estrogen replacement therapy. As weak estrogen agonists/antagonists with a range of other enzymatic activities, the isoflavonoids provide a useful model to investigate the actions of endocrine disruptors. Activational and organizational effects of these compounds on the brain are reviewed. Isoflavonoids act in vivo through both ERalpha and ERbeta. Their neurobehavioural actions are largely anti-estrogenic, either antagonizing or producing an action in opposition to that of estradiol. Small, physiologically relevant exposure levels can alter estrogen-dependent gene expression in the brain and affect complex behavior in a wide range of species. Implications for these findings in humans, particularly in infants, remain uninvestigated and are a subject of increasing public interest.
www.ncbi.nlm.nih.gov/pubmed?term=Phytoestrogen action in the adult and developing brain

2008, Endocrine disrupting chemicals (EDCs) exert hormone-like activity and exposure to these compounds may induce both short- and long-term deleterious effects. The EDCs examined included estradiol, androgen active compounds, soy phytoestrogens, and atrazine. All EDCs impaired reproduction. Male sexual behavior proved to be a sensitive index of EDC exposure and embryonic exposure to a variety of EDCs consistently resulted in impaired male sexual behavior. Exposure to EDCs during embryonic development has consequences beyond impaired function of the reproductive axis.
www.ncbi.nlm.nih.gov/pubmed/18006066

2004, Soy causes agonistic and antagonistic properties on ER (Estrogen Receptor) alpha and ER Beta in human cells and functions as an endocrine disruptor. www.ncbi.nlm.nih.gov/pubmed/15084758

2002, Concerns have been raised about the potential adverse effects on reproductive health and immune status of farm animals following exposure to environmental compounds that disrupt normal hormonal actions. These compounds range from natural plant estrogens, (genistein), to growth promoting pharmaceuticals to chemicals spread in water, sewage, sludge or detergents, plastics, pesticides (DDT), and industrial chemicals. These compounds are commonly termed 'endocrine disrupting compounds or endocrine disruptors' due to their ability to disrupt hormone synthesis, storage or metabolism. Susceptibility of target tissues is related to the stage of development, cumulative exposure dose and the immune status of the individual. Effects that are observed in the adult may be due to exposure to endocrine disruptors during fetal life. www.ncbi.nlm.nih.gov/pubmed/12142238

2010, Soy As An Endocrine Disruptor: Cause For Caution: Endocrine disrupting compounds (EDCs_ alter the function of the endocrine system and consequently cause adverse health effects. Phytoestrogens, natural plant compounds abundantly found in soy and soy products, behave as weak estrogen mimics or as anti-estrogen. They are considered to be EDCs. Supporting evidence that consumption of phytoestrogens is beneficial is indirect and inconsistent. Lifetime exposure to estrogenic substances, especially during critical periods of development, has been associated with formation of malignancies and several anomalies of the reproductive systems. Phytoestrogen consumption in infants, through soy-based formulas is of particular concern. Possible adverse effects should not be taken lightly.
www.ncbi.nlm.nih.gov/pubmed/21175082

1997, Man-made chemicals potential risk to human health include phytoestrogens comparing to plastics, pesticides etc. www.ncbi.nlm.nih.gov/pubmed/9414467

2000, NCTR Genistein principal soy isoflavone in diet to male and female rats. Endocrine responsive tissues including brain, liver, mammary, ovary, prostate, testis, thyroid and uterus showed significant dose-depended increases in total genistein concentration. Female liver contained the highest amount and male whole brain contains the least blood concentrations and physiologic effects of genistein. www.ncbi.nlm.nih.gov/pubmed/10917909

2004, Among the issues raising concerns about human exposure to soy phytoestrogens is how such exposure may affect responsiveness and sensitivity of the exposed subjects to additional xenobiotics, particularly drugs and environmental chemicals with estrogenic or other endocrine disruptor activities. www.ncbi.nlm.nih.gov/pubmed/15320740

2004, Feeding with a soy formula should not be recommended for the prevention of allergy or food intolerance in infants at high risk of allergy or food intolerance: www.ncbi.nlm.nih.gov/pubmed/15266499

2007, Endocrine disrupting chemicals (EDCs) cause defects in sexual behavior and reproductive ability due to their steroid-like or anti-steroid like properties. In addition, endocrine systems such as the hypothalamus-pituitary-thyroid (HTP) axis may be targets of endocrine disruption. There may be multiple targets for interference by various EDC substances suspected of having endocrine disruptor activity, such as genistein as well as glycitein and daidzein (soybean isoflavones). A striking example is genistein, on one had inhibits thyroid peroxidase enzyme in the thyroid and on the other hand also displays estrogenic and anti-estrogenic effects by interacting with Estrogen Receptor-beta. EDC can act in a transgenerational manner by epigenetic and modification of genes. www.ncbi.nlm.nih.gov/pmc/articles/PMC2174406/

2003, Native soybean lectins (cause intestinal disorders, diarrhea, nausea, vomiting, nutritional deficiencies, immune allergic reactions, possible death) could potentially have deleterious effects on young animals. www.ncbi.nlm.nih.gov/pubmed/12710487

2002, In postmenopausal subjects, mean lutenizing hormone (LH)secretion decreased after discontinuing soy, suggesting a residual estrogenic effects. In a premenopausal woman enhanced LH secretion was observed after soy treatment, suggesting there may be subpopulations of women who are highly sensitive to soy isoflavones. www.ncbi.nlm.nih.gov/pubmed/11925465

20. Soy-Cause Of GENE MUTATIONS:

1998, FDA NCTR Reports: Our results may be interpreted that soy phytoestrogen genistein is a chromosomal mutagen. www.ncbi.nlm.nih.gov/pubmed/9729267

2006, National Institute of Mind Health Confirms: “Tiny, Spontaneous Gene Mutation May Boost Autism Risk. Our results show conclusively that these tiny glitches are frequent in autism, occurring in at least 10% of the cases, and primarily in the sporadic form of the disease, which accounts for 90% of affected individuals.” www.nimh.nih.gov/press/gene-mutations-autism.cfm (IACC Note: URL is not valid.)

2004, Phytoestrogens are a matter of public concern, results point to genotoxicity of phytoestrogens. www.ncbi.nlm.nih.gov/pubmed/15177650

1991, Genotoxic effects of genistein: A variety of genotoxic effects of phytoestrogens have been reported. Genistein effects occur at relevant low dietary concentrations. No dose is without risk, the dose defines the poison. www.ncbi.nlm.nih.gov/pubmed/17688899

2004, Genotoxicity, DNA Damage: Recent studies indicated that genistein and/or daidzein induced cancer of reproductive organs in rodents…we examined the ability of genistein daidzein and their metabolites to cause DNA damage and cell proliferation. DNA damage by isoflavone metabolites plays a role in tumor initiation by isoflavones via estrogen receptors to estrogen response elements. www.ncbi.nlm.nih.gov/pubmed/14992594

2003, Genotoxic activity of soy daidzein, exhibit genotoxic potential in vitro www.ncbi.nlm.nih.gov/pubmed/14644352

2007, "Concerns" about potential detrimental or other genotoxic effects persist about soy-derived phytoestrogens. This review focuses on soy phytoestrogen, genistein, critically examining dose as a crucial determinant of cellular effects. In toxicology, the well accepted principle of "the dose defines the poison" applies to many toxicants and can be invoked to distinguish genotoxic effects of natural dietary products such as genistein. www.ncbi.nlm.nih.gov/pubmed/17688899

2008, Developmental effects of exposure to endocrine disruptors can influence adult characteristics in mammals, but could also have evolutionary consequences. The effects of a continuous pre-and post-natal exposure to high levels of dietary soy isoflavones was evaluated on sexual maturity, morphometric parameters and DNA methylation status in mice. Individuals from a population subjected to a high consumption of soy isoflavones (plant-estrogens) can show alterations in characters that may be of importance from an evolutionary perspective, such as epigenetic and morphometric characters or sexual maturation. www.ncbi.nlm.nih.gov/pubmed/18793434

21. Soy-Damage Caused to Thymus, Thyroid, and IMMUNE SYSTEM:

Congenital hypothyroidism is proven to cause mental retardation. Maternal thyroid function during pregnancy is crucial for normal neurodevelopment of the fetus. The "Hypothalamus-Pituitary-Thyroid" (HPT) axis is functional early in gestation and remains immature until after birth. There is a critical period for thyroid hormone mediated human brain development that begins in utero and extends through 2-3 years of age. Excessive or deficient thyroid hormone levels during this period can cause irreversible brain damage. Soy causes deficient thyroid levels.

2007, Endocrine Disruptors and the Thyroid Gland: It is now shown that there may be multiple targets of interference by various Endocrine Disrupting Chemicals (EDC) with the complex regulatory network of thyroid hormone synthesis, metabolism, distribution, and action on the various levels of endocrine regulation and feedback control. Complex biological developmental programs controlled by thyroid hormone may be disturbed by EDC action. Chosen for analysis was an environmentally and nutritionally relevant collection of substances suspected to have endocrine disrupting activity because of their steroid-like or anti-steroid effects. These substances included genistein as well as glycitein and daidzein from soybean. These substances also interfere with multiple targets at various levels of the HPT axis in a tissue-specific manner.

The soy isoflavone genistein decreased iodide accumulation by 52%. Iodide uptake was also inhibited in the presence of this endocrine disruptor chemical. Thyroid peroxidase (TPO) also seems to be the target of goitrogens from isoflavone genistein from soybeans. It was already known four decades ago that feeding infants with soy milk caused goiter in those with inadequate iodine. Genistein, an isoflavone of soy could be responsible for the pathogenesis of this type of childhood goiter as well known for its endocrine activity exerted via interaction with estrogen and other nuclear receptors also inhibits TPO in vitro and in vivo. One EDC affects more than on target in the HPT axis or even affects more than one endocrine axis, a striking example is genistein. Our results show that hypothalamic-pituitary-thyroid (HPT) axis is a relevant target of (soy) endocrine disruptor action. Genistein inhibits TPO enzyme activity and also binds thyroid hormones, displaying estrogenic and anti-estrogenic effects by interacting with Estrogen Receptor-beta. Taken together, there seems to be synergistic as well as antagonistic interference at several levels of thyroid hormone synthesis, action, and regulation. www.ncbi.nlm.nih.gov/pmc/articles/PMC2174406/

2009, It's not advisable to assume that soy is safe for thyroid patients. It's also clear that soy does have the potential to cause thyroid problems in a segment of the population that is susceptible due to iodine deficiency or other conditions. www.thyroid.about.com/cs/soyinfo/a/soy_4.htm

1959, A 10 month old infant reared on soybean product from birth developed a goiter and hypothyroidism. Studies suggest that a goitrogenic agent was present in this particular soybean product that interfered with thyroid hormone synthesis in susceptible individuals. http://pediatrics.aapublications.org/content/24/5/752.abstract

1999, Autoimmune disorders and evaluation of medical risk factors in autism. Autism is a neurologic disorder that is often associated with autoimmune disorders (hypothyroidism) in the patient, in the patients' relatives. The number of autoimmune disorders was greater in families with autism. An increased number of autoimmune disorders suggests that in some families with autism, immune dysfunction could interact with various hormone disruptor factors to play a role in autism pathogenesis. www.ncbi.nlm.nih.gov/pubmed/10385847

2002, The phytoestrogen genistein induces thymic and immune deficiency; These results raise the possibility that serum genistein concentrations found in soy-fed human infants may be capable of producing thymic and immune abnormalities, as suggested by previous reports of immune impairments in soy-fed human infants. www.ncbi.nlm.nih.gov/pubmed/12032332 (without the thymus not enough T-cells are produced. The spleen and lymph nodes are at risk, and immune system fails).

2002, Soy exposure during pregnancy and lactation causes long-lasting adverse effects into adulthood. Soy-cause of thymus masses. www.ncbi.nlm.nih.gov/pmc/articles/PMC2039948/

1986, Zinc is required to confer biological activity on thymic hormone molecules. Thyroid status modulates thymic endocrine function in humans. (Soy phytates inhibit zinc as studies conclude above). http://jcem.endojournals.org/cgi/conten/abstract/62/3/474 (IACC Note: URL is not valid.)

2008, Soy products increase the risk of thyroid disease, and this danger is particularly great for infants on soy formula. Researchers have identified that soy isoflavones act as potent anti-thyroid agents, and are capable of suppressing thyroid function and causing or worsening hypothyroidism.. Because soy phytoestrogen that acts in the body much like a hormone, it is no surprise that it interacts with the delicate balance of the thyroid's hormonal systems.

www.thyroid-info.com/articles/soydangers.htm.

2006, Modulation of immune response following dietary genistein exposure in 2 generations: evidence of thymic regulation. Results demonstrate that genistein can modulate the immune system in both adult and developing mice in a dose-specific manner. Genistein may modulate the immune system by functioning as either an estrogen agonist or antagonist. www.ncbi.nlm.nih.gov/pubmed/161623809

2010, Soy-based infant formula contain high levels of the estrogenic isoflavone genistein leading to "concern" that neonatal genistein exposure could cause acute and/or long-term adverse effects on reproductive and other organs. Neonatal genistein treatment caused increased relative uterine weight, down-regulation of progesterone receptor in uterine epithelia, genistein was also seen in the neonatal ovary, and thymus, which had an increase in the incidence of multioocyte follicles (MOF) and decrease in thymic weight. Increased MOF's persisted into adulthood in neonatally treated genistein females. www.ncbi.nlm.nih.gov/pubmed/20357267

2004, Soy fed to infants with congenital hypothyroidism Infants fed soy formula had prolonged increases in thyroid stimulating hormone, (abnormal thyroid function) when compared to infants fed non-soy formula. www.ncbi.nlm.nih.gov/pubmed/14709499

1995, Persistent hypothyroidism in an infant receiving soy formula: Patient with congenital hypothyroidism who remained persistently hypothyroid while on a soy formula diet despite large doses of L-thyroxine (or Levothyroixin) a synthetic hypothyroid drug.
http://pediatrics.aapublications.org/content/96/1/148.short

2011, There is some scientific evid3ence that soy may adversely effect thyroid function and interfere with thyroid hormone absorption. Thyroid hormones affect metabolism, growth, brain development, breathing and body temperature. So low thyroid hormone levels can result in mental retardation and stunted growth. Certain types of chemicals in soy, especially isoflavones, may disrupt the normal action of thyroid hormones., increasing the risk for thyroid problems or goiter. Genistein and daidzein were found to be the chemicals in soy that inhibited thyroid peroxidase. www.livestrong.com/article/407844-thyroid-disease-and-soy-products

2008, Endocrine disrupting chemicals (EDCs) exert hormone-like activity and exposure to these compounds may induce deleterious effects. The EDCs examined included estradiol, androgen active compounds, soy phytoestrogens, and atrazine. The EDCs are known to impact both the immune and thyroid systems. www.ncbi.nlm.nih.gov/pubmed/18006066

2006, Concerns have been expressed that soy may be contraindicated for some subsets of the population. One concern is that soy may adversely affect thyroid function and interfere with the absorption of synthetic thyroid hormone. In individuals with compromised thyroid function, food may increase risk of developing clinical hypothyroidism. www.ncbi.nlm.nih.gov/pubmed/16571087

2010, Soybean phytoestrogens, isoflavones genistein and daidzein were reported to affect adversely thyroid function in the presence of other goitrogenic factors. Both genistein and daidzein can induce microfollicular changes in the thyroid tissue and reduce the level of thyroid hormones in middle-aged male rats. TSH cells increased cellular volume while Volume of T(4) and T(3) levels decreased….. (a cause of hypothyroidism and a number of cascading adverse effects).
www.ncbi.nlm.nih.gov/pubmed/20463299

2008, Soy phytoestrogens or isoflavones have been definitely shown to depress thyroid function and to cause infertility in every animal species studied so far. www.genistein.net/cancer.html

1997, FDA, NIEHS report, Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action. Because inhibition of thyroid hormone synthesis can induce goiter and thyroid neoplasia in rodents, delineation of ant-thyroid mechanisms for soy isoflavones may be important for extrapolating goitrogenic hazards identified in chronic rodent bioassays to humans consuming soy products. www.ncbi.nlm.nih.gov/pubmed/9464451

2002, FDA NIEHS Drs. Doerge and Sheehan report: Goitrogenic and estrogenic activity of soy: Genistein, the major soy isoflavone has a frank estrogenic effect in women. Additional factors appear necessary for soy to cause overt thyroid toxicity. Safety testing of soy products is not required. The possibility that widely consumed soy products may cause harm in the human population via estrogenic and goitrogenic activities is of concern. Human research into soy toxicity is the best way to address these concerns. www.ncbi.nlm.nih.gov/pubmed/12060828

1990, Autoimmune thyroid disease: Infant feeding of soy formula may affect autoimmune diseases later in life. This retrospective analysis documents the association of soy formula feeding in infancy and autoimmune thyroid disease Dr. Fort Study. www.ncbi.nlm.nih.gov/pubmed/2338464

2002, Johns Hopkins, Primary goal of this study was to compare effects of perinatal exposure with life-long exposure to genistein, an estrogenic compound in soy on the endocrine and immune system in rat adulthood. These data illustrat4e that exposure to genistein during pregnancy and lactation exerts long-lasting effects on the endocrine and immune systems in adulthood.
www.ncbi.nlm.nih.gov/pmc/articles/PMC2039948

2002, Frequency of feedings with soy-based milk formulas in early life was significantly higher in children with autoimmune thyroid disease. Inappropriate thyroid hormone levels can also have a devastating effect on the developing human brain especially during the first 12 weeks of pregnancy when the fetus depends on the mother's thyroid hormones for brain development. www.rense.com/general3/soy.htm

2001, The morphological and biochemical alterations in the neurons of the developing hypothyroid brain are comparable to those seen in several neurodegenerative diseases.
www.ncbi.nlm.nih.gov/pubmed/11448519

1993, Fetal thyroid hormones play an essential role in fetal brain development. It is possible that maternal soy hormone disruptor consumption influence fetal brain development. There is a "critical period" in which appropriate thyroid hormone levels are absolutely essential for normal brain development. In humans this period is considered to begin late in gestation and extend through 1-3 years of age. Deficiencies of thyroid hormone during this critical period cause serious damage to the structural development and organization of the brain.
Edrv.endjournals.org/content/14/1/94/short (IACC Note: URL is not valid.)

2009, NIEHS experts Daniel Doerge and Daniel Sheehan call for rigorous, high-quality experimental and human studies into soy toxicity. It's not advisable to assume that soy is universally safe for thyroid patients. It's also clear that soy does have potential to cause thyroid problems. Soy can be a trigger for developing hypothyroidism. http://thyroid.about.com/cs/soyinfo/a/soy_4.htm

2008. Hypothyroidism during early development results in multiple morphological and functional alterations in the developing brain. Hyperactive locomotor behavioral patterns resulted in chronic hypothyroid, and affects spatial memory in a negative manner.
http://ep.physoc.org/content/93/11/1199.abstract

2001, Hypothyroidism in the developing rat brain is associated with marked oxidative stress and aberrant intra-neuronal accumulation of neurofilaments.
www.ncbi.nlm.nih.gov/pubmed?term=hypothyroidis in the developing rat brain is associated with marked stress and aberrant intraneuronal accumulation of neurofilaments

Eileen Nicole Simon

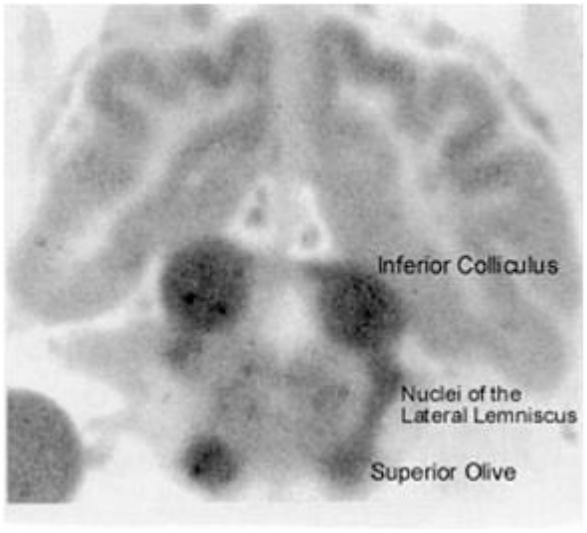
January 14, 2013

1. Developmental language disorder is the most serious handicap for children with autism, and this should be the primary focus of research.
2. White matter (myelin) in the language circuits of the brain develops most rapidly during the first 18 months after birth, which is when children normally begin to speak [Su et al. 2008].
3. In infants at high risk, white matter appeared greater at 6 months in those later diagnosed with autism, but development then declined over the next 18 months [Wollf et al. 2012].
4. The lag in myelination after 6 months of age should be compared with the poor development of the cerebral cortex in monkeys subjected to asphyxia at birth [Faro & Windle 1969].
5. The progression of changes only became noticeable in the brains of monkeys 10 months of age or older. Damage of auditory nuclei and the thalamus remained evident in the brainstem.
6. Disturbed maturation of the brain in monkeys was most evident in the corpus callosum and areas of the cerebral cortex that receive projections from the thalamic nuclei.
7. These were among the sites of diminished white matter growth observed by Wollf et al. in the MRI scans of children who developed autism.
8. The primary sites of damage in the brains of monkeys subjected to asphyxia were (a) nuclei in the brainstem auditory pathway and (b) the thalamic nuclei [Ranck & Windle 1959, Myers 1972].
9. The monkeys asphyxiated at birth recovered from early developmental delays (considered to be minimal), but poor manual dexterity and short memory spans persisted.
10. The experiments with monkeys should be repeated but now, rather than sacrificing the animals, MRI monitoring of white matter development should be done [Chanraud et al. 2010].
11. To those who would object to such experimentation, the obstetric protocol for clamping the umbilical cord of newborn human infants should be pointed out.
12. Clamping the umbilical cord immediately after birth was adopted as a standard practice in obstetrics almost 30 years ago, when the increase in autism prevalence appears to have begun.
13. Most children obviously suffered no harm from this procedure. However, many obstetricians wisely continued to wait for the first breath before clamping the cord. Not all infants breathe immediately at birth, and many require resuscitation.
14. The procedure of when (or if) to clamp the umbilical cord is currently under revision [ACOG 2012].
15. Trophic neurotransmitters produced by brainstem auditory nuclei guide maturation of target areas in the cerebral cortex, the language areas in the human brain. [Friauf & Lohman 1999].
16. Brainstem nuclei in the auditory pathway are also essential for processing (not just transmitting) incoming acoustic signals [Chandrasekaran et al. 2012].
17. Loss of the ability to comprehend spoken language has now been described in several case reports following injury of auditory nuclei in the midbrain [references 10-22 below].
18. Consider how much more serious such an injury would be for an infant.
19. Brainstem injury has been reported in human cases due to circulatory arrest or birth injury [references 23-31 below]. Note that Natsume et al. (1995) reported both neuropathological and MRI data. MRI investigations now likely will supersede neuropathology.
20. I previously suggested two papers published in 2011, Kulesza et al. on malformation of the superior olive in 9 people with autism, and Lukose et al. on producing the same malformation in rats exposed to valproic acid during gestation. These are important papers that I believe should be cited in the strategic plan [references 32 and 33 below].

References

1. Su P, Kuan CC, Kaga K, Sano M, Mima K. Myelination progression in language correlated regions in brain of normal children determined by quantitative MRI assessment. Int J Pediatr Otorhinolaryngol. 2008 Dec;72(12):1751-63.
2. Wolff JJ, Gu H, Gerig G, et al. (IBIS Network, www.ibis-network.org). Differences in white matter fiber tract development present from 6 to 24 months in infants with autism. Am J Psychiatry. 2012 Jun;169(6):589-600.
3. Faro MD, Windle WF. Transneuronal degeneration in brains of monkeys asphyxiated at birth. Exp Neurol. 1969 May;24(1):38-53.
4. Ranck JB, Windle WF. Brain damage in the monkey, Macaca mulatta, by asphyxia neonatorum. Exp Neurol. 1959 Jun;1(2):130-54.
5. Myers RE. Two patterns of perinatal brain damage and their conditions of occurrence. Am J Obstet Gynecol. 1972 Jan 15;112(2):246-76.
6. Chanraud S, Zahr N, Sullivan EV, Pfefferbaum A. MR diffusion tensor imaging: a window into white matter integrity of the working brain. Neuropsychol Rev. 2010 Jun; 20(2):209-25.
7. ACOG Committee Opinion 543 Timing of Umbilical Cord Clamping After Birth (December 2012) http://www.acog.org/Resources_And_Publications/ Committee_Opinions_List
8. Friauf E, Lohmann C. Development of auditory brainstem circuitry. Activity dependent and activity-independent processes. Cell Tissue Res. 1999 Aug;297(2): 187-95.
9. Chandrasekaran B, Kraus N, Wong PC. Human inferior colliculus activity relates to individual differences in spoken language learning. J Neurophysiol. 2012 Mar; 107(5):1325-36.
10. Howe JR, Miller CA. Midbrain deafness following head injury. Neurology. 1975 Mar; 25(3):286-9.
11. Jani NN, Laureno R, Mark AS, Brewer CC. Deafness after bilateral midbrain contusion: a correlation of magnetic resonance imaging with auditory brain stem evoked responses. Neurosurgery. 1991 Jul;29(1):106-8.
12. Nagao M, Kita Y, Kamo H. Haemorrhage in the inferior colliculus. et al. Neuroradiology. 1992;34(4):347.
13. Meyer B, Kral T, Zentner J. Pure word deafness after resection of a tectal plate glioma with preservation of wave V of brain stem auditory evoked potentials. J Neurol Neurosurg Psychiatry. 1996 Oct;61(4): 423-4.
14. Hu CJ, Chan KY, Lin TJ, Hsiao SH, Chang YM, Sung SM. Traumatic brainstem deafness with normal brainstem auditory evoked potentials. et al. Neurology 1997 May;48 (5):1448–1451.
15. Johkura K, Matsumoto S, Hasegawa O, Kuroiwa Y. Defective auditory recognition after small hemorrhage in the inferior colliculi. J Neurol Sci. 1998 Nov 26; 161(1): 91-6.
16. Masuda S, Takeuchi K, Tsuruoka H, Ukai K, Sakakura Y. Word deafness after resection of a pineal body tumor in the presence of normal wave latencies of the auditory brain stem response. Ann Otol Rhinol Laryngol. 2000 Dec;109(12 Pt 1): 1107-12.
17. Vitte E, Tankéré F, Bernat I, Zouaoui A, Lamas G, Soudant J. Midbrain deafness with normal brainstem auditory evoked potentials. Neurology 2002 Mar 26;58(6):970–3.
18. Hoistad DL, Hain TC. Central hearing loss with a bilateral inferior colliculus lesion. Audiol Neurootol 2003 Mar-Apr; 8(2):111-223.
19. Musiek FE, Charette L, Morse D, Baran JA. Central deafness associated with a midbrain lesion. J Am Acad Audiol 2004 Feb; 15(2):133-151.
20. Pan CL, Kuo MF, Hsieh ST. Auditory agnosia caused by a tectal germinoma. Neurology. 2004 Dec 28;63(12):2387-9.

21. Kimiskidis VK, Lalaki P, Papagiannopoulos S, Tsitouridis I, Tolika T, Serasli E, Kazis D, Tsara V, Tsalighopoulos MG, Kazis A. Sensorineural hearing loss and word deafness caused by a mesencephalic lesion: clinicoelectrophysiologic correlations. Otol Neurotol. 2004 Mar;25(2):178-82.
22. Pillion JP. Speech processing disorder in neural hearing loss. Case Report Med. 2012;2012:206716. doi: 10.1155/2012/206716. Epub 2012 Dec 6.
23. Neubuerger KT. Lesions of the human brain following circulatory arrest. J Neuropathol Exp Neurol. 1954 Jan;13(1):144-60.
24. Gilles FH. Selective symmetrical neuronal necrosis of certain brain stem tegmental nuclei in temporary cardiac standstill [Abstract of presentation at the American Association of Neuropathologists: 38th Annual Meeting. Atlantic City. New Jersey]. J Neuropathol Exp Neurol 1963 Apr; 22(2):318.
25. Gilles FH. Hypotensive brain stem necrosis. Selective symmetrical necrosis of tegmental neuronal aggregates following cardiac arrest. Arch Pathol. 1969 Jul;88(1):32-41.
26. Griffiths AD, Laurence KM. The effect of hypoxia and hypoglycaemia on the brain of the newborn human infant. Dev Med Child Neurol. 1974 Jun;16(3):308-319.
27. Schneider H, Ballowitz L, Schachinger H, Hanefield F, Droeszus J-U. Anoxic encephalopathy with predominant involvement of basal ganglia, brain stem and spinal cord in the perinatal period. Report on seven newborns. Acta Neuropathol. 1975 Oct 1;32(4):287-98.
28. Leech RW, Alvord EC Jr, Anoxic-ischemic encephalopathy in the human neonatal period, the significance of brain stem involvement. Arch Neurol. 1977 Feb;34(2): 109-13.
29. Janzer RC, Friede RL. Hypotensive brain stem necrosis or cardiac arrest encephalopathy? Acta Neuropathol (Berl). 1980;50(1):53-6.
30. Roland EH, Hill A, Norman MG, Flodmark O, MacNab AJ. Selective brainstem injury in an asphyxiated newborn. Ann Neurol. 1988 Jan;23(1):89-92.
31. Natsume J, Watanabe K, Kuno K, Hayakawa F, Hashizume Y (1995) Clinical, neurophysiologic, and neuropathological features of an infant with brain damage of total asphyxia type (Myers). Pediatr Neurol. 1995 Jul;13(1):61-4.
32. Kulesza RJ Jr, Lukose R, Stevens LV. Malformation of the human superior olive in autistic spectrum disorders. Brain Res. 2011 Jan 7;1367:360-71.
33. Lukose R, Schmidt E, Wolski TP Jr, Murawski NJ, Kulesza RJ Jr. Malformation of the superior olivary complex in an animal model of autism. Brain Res. 2011 Jun 29;1398:102-12.

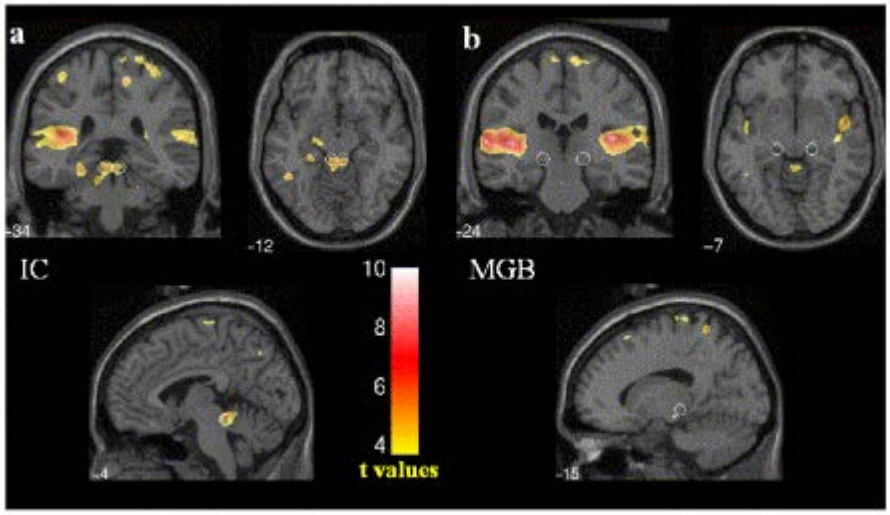


Blood Flow in the Brain

From the seminal paper by Seymour S. Kety (Bull NY Acad Med 1962 38:799-812). Autoradiogram, 60 seconds after injection of a radioactive tracer into the circulation of a cat. The greatest perfusion (darkest areas) is seen in nuclei of the brainstem auditory pathway.
This technique has revealed that the highest blood flow in the brain is to structures of the auditory pathway in several other mammalian species, including monkeys.

Other subcortical areas have only slightly lower blood flow, thalamus, mammillary bodies, caudate nucleus, hippocampus.

High blood flow makes these areas most vulnerable to toxic substances and factors that disrupt aerobic metabolism. Impairments in these brain structures may underly sensory and motor handicaps of children with autism.



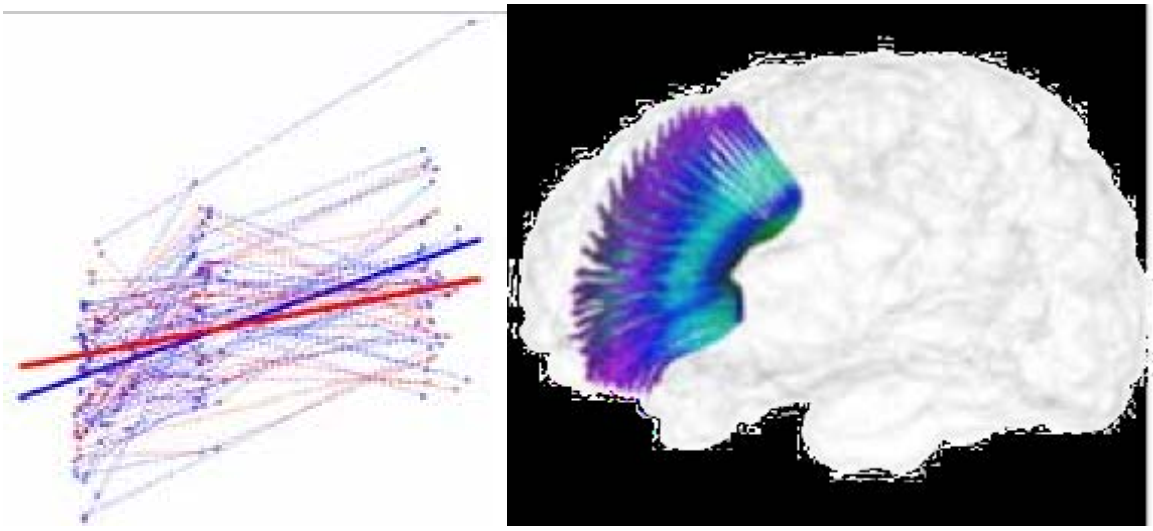
From: Budd TW et al. Neuroimage 2003; 20:1783

The inferior colliculi on functional MRI (fMRI) scans:
(a) Three orthogonal slices, coronal, horizontal, sagittal – centered on the anatomically defined inferior colliculi (IC), white circles superimposed,
(b) Slices centered on the anatomical center of medial geniculate bodies (MGB), white circles superimposed.

The special brightness of the inferior colliculi (a) may be because they have the highest blood flow in the brain even in the absence of stimulation. The medial geniculate bodies (b) in comparison are barely visible.

Excerpt of FIGURE 2 from Wolff et al. (2012):
Trajectories of fractional anisotropy in white matter of corpus callosum subdivisions in 92 high-risk infants with and without evidence of autism spectrum disorders (ASDs) at 24 months of age.

Heavy lines represent mean values, red ASD-positive, blue ASD-negative



Left: Fractional anisotropy (Y-axis) vs age (X-axis), measure of white matter development, Y axis (frontal lobes) versus age in months (3 - 27 months), X axis.
Right: Target area in cerebral cortex

Initial growth in ASD-positive children (red) slowed after 6 months of age. Growth in ASD-negative infants (blue) continued at a faster rate than for the children who were diagnosed with ASD at 24 months of age.

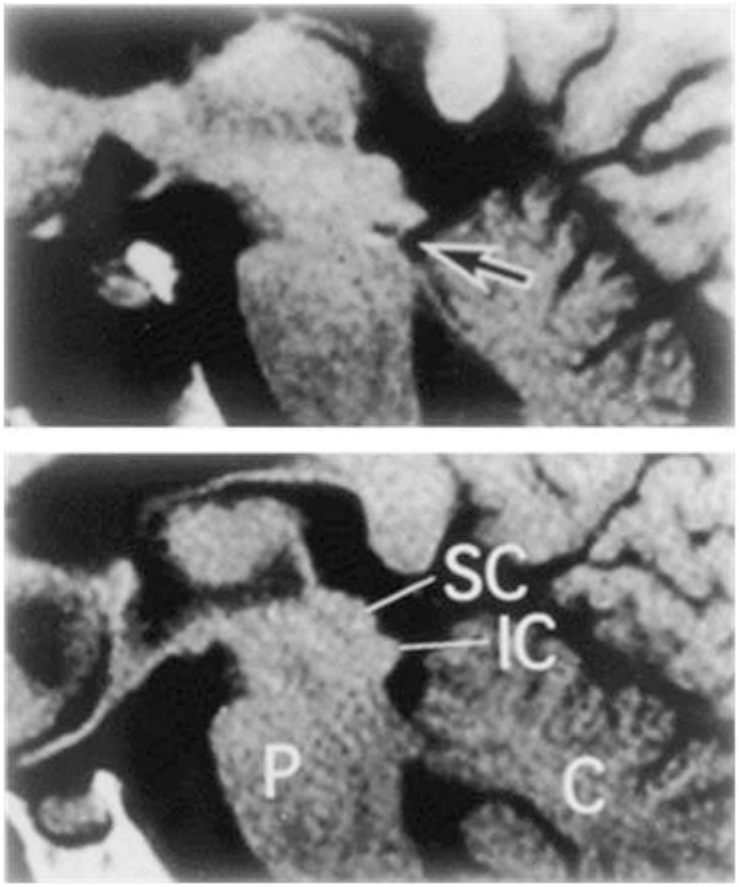


Figure 4 from Johkura et al. (1998)
Top: T-weighted MRI showing a small punctate hematoma in the inferior colliculi (arrow).
Bottom: A comparison with a normal subject cut in the same plane to show the normal shape and location of the inferior colliculi. SC, superior colliculus; IC, inferior colliculus; P, pons; C, cerebellum.

Case report (excerpt): A 46-year-old man lost consciousness in a skiing accident. When he regained consciousness five days after the accident, he complained that he was unable to recognize any sounds. Otherwise, he showed no focal neurologic signs. Six months after the skiing accident, he was alert and cooperative, although he was unable to understand verbal and many nonverbal sounds. His cognitive functions were normal; he was able to speak, read, write and sing. His neurologic examination was otherwise normal.

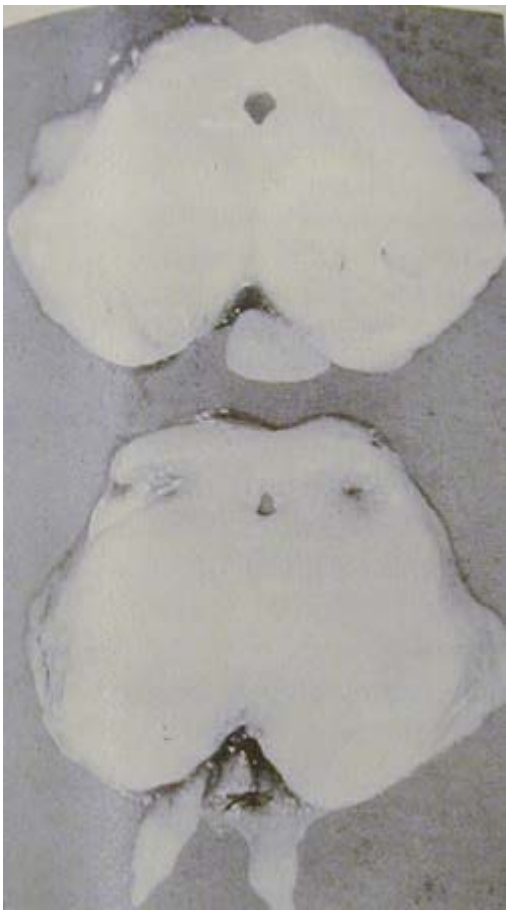


Figure 1 from Leech & Alvord (1977), p111:
Bottom: Damage of the inferior colliculi in a human infant.

AUTISM AND COMPLICATIONS AT BIRTH

Complications at birth have long been reported as part of the background of children who later become autistic. Below are excerpts from published reports on autism associated with complications at birth.

Two common conclusions drawn in these papers are (1) That no unifying feature can be identified, and (2) That some problem with the mother or her infant was a predisposition for complications.

However, fear of oxygen lapse during labor and delivery is clearly a unifying feature, whether the birth is by a breech presentation or emergency c-section. Problems with the mother, such as small pelvic size, or infant, such as large head size are problems, but should these factors be considered abnormalities specific to the brain disorder in autism?

Why is the clear evidence of anoxia at birth so pointedly dismissed?

1. Guinchat V, Thorsen P, Laurent C, Cans C, Bodeau N, Cohen D. Pre-, peri- and neonatal risk factors for autism. Acta Obstet Gynecol Scand. 2012 Mar;91(3): 287-300.

"During the perinatal and neonatal periods, the risk factors for PDD were preterm birth, breech presentation, planned cesarean section, low Apgar scores, hyperbilirubinemia, birth defect and a birthweight small for gestational age."

2. Gardener H, Spiegelman D, Buka SL. Perinatal and neonatal risk factors for autism: a comprehensive meta-analysis. Pediatrics. 2011 Aug;128(2):344-55. Epub 2011 Jul 11.
"The factors with the strongest evidence for an association with autism risk included abnormal fetal presentation, umbilical-cord complications, fetal distress, birth injury or trauma, multiple birth, maternal hemorrhage, summer birth, low birth weight, small for gestational age, congenital malformation, low 5-minute Apgar score, feeding difficulties, meconium aspiration, neonatal anemia, ABO or Rh incompatibility, and hyperbilirubinemia."
3. Dodds L, Fell DB, Shea S, Armson BA, Allen AC, Bryson S. The role of prenatal, obstetric and neonatal factors in the development of autism. J Autism Dev Disord. 2011 Jul;41(7):891-902.
". . . The only factor relevant to the labor and delivery time period in the final model was type of labor." (induced labor or no labor)

4. Haglund NG, Källén KB. Risk factors for autism and Asperger syndrome. Perinatal factors and migration. Autism. 2011 Mar;15(2):163-83.
"Obstetric sub-optimality (prematurity, low Apgar scores, growth restriction, or macrosomia) was positively associated with autism but not with Asperger syndrome."

5. Zhang X, Lv CC, Tian J, Miao RJ, Xi W, Hertz-Picciotto I, Qi L. Prenatal and perinatal risk factors for autism in China. J Autism Dev Disord. 2010 Nov;40(11):1311-21.
" Seven characteristics at the time of delivery were significantly associated with autism in the unadjusted analyses and all these characteristics had an odds ratio of at least 2 except for cesarean delivery: abnormal gestational age including preterm (16.9% in cases vs. 4.2% in controls) and postterm (8.4% in cases vs. 4.2% in controls), nuchal cord (23.2% in cases vs. 6.3% in controls), cesarean delivery (50.0% in cases vs. 35.8% in controls), delayed crying (11.6% in cases and 2.1% in controls), newborn complications (29.5% in cases and 4.2% in controls), apnoea (11.6% in cases and 1.1% in controls), and neonatal jaundice (11.6% in cases and 1.1% in controls)"

6. Indredavik MS, Vik T, Evensen KA, Skranes J, Taraldsen G, Brubakk AM. Perinatal risk and psychiatric outcome in adolescents born preterm with very low birth weight or term small for gestational age. J Dev Behav Pediatr. 2010 May;31(4):286-94. "Lower birth weight, shorter gestation, and intraventricular hemorrhage were risk factors for psychiatric problems in the very low birth weight group. Lower Apgar score increased the risk for autism spectrum symptoms and internalizing symptoms."

7. Bilder D, Pinborough-Zimmerman J, Miller J, McMahon W. Prenatal, perinatal, and neonatal factors associated with autism spectrum disorders.Pediatrics. 2009 May; 123(5):1293-300. "Children with an ASD were more likely to have a breech presentation . . . and be born by primary cesarean delivery . . . The significance of primary cesarean delivery was lost when excluding those children presenting breech (which is an indication for performing a cesarean delivery)."

8. van Handel M, Swaab H, de Vries LS, Jongmans MJ.Long-term cognitive and behavioral consequences of neonatal encephalopathy following perinatal asphyxia: a review. Eur J Pediatr. 2007 Jul;166(7):645-54.
"Most outcome studies have focused on neurological functioning and severe deficits in young children (<4 years). In general, very few children with mild encephalopathy show neurological impairments or have developed severe mental or motor retardation at preschool age. ... Only a few studies looked at the behavioral consequences of NE. Those studies found elevated rates of hyperactivity and autism in children with moderate NE."

9. Kolevzon A, Gross R, Reichenberg A.Prenatal and perinatal risk factors for autism: a review and integration of findings. Arch Pediatr Adolesc Med. 2007 Apr;161(4): 326-33.
"According to our review, 3 parental characteristics and 2 obstetric conditions emerge as potential risk factors for autism: namely, paternal age, maternal age, maternal immigration, growth restriction, and newborn hypoxia. In analyses that adjusted for confounding variables, these factors usually remained statistically significant."

10.Maimburg RD, Vaeth M. Perinatal risk factors and infantile autism. Acta Psychiatr Scand. 2006 Oct;114(4):257-64.
"We also found strong associations between children with infantile autism and mothers with foreign citizenship, children with congenital malformations and children who needed treatment at Neonatal Intensive Care Unit (NICU) after birth. When the caesarean sections were categorized into scheduled and unscheduled procedures, we found only scheduled caesarean sections to be associated with infantile autism."

11.Badawi N et al. Autism following a history of newborn encephalopathy: more than a coincidence? Dev Med Child Neurol. 2006 Feb;48(2):85-9.
"... in a population-based study of moderate and severe term newborn encephalopathy (NE) in Western Australia ...infants with NE were 5.9 (95% CI 2.0–16.9) times more likely to be diagnosed with an ASD than controls... this was not an expected association at the outset of the study"

12.Sugie Y et al. Neonatal factors in infants with Autistic Disorder and typically developing infants. Autism. 2005 Dec;9(5):487-94. "Frequent neonatal complications included hyperbilirubinemia, history of phototherapy, premature birth (less than 37 weeks), asphyxia, post-term birth of 42 weeks or longer, fetal distress, and complications of respiratory distress."

13.Larsson HJ et al. Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status. Am J Epidemiol. 2005;161:916-25. "In the unadjusted analyses, breech presentation, lowApgar score (less than or equal 7) at 5 minutes, low birth weight (less than or equal 2,500 g), gestational age at birth of less than 35 weeks, and being small for gestational age were associated with a statistically significantly increased risk of autism..."

14.Gillberg C, Cederlund M. Asperger syndrome: familial and pre- and perinatal factors. J Autism Dev Disord. 2005 Apr;35(2):159-66.
"Five children had had an Apgar score of 6 or under at 1, 5 , or 10 minutes, and 3 of these had scores of 1 or 2 (i.e., they had severe postnatal asphyxia). ... Of the 100 individuals, 58 had one or more remarks in their birth- or perinatal records about a serious problem in the peri-/neonatal period."

15.Cederlund M, Gillberg C. One hundred males with Asperger syndrome: a clinical study of background and associated factors. Dev Med Child Neurol. 2004 Oct;46(10): 652-60.
“For 58 of 99 children, some kind of abnormality was noted in their neonatal record. ... Twenty-two had had hyperbilirubinemia (plasma bilirubin more than 200µmol/l), ... Hyperbilirubinemia occurs in about 10% of newborn infants... Forty-five of 92 children (49%) for whom fairly detailed data about early language development were available, clearly did not have normal language development at 2 years of age. It cannot be concluded that the remainder had normal language development.”

16.Glasson EJ et al. Perinatal factors and the development of autism: a population study. Arch Gen Psychiatry. 2004 Jun;61(6):618-27.

"Cases were more likely to have experienced fetal distress during labor (OR, 1.64; 95% CI, 1.15-2.34). Apgar scores calculated at 1 minute showed that significantly more cases achieved a score of 6 or less (54 [19.5%] of 277 cases with data recorded since 1991..." "[12.9%] of 512 control subjects with data recorded since 1991)(OR, 1.6; 95% CI, 1.1-2.4), and cases were more likely to have taken more than 1 minute before the onset of spontaneous respiration (OR, 1.4; 95% CI, 1.0-1.9)."

17.Wilkerson DS et al. Perinatal complications as predictors of infantile autism. Int J Neurosci. 2002 Sep;112(9):1085-98.
"… 5 items were found to significantly predict group membership (prescriptions taken during pregnancy, length of labor, viral infection, abnormal presentation at delivery, and low birth weight)."

18.Hultman CM et al. Perinatal risk factors for infantile autism. Epidemiology. 2002 Jul; 13(4):417-23.
"The risk of autism was associated with daily smoking in early pregnancy (OR = 1.4; CI = 1.1-1.8), maternal birth outside Europe and North America (OR = 3.0; CI = 1.7-5.2), cesarean delivery (OR = 1.6; CI = 1.1-2.3), being small for gestational age (SGA; OR = 2.1; CI = 1.1-3.9), a 5-minute Apgar score below 7 (OR = 3.2, CI = 1.2-8.2), and congenital malformations (OR = 1.8, CI = 1.1-3.1)." Note: The OR (odds ratio) was greatest for 5-min Apgar score below 7."

19.Zwaigenbaum L et al. Pregnancy and birth complications in autism and liability to the broader autism phenotype. J Am Acad Child Adolesc Psychiatry 2002 May;41(5): 572-9
"Children with autism spectrum disorders have lower optimality (higher rates of complications) than unaffected siblings…"

20.Greenberg DA et al. Excess of twins among affected sibling pairs with autism: implications for the etiology of autism. Am J Hum Genet 2001 Nov;69(5):1062-7 "In a sample of families selected because each had exactly two affected sibs, we observed a remarkably high proportion of affected twin pairs, both MZ and DZ…"

21.Bodier C et al. Autisme et pathologies associées. Étude clinique de 295 cas de troubles envahissants du developpment. [Autism and associated pathologies. Clinical study of 295 cases involving development disorders] Presse Médicale 2001 Sep 1; 30(24 Pt 1):1199-203. French.
"Among the children with a serious medical condition, 34.4% also had ante- or perinatal antecedents. Among the 33% without any medical factor, 77% also had ante- or perinatal antecedents."

22.Juul-Dam N et al. Prenatal, perinatal, and neonatal factors in autism, pervasive developmental disorder-not otherwise specified, and the general population. Pediatrics. 2001 Apr;107(4):E63.
"… specific complications that carried the highest risk of autism and PDD-NOS represented various forms of pathologic processes with no presently apparent unifying feature."

23.Matsuishi T et al. Brief report: incidence of and risk factors for autistic disorder in neonatal intensive care unit survivors. J Autism Dev Disord. 1999 Apr;29(2):161-6
"AD was identified in 18 of the 5,271 children and the incidence was 34 per 10,000 (0.34%). This value was more than twice the highest prevalence value previously reported in Japan. Children with AD had a significantly higher history of the meconium aspiration syndrome (p = .0010) than the controls. Autistic patients had different risk factors than CP." Note: CP (cerebral palsy) occurred in 57 of the 5,271 children."

24.Bolton PF et al. Obstetric complications in autism: consequences or causes of the condition? J Am Acad Child Adolesc Psychiatry. 1997 Feb;36(2):272-81.
"…[obstetric] optimality score (OS), were compared in two groups: 78 families containing an autistic proband (ICD-10 criteria) and 27 families containing a down syndrome (DS) proband… RESULTS: Autistic and DS probands had a significantly elevated OS compared with unaffected siblings, regardless of birth order position. The elevation was mainly due to an increase in mild as opposed to severe obstetric adversities."

25.Ghaziuddin M et al. Obstetric factors in Asperger syndrome: comparison with highfunctioning autism. J Intellect Disabil Res. 1995 Dec;39 (Pt 6):538-43.
"Males with AS showed a trend toward lower Apgar scores at one minute …"

26.Lord C et al. Pre- and perinatal factors in high-functioning females and males with autism. J Autism Dev Disord. 1991 Jun;21(2):197-209.
"These data provide slight support for the contribution of nonspecific pre- and perinatal factors to other etiological bases of autism."

27.Steffenburg S et al. A twin study of autism in Denmark, Finland, Iceland, Norway and Sweden. J Child Psychol Psychiatry. 1989 May;30(3):405-16.
"In most of the pairs discordant for autism, the autistic twin had more perinatal stress."

28.Levy S et al. A comparison of obstetrical records of autistic and nonautistic referrals for psychoeducational evaluations. J Autism Dev Disord. 1988 Dec;18(4):573-81.
"Abnormal presentation at birth is the only factor that occurred more frequently for the autistic sample…"

29.Lobascher ME et al. Childhood autism: an investigation of aetiological factors in twenty-five cases. Br J Psychiatry. 1970 Nov;117(540):525-9.
"There were more complications of labour in the experimental group than the controls (p=0.001) ...Abnormal conditions of the child noted at delivery occurred significantly more frequently in the experimental group, e.g. difficulty with resuscitation, cord around neck, fractured skull, cyanosis, head moulding, bruising, jaundice (p<0.0004)."

Note: Personally Identifiable Information (PII) has been redacted in this document

Eileen Nicole Simon

January 24, 2013

Attached is an article on how clamping the umbilical cord at birth came about. Please provide this to members of the IACC with my comments that follow:

Clamping the umbilical cord is clearly a practice that came about with no evidence of its safety. Clamping the cord before the first breath risks causing a lapse in respiration. The IACC might possibly be able to suggest that this procedure no longer be allowed. Resuscitation should be done at the delivery bed with the cord left intact.

Resuscitation by ventilation of the lungs risks over inflation of lobes near the airways with failure to expand deeper (distal) lobes. Blood must be flowing in the capillaries around the alveoli for oxygen to be taken up by hemoglobin. Placental transfusion should provide this blood, unless it is prevented by clamping.

The dangers of cord clamping and resuscitation by ventilation are currently being revealed in research based on randomized controlled groups of human infants.

What should have been recognized long ago is that a lapse in respiration leads to a distinct pattern of damage within the brainstem auditory pathway. Long ago this pattern of damage should have been recognized as relevant to delayed language development in children with "minimal cerebral dysfunction" (MCD), which is now referred to as pervasive developmental disorder (PDD).

Developmental language disorder is the most serious handicap for children with autism. The neurological basis for this must be sought. The idea that language development in autism is hindered by social obliviousness is leading nowhere.

Research on echolalic speech and "pronoun reversal" should be encouraged. Pronoun reversal is simply one aspect of echolalic speech. The child (or adult) simply repeats verbatim phrases that are relevant to a particular situation.

"You don't want to go to the playground?" means "I don't want to go to the playground." The child repeats what he has heard. [PII redacted] asked parents to explain the meanings of what he referred to as "metaphorical phrases". "What's the matter, did your wagon get stuck?" was a universal phrase of frustration used by my son [PII redacted], even for things like difficulty squeezing toothpaste out of the tube. The echolalic autistic child (or adult) can hear and remember long phrases, but recognition of syllable boundaries is missing. Analysis of such boundaries has been reported to take place in nuclei of the brainstem pathway.

Research based on specific functions within specific systems of the brain should be sought to understand the language handicap of autistic children. Difficulties at birth must not be dismissed as irrelevant. Impairment of brainstem auditory nuclei caused by even a brief lapse in respiration at birth is relevant to disordered language development.

Sincerely,
Eileen Nicole Simon, PhD, RN

Dawn Loughborough

January 24, 2013

Autism is Medical

My name is Dawn Loughborough. I am the mother of a child with autism. I am here today to convey medical concerns and Autism. As a coordinating agency, IACC should work to coordinate medical concerns in Autism. What families would like is a physiological model for Autism as a special patient population.

Coordinating such an approach will help ready hospitals and clinics in the mainstream medical practices for patients with Autism, improve quality of care, and lower costs of autism treatments. It would help physicians and staff to better serve the autism patient population on concerns that impact delivery of care such as emergency room care metabolic considerations for medicines and anesthesia.

We desire an Integrative Autism Medical Care model similar to St Jude's Hospital quality of care approach to children's cancer where the finest teams work together to facilitate clinical treatments that inform mainstream medical institutions. If we are going to continue to deny and ignore the environmental and vaccine causation concerns, we need to put medical care in place to manage the resulting health outcomes and be responsible for these families' quality of life.

Quite often, our children have massive inflammation which alters the immune system and the nervous system both. These children cannot detoxify well. They have sensitivities and sensory problems.

It is very hard to say vaccine injury is happening without huge industrial-political back lash, but in reality, all science starts with observation. And the overwhelming observation coming from parents is that their children are changing after vaccines. Whether it is a genetic predisposition, illness, quality of vaccine, or sensitivity to one or more vaccine components, children are having adverse events and it is causing Autism. Federal awards from the National Vaccine Injury Compensation Program (NVICP) should inform IACC further. Fifty percent of Americans are vaccinating on alternative schedules because they have lost faith in the national vaccine program.

The relevance here is that IAAC exists to coordinate Autism. Autistic children are physically ill and require accurate diagnosis and appropriate treatment and quality of care. How do we know what to do if they have never been tested for things like mitochondrial disorder? Continuing to treat autism from a psychological model denies basic medical care to a generation of children. In addition to appropriate medical treatment, integrative services such as speech therapy, occupational therapy, well being and social development interventions are imperative.

Here are some general concerns that come from not talking about this and not coordinating medical solutions:

1. Intake Analysis Lacks Collection of Medical/ Physiological Data
Medical intake diagnostics for regressive autism are missing from mainstream medicine. We have psychological intake, but we do not have physiological intake. Caregiver observations need to be accounted for and pathways for appropriate medical treatment discussed.

2. Medical Management of Adverse Events
Flu shots are known to sometimes trigger Guillaine-Barre Syndrome which affects the nervous system and can paralyze patients, but physicians can now treat GBS early on with steroids and help patients avoid or recover faster… but childhood vaccines aren't identified in this manner which impedes knowing the signs of vaccine injury that may lead to chronic illnesses, like autism, when not treated.

Emergency room staff and pediatrician's offices need to be trained to recognize vaccine reaction so that they may start interventions immediately.

3. Medical Screening Needs to be Developed
Mitochondrial disorders are not rare, but rather a common issue with regressive autism. Our children should be screened for mitochondrial disorders. Additional screenings can be developed in future.

4. Seizures are Underdiagnosed
60% of autistic patients have seizure disorder or abnormal brain activity often affecting speech and movement and social disorders. Many children do not have their seizures detected because they are not referred to a neurologist for an EEG to look at their brain activity. All children with autism and speech or movement problems should be presented the opportunity to have a 24 hour EEG.

5. Gastrointestinal and Immune System Problems are Disregarded
Severe Gastrointestinal symptoms occur in a large percentage of autistic children. These children can have bowel disease, malabsorption, nutritional deficiencies, severe pain, inflammation, bleeding, diarrhea, constipation and immune dysfunction. Many children exhibit self-injurious behaviors in response to this pain. Proper investigation of and diagnoses is rarely made and most of our children are sent off with laxatives as their only intervention later in life leading to motility issues such as Hirshsprungs disease. This lack of investigation is nothing short of medical neglect. Endoscopy and colonoscopy are the standard that would be applied to any other patient presenting with the same persistent, severe symptoms. Autistic children and adults suffering, some for many years, when treated appropriately, drastically improve.

Faulty immune systems cause many symptoms and illnesses in the autistic child. All children should be baseline tested prior to receiving multiple vaccinations at once.

Many children who have autism have overloaded immune systems and are highly sensitive with extensive allergies to foods like gluten, casein, corn and soy, and other additives used in medicines including but not limited to dyes, glutamate, artificial sweeteners, and actual constituents themselves.

6. Detox Mechanisms are Sub Par
Children with Autism are terrible at detoxifying. They need system supports to assist with proper detoxification such as comes from [vitamin] B12 shots or glutathione. They are not effective excretors. They have a lot of metals in their systems. There are novel and emerging medical therapies to help with excretion.

7. Current Infectious Disease Management is Not Specific to Individual Needs
Policies currently in place by pediatric associations and individual practices exclude the very patient population that requires extensive coordination of care by a medical home and primary pediatrician. Parents who care for children with severe illness of injury following vaccination are told they must continue to vaccinate their child or they are forced from the pediatrician's practice. This results in children going without appropriate medical care.

I hope this shines some light on some of the very basic issues families are dealing with. Since 1998, I have had parent mentoring conversations with these families and this is our reality. We are everywhere. Thank you for this agency's time.