

# **COMPLEMENTARY ALTERNATIVE TREATMENT FOR SCHIZOPHRENIA: A REVIEW**

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Various segments of the schizophrenic population fall into subgroups of distinct biochemical imbalance. We often see subgroups of essential fatty acid deficiency, inadequate nutrition, dysglycemia, food intolerance, digestive compromise, malabsorption, under-methylation, vitamin B3 deficiency, vitamin C deficiency, heavy metal toxicity, B6 deficiency, zinc deficiency, brain hypothyroidism, and hypoadrenia. Complementary alternative medicine (CAM) has a key role in the treatment of schizophrenia. The goal of optimal complementary treatment is to correct the biochemical imbalance. In schizophrenia, we assess cases with lab tests and target our treatment accordingly. CAM treatment involves the use of nutritional supplements and other nutraceuticals. Dietary changes are also implemented in treatment.

## **The Essential Fatty Acid (EFA) Deficient Schizophrenic**

Chronic schizophrenics have increased phospholipid neuron membrane break down (oxidative stress) which concentrates in the frontal cortex and other brain areas (Fendri et al, 2006; Gattaz et al, 1995). Pro-inflammatory cytokine involvement in the development may set the stage for oxidative stress from early development onward (Song & Zhao, 2007; Das, 2004). Omega 3 fats have a neuroprotective and anti-inflammatory role. 60 % of the dry weight of the brain is fat. EFA's, including omega-3 and omega-6, are good fats, not saturated with hydrogen, and unfortunately, not readily provided in the American diet. Investigators are learning that there is an integral need for omega-3 supplementation for schizophrenia, mood, and behavior disorders (Song & Zhao, 2007; Greenwood & Young, 2001). EFA's are important components of nerve cell walls and they are involved in neurotransmitter electrical activity and post-receptor phospholipid mediated signal transduction.

Eicosapentaenoic acid (EPA) is an omega 3 fat and it is slightly more unsaturated than omega-6 fat. Brain membrane structure is compromised in chronic schizophrenia and EPA has demonstrated some potential in keeping brain neuron degeneration at bay and in reducing psychotic symptoms (Freeman, 2000; Horrobin, 2000; Bennett & Horrobin, 2000; Richardson et al, 2000; Puri et al, 2000; Horrobin, 1998; Puri et al, 1997).

Omega-3 EFA's may eventually gain notice as "a safe and efficacious treatment for psychiatric disorders in pregnancy and in breast feeding [moms]" (Freeman, 2000; Koletzko et al, 2001).

Fish have high amounts of omega 3's and the higher EPA supplements are derived from fish. Many EPA fish oil products contain antagonistic fats and the more pure EPA supplements have been found useful in schizophrenia treatment (Horrobin, 2000).

A balanced essential fatty acid profile may also be mediated by vitamin B3 but more research is needed to identify the role of B3 on the EFA profile of schizophrenics (Smesny et al, 2005).

## **The Schizophrenic with Inadequate Nutrition**

Neurotransmitter production is dependant on amino acid protein building blocks (phenylalanine, tyrosine, tryptophan, etc.) supplied from the diet. The catecholamines dopamine, norepinephrine, and epinephrine are derived from phenylalanine and tyrosine. Catecholamines are involved in

executive functions and motivation. Serotonin, the 'feel good' neurotransmitter, is derived from the amino acid tryptophan. Protein nutrition is very important for schizophrenia and general mental well-being. I have seen many schizophrenics respond when they start increasing protein intake with each meal. A diet that has 40% protein, 40% carbohydrate, and 20% fat is ideal for most schizophrenics.

Many schizophrenics do not eat three meals a day and their diet is invariably carbohydrate dominant. Carbohydrate dominant North American diets release glucose to the bloodstream quickly. Most schizophrenics require a dietary change that incorporates complex carbohydrates. They also do well to avoid high glycemic load foods; junk food, white sugar, white rice, and white bread. If they have a poor appetite, this can lead to inadequate nutrition. Poor appetite is associated with zinc loss.

Fat nutrition is important in schizophrenia. Cold water fish with teeth have a fat profile suitable for schizophrenia. Salmon, tuna, mackerel, herring, cod, and trout provide the highest omega-3 profile. Other high EFA sources include scallops, shrimp, flaxseed, walnuts, winter squash, and kidney beans.

Inadequate nutrition can occur with gastrointestinal compromise, mal-absorption, and low thyroid function.

### **The Dysglycemic Schizophrenic**

The brain's demand for glucose is so immense that about 20% of the total blood volume circulates to the brain, an organ that represents only 2% of body weight. The brain demands a substantial amount of glucose to maintain its high metabolic rate. Gluco-sensing neurons regulate glucose availability in the brain as a fail-safe mechanism to ensure homeostasis of brain glucose levels (Rao et al, 2006).

In schizophrenia, it seems likely that glucose transporters are compromised with consequent intraneuronal glucose deficits (McDermott & de Silva, 2005). McDermott and de Silva mention that this hypoglycemic state has the potential to cause "acute symptoms of misperceptions, misinterpretations, anxiety and irritability - the usual features of prodromal and first onset schizophrenia." Epidemiological investigations show us that schizophrenics are at increased risk for dysglycemia (Voruganti et al, 2007). Psychiatric meds also have some potential to induce hyperglycemic or insulin resistant states and this can be addressed, at least in part, with nutrition (Bergman & Ader, 2005). Schizophrenics with hyperglycemia, much like diabetics, present with hypoglycemic mental symptoms because the glucose doesn't get into brain neurons. Brain neurons starved for energy behave differently and mental function declines (Cox et al, 2002; Mitrakou et al, 1991). It is not clear if dysglycemia has a causative role in schizophrenia but it can be deemed an aggravating factor.

The hypoglycemic state involves a sharp rise of simple sugars in the blood followed by a sharp decline which robs the neurons of their main energy source. The sharper the decline, the greater the effect on brain cells. Typical hypoglycemic symptoms include irritability, poor memory, late afternoon blues, poor concentration, tiredness, cold hands, muscle cramping, and 'feeling better when arguing'.

It is said that hypoglycemia is 100% treatable in compliant patients. This emphasizes the need to address diet. The dysglycemic schizophrenic requires three solid meals (of 40% protein) a day and sometimes additional protein-containing snacks. Many schizophrenics need to be educated on complex versus fast carbohydrates. This entails avoiding junk food and sugar. When schizophrenics increase protein, they release glucose to the brain at a steady rate and their sugar

cravings lessen. Supplements such as chromium and zinc are useful for sugar balance. Botanical medicine is useful to treat advanced hypoglycemia.

### **The Food Intolerant Schizophrenic**

Some schizophrenics, just like the general population, have the potential to exhibit mild or severe food intolerance symptoms (Hardman & Hart, 2007; Jackson et al, 2007; Cade et al, 2000; Crowe & Perdue, 1992; Hall, 1976). The digestive tract reacts to food allergens by eliciting an immune response. Undigested food by-products can be toxic (e.g. opioid peptide exorphins), pass through the gut wall, enter the bloodstream, and reach the brain with subsequent influences on brain function (Takahashi et al, 2000; Cade et al, 2000; Dohan, 1988; King, 1984). I have several clients who have increased severity and frequency of hallucinations, delusions, depression, anxiety, irritability, and insomnia when they eat intolerant foods. We also see schizophrenics that experience a wide range of food related physical symptoms such as headaches, skin eruptions, palpitations, weakness, painful digestion, constipation, diarrhea, and arthralgia. Common intolerant foods in schizophrenia include gluten, dairy, and eggs (Jackson et al, 2007; Cade et al, 2000; Ross-Smith & Jenner, 1980). Other common food intolerances include tree nuts, citrus, fish, legumes and crustaceans. It is helpful to survey patient responses with a seven-day diet diary. Often schizophrenics are tired, weak, irritated, or moody after eating intolerant foods. Typically they either hate the intolerant food or crave it and this may be due to the toxic effects of opioid exorphin peptides. It is not uncommon to see patients that have fasted in the past and report feeling better. This is a good indication that they have a food intolerance. An elimination diet followed by provocation is helpful to assess the case clinically. Elaborate lab testing need not be implemented but IgG Elisa testing can be quite useful to assess food intolerances that are less obvious (Hardman & Hart, 2007; Atkinson et al, 2004). IgG responses are provoked when there is a delayed response. IgG testing rates the severity of the delayed reactions and provides a rotation diet recommendation. Many investigators have noted the improvement with dietary restriction of food intolerants. Approximately 10% of schizophrenics in our clinic will experience profound improvement after removing intolerant foods. More research is needed to understand the pathophysiology, epidemiology, and clinical presentation of the food sensitive subset of schizophrenics (Kalaydjian et al, 2006).

### **The Schizophrenic with Digestive Compromise and Malabsorption**

I constantly see gastrointestinal problems in schizophrenia including constipation, spastic obstipation, bloating, cramping, abdominal discomfort, IBS, and GERD. Compromised gastrointestinal function leads to malabsorption of nutrients. These patients often require higher doses of nutrients and medications. Lack of stomach acid can reduce intrinsic factor and diminish B12 utilization which is essential for methylation and neurotransmitter formation. Poor bowel transit locks in toxins and they build-up, tax the immune system, and reduce the absorptive surface area. Poor bowel transit may be due to lack of peristalsis, low thyroid function, or magnesium deficiency. Adequate water intake is about two liters per day for the average adult. This is essential to keep toxins moving out and, bowel contents hydrated. CAM treatment for digestive dysfunction and low thyroid function helps to alleviate digestive symptomology and also reduces the need for high nutrient dosing. Intact gastrointestinal health is a prerequisite for improved outcome in schizophrenia.

### **The Under-Methylated Schizophrenic**

In our clinic, we see approximately 30% of schizophrenics with methylation compromise as indicated by elevated fasting homocysteine levels. Without the ability to methylate efficiently, many schizophrenics are caught up in a state of neurotransmitter deficiency (Haidemenos et al, 2007; Herrmann & Obeid, 2007; Herrmann et al, 2007; Neeman et al, 2005; Regland et al, 1994;

Freeman et al, 1975). Schizophrenic researchers are well aware that certain brain tracts are overstimulated while others are understimulated (hypofrontality). If we can methylate efficiently, we have the machinery to form neurotransmitters in areas of the brain that are understimulated and neurotransmitter deficient.

Nutritional treatment with B12 and folic acid can restore methylation status. In schizophrenia, investigators have found genetic polymorphisms that disrupt folic acid pathways (Gilbody et al, 2007; Roffman et al, 2007). These schizophrenics have a greater need for folic acid supplementation.

Some evidence suggests that high circulating levels of homocysteine increase the level of homocysteic acid and cysteine sulphonic acid, both of which are NMDA receptor agonists that contribute to neuronal excitotoxicity (Parnetti & Bottiglieri, 1997). It is not known if neuronal degeneration in chronic schizophrenia is due to elevated homocysteine levels. It is also unclear if NMDA-induced excitotoxicity plays a causative role in schizophrenia. More research on methylation in schizophrenia is required to fully understand the pathophysiology.

### **The Vitamin B3 and C Deficient Schizophrenic**

Schizophrenics are poor at filtering the influx of sensory information and this causes perceptual dysfunction (hallucinations, illusions). Overstimulated brain pathways have excess neurotransmitter and symptoms are, in part, caused by neurotransmitter overstimulation of the prefrontal cortex. Many neurotransmitter pathways are involved; some overstimulated, others understimulated. In a schizophrenic brain, vitamin B3 and C (ascorbate) together have the potential to intervene and limit the production and oxidation of excess catecholamines in the brain.

Vitamin B3 is one of the few methyl acceptors in the body. As a methyl acceptor, B3 can limit, in a regulated fashion, neurotransmitter production (Zaremba & Hogue-Angeletti, 1982). When under stress, B3 can also limit adrenal gland conversion of noradrenaline to adrenaline. This acts as a fail-safe mechanism to prevent excessive adrenaline production and consequent readily autoxidizable catecholamine end-products (Wakefield et al, 1986).

A catecholamine rich cerebral environment is prone to oxidation and oxidized metabolites are neurotoxic and hallucinogenic to humans (Paris et al, 2007; Graumann et al, 2002; Smythies, 1997; Smythies, 1996). Oxidized catecholamines and toxic indoles may contribute to synaptic deletion (Smythies, 2000). In the healthy brain, oxidized catecholamines convert back to a stable form (neuromelanin), a process that has the effect of 'neutralizing' or 'storing' unwanted toxins (Smythies, 2000; Smythies, 1996). Smythies proposes that neuromelanin neutralization is compromised in schizophrenia and it may play a causative role (Smythies, 1997; Smythies, 1996). Both vitamin B3 and C (ascorbate) have the potential to reduce oxidized catecholamine intermediates (Siraki & O'Brien, 2002). In the adrenal gland, vitamin C is found in high concentrations to keep oxidation at bay (Wakefield et al, 1986).

As a separate mechanism of action, B3 and ascorbate are antagonistic to copper and can help to limit dopamine overproduction which overstimulates the prefrontal cortex and disturbs executive functions. Excess copper is very common in schizophrenia and copper is a cofactor in dopamine production. When dopamine pathways are overstimulated, serotonin (the opposing 'feel good' master neurotransmitter system) can become downregulated. This may in part account for some of the negative symptoms of schizophrenia.

Vitamin B3 (NAD) can be found in several supplemental forms; as niacin, niacinamide, inositol hexaniacinate, and NADH. NADH is the reduced form and it is more active than NAD. NADH is

dosed in the mg range. The other forms of B3 can be dosed in the gram range. Niacin and inositol hexaniacinate are dosed safely in the gram range in the treatment of intermittent claudication, hypercholesterolemia, and Raynaud's. Sufficient doses of B3 for schizophrenia are also in the gram range. Niacinamide and inositol hexaniacinate are flush-free. Pure niacin causes flushing due to the release of peripheral histamine stores. When dosed properly, pure niacin causes and head down flushing response during day 1 and day 2 and this subsides with subsequent gram range dosings. The inositol hexaniacinate form of B3 is well tolerated and has a great safety profile. Numerous investigators report the use of inositol hexaniacinate in the 4 gram daily range without a single adverse reaction (Sunderland et al, 1988; Ring et al, 1981; Holti, 1979). Inositol hexaniacinate also promotes brain blood flow which can be an important issue in schizophrenia with hypofrontality. Vitamin B3 has an interesting side-effect of longevity. The Mayo Clinic found significant reductions in mortality in subjects with high baseline cholesterol who used niacin alone (Berge & Canner, 1991; Pauling, 1986).

The B3 deficient state is typified in the disease pellagra, the rarely seen vitamin B3-dependant disease state. Classic symptoms of pellegra include psychosis, hallucinations, depression, anxiety, confusion, memory loss, anorexia, and fatigue (Pitche, 2005; Hoffer, 2000). Pellagrins and schizophrenics respond well to B3.

The positive results of B3 treatment have been noted in six double-blind trials on schizophrenic cohorts and an optimal dosing strategy is indicated (Hoffer, 1999; Hoffer, 1999(Mar); Hoffer, 1998; Hoffer, 1994; Hoffer, 1994(Jan); Hoffer, 1991; Hoffer, 1989; Hoffer, 1987; Hoffer, 1981; Hoffer, 1980; Hoffer, 1976; Hoffer, 1976(May); Hoffer, 1973; Hoffer, 1967; Hoffer, 1967(Jan); Hoffer & Osmond, 1966; Hoffer & Osmond, 1960; Hoffer et al, 1957).

Vitamin B3 and C are anti-stress vitamins. Practitioners who use vitamin B3 and C treatment continue to notice positive reponses (Dardanelli & Del Pilar Garcia, 2001; Wenzel, 2000; Hoffer, 1999; Walsh, 1997).

## **Heavy Metal Toxic Schizophrenia**

Heavy metals are associated with schizophrenic pathology (Kunert et al, 2007; Wolf et al, 2006; Stanley & Wakwe, 2002; Yao et al, 2001; Wallwork, 1987). It is not uncommon to see toxic levels of copper, lead, mercury, aluminum, arsenic, and cadmium in schizophrenics. We find some of the most advances schizophrenic cases having as many as three or four heavy metals. Heavy metal toxicity is also associated with ADHD, anxiety, OCD, depression, bipolar disorder, and dementia.

Free radical-mediated neurotoxicity and oxidative stress are implicated as causative factors of schizophrenia (Prabakaran et al, 2004; Yao et al, 2001). Most heavy metals are free radicals that induce oxidative stress and have an affinity for brain tissue (Aschner et al, 1997). Heavy metal free-radicals have the ability to compromise and/or destroy brain tissue and in so doing, decrease the availability of viable brain tissue.

Heavy metals are excreted by using the body's metal removing protein, metallothionein (Aschner et al, 1997; Ebadi, 1995). In the process of ridding heavy metals, this protein loses zinc (Chimienti et al, 2001). Zinc loss in schizophrenia in turn compromises the ability to transcribe proteins and make neurotransmitters. Investigators are recognizing compromised brain protein transcription pathways in the schizophrenia (Prabakaran et al, 2004; Aschner, 1996). Zinc deficiency is associated with schizophrenia and several other psychiatric pathologies including mood dysfunction and dementia (Ebadi, 1995).

Lead disrupts mental function (Goyer, 1995). Toxic lead levels are associated with psychosis (Bahiga et al, 1978). Lead toxicity is also associated with behavior disturbance, mood disorder,

learning disabilities, insomnia, immune compromise, brain damage, and delayed infant development. Lead also has been found to disrupt the carriage of thyroid hormone (T4) into the brain (Zheng et al, 2001; Zheng et al, 1999). If you are a city dweller, you are exposed to lead. The risk of lead toxicity rises with age. With widespread pesticide use, lead is accumulating in the food chain. Lead is found in paints, print colors, glass, batteries, rust protectants, alloys, old water piping, and old bathtubs (Wenzel & Pataracchia, 2005).

Mercury disrupts dopamine and norepinephrine metabolism (Rajanna & Hobson, 1985). Mercury is toxic and has no therapeutic use. It is not uncommon to find elevated mercury in patients with schizophrenia. Mercury is found in fluorescents, vaccines, thermometers, and exposed fish, animals, and plants. Dental fillings contain on average about 40% mercury which has the potential to leach with electrolytic decay. Mercury often causes headaches, nervous irritability, memory decline, depression, rapid fatigue, nausea, stomach aches, and allergic susceptibilities (Wenzel & Pataracchia, 2005). Mercury has a strong affinity for the brain but also sequesters in the liver, kidney, and spleen.

Aluminum can be toxic in patients with schizophrenia, mood disorders, Alzheimer's Disease, and digestive system pathologies. Aluminum disrupts enzyme function and is well documented to disrupt cognition, learning, and memory. Aluminum sources include aluminum cookware (especially when you heat and deglaze with an acid like vinegar or wine), drinking boxes, processed cheese, deodorants, and drinking water (aluminum is more soluble in our acidic magnesium deficient drinking water) (Foster, 2004).

Copper in excess has a toxic effect and in schizophrenics, it contributes to excess catecholamine oxidation, the end products of which are unstable toxic hallucinogens (Wolf et al, 2006; Rigobello et al, 2001). We find copper toxicity to be the most common heavy metal disruption in schizophrenia. It is also associated with ADHD, autism, depression, anxiety, bipolar disorder, and paranoia. With copper toxicity we see clinical zinc deficiency (Johnson, 2001). Copper is abundant in food and water as it is found in soil, pesticides, and animal feed. Since World War II we have been exposed to greater levels of copper due to copper piping in modern homes and the widespread use of birth control pills (estrogen based). Estrogen dominance is associated with higher circulating copper levels and copper is thought to transfer via placenta from generation to generation (Johnson, 2001). Other copper sources include copper tea pots, copper sulphate treated jacuzzi's or swimming pools, drinking water, dental fillings, prenatal vitamins, and copper IUD's. Neuroleptics, antibiotics, antacids, cortisone, tagamet, zantac, and diuretics can encourage a copper dominant biochemistry.

The liver produces the copper regulating proteins metallothionein and ceruloplasmin and, with low thyroid function, hepatic protein synthesis is diminished. The body attempts to remove excess copper by excreting it out of the liver via gall bladder excretion to the bowel. CAM treatment involves vitamin B3, vitamin C, and zinc which are helpful clinically because they are physiologically antagonistic to copper.

Schizophrenics relapse when thyroid function is low (Heinrich & Grahm, 2003). Poor thyroid function encourages heavy metal retention. CAM treatment for heavy metal toxicity involves mobilizing and eliminating the heavy metal, but this is best done after thyroid function has been optimized. When the thyroid is functioning optimally, the organs involved in metal removal are more efficient. CAM treatment also involves the obvious avoidance of environmental exposures.

### **Zinc & B6 Deficient Schizophrenia**

Zinc is important to several biochemical pathways as over 200 enzymes are zinc dependant. Zinc and iron are the most concentrated metals in the human brain. Zinc deficiency is very common in

schizophrenia (Stanley & Wakwe, 2002; Ebadi, 1995; Wallwork, 1987). Insufficient levels of zinc are also associated with depression, dementia, mental retardation, learning disabilities, lethargy, and apathy (Pfeiffer & Braverman, 1982). Zinc is essential for the synthesis of serotonin and melatonin (Johnson, 2001). Zinc is crucial to brain development as it plays a major role in protein synthesis (Johnson, 2001; Pfeiffer & Braverman, 1982). In the brain, zinc lowers excitability by moderating NMDA receptor release of excitatory glutamate. Zinc is involved in the synthesis of inhibitory GABA by the modulation of glutamate decarboxylase activity. Among the zinc-dependant proteins are metallothionein which is essential for heavy metal regulation and zinc bioavailability. The synthesis of Zn-thionein and CuZnSOD is essential in averting oxidative damage (Johnson, 2001). Zinc protects against fatty acid peroxidation which destroys neuron structure and function. Zinc is involved in neuronal plasma membrane structure and functioning and may play a key role in blood-brain-barrier integrity (Noseworthy & Bray, 2000). Zinc has a role in biogenic amine storage (in synaptic vesicles) and in axonal transport. The biogenic amine histamine regulates nucleus accumbens activity which is responsible for filtering sensory information and communicating with the amygdala, ventral tegmentum, and hypothalamus. Zinc is involved in the limbic system metabolism which regulates emotions. Hormonal metabolism of the hypophysis and hypothalamus are dependant on zinc as well.

B6 is involved in the decarboxylation of tyrosine, tyrtophan, and histadine into the neurotransmitters nor-epinephrine, serotonin, and histamine (Marz, 1997). B6 deficiencies are associated with schizophrenia, depression, and behavior disorders. It is a cofactor in homocysteine re-methylation (Levine et al, 2006). B6 has been found useful in memory acquisition, with just a 20mg dose (Deijen et al, 1992). It has demonstrated usefulness in controlling neuroleptic-induced akathisia and drug-induced movement disorders (Lerner et al, 2004; Lerner et al, 1999; Sandyk & Pardeshi, 1990). B6 is essential for the synthesis of antioxidants such as metallothionein, glutathionein, and CoQ10 which help to prevent neuronal oxidative stress. B6 and zinc are involved in the synthesis of glutamic acid decarboxylase (GAD) which blocks excitotoxicity which causes secondary oxidative damage. B6 is essential for glutathione peroxidase and glutathione reductase which help prevent mitochondrial decay.

The master neurotransmitters of the brain are derived from protein building blocks and assembled with exact instructions by means of messenger RNA (mRNA) transcription of neuronal DNA templates. Brain tissue samples of schizophrenics have been assessed with high-dimensional biology and found compromised in basic mRNA transcription and protein synthesis (Prabakaran et al, 2004). These pertebations influence an array of neuronal changes in the schizophrenic brain among which are, neurotransmitter synthesis and mitochondrial functioning. Oxidative stress can cause these pertebations and the insuing changes in neuronal structure and function may be integral to understanding schizophrenic pathophysiology. It is interesting to note that both zinc and vitamin B6 are needed by the body as cofactors in neurotransmitter synthesis; zinc is needed for transcription and B6 is needed for transamination.

Previous investigators have described B6 and zinc depletion in the context of pyrrolluria. In this metabolic syndrome, B6 and zinc interact with 2,4-dimethyl-3-ethylpyrrole and are readily excreted (Wenzel, 2000; Jackson et al, 1997; Edelman, 1996; Hoffer, 1994(Apr); Pfeiffer, 1975; Sohler et al, 1974; Pfeiffer, 1973; Sohler et al, 1970).

### **Brain Hypothyroidism & Hypoadrenia in Schizophrenia**

Thyroid and adrenal function are compromised in many schizophrenics (Heinrich & Grahm, 2003; Mello et al, 2003). The thyroid and adrenal are pivotal endocrine glands. Many symptoms common to adrenal dysfunction are seen in thyroid dysfunction and vice versa. The adrenal works in concert with the thyroid gland and often both glands need to be supported together (Abdullatif et al, 2006; Candrina et al, 1987).

Hypothalamic-Pituitary-Adrenal axis dysregulation is integrally associated with schizophrenia (Heinrich & Grahm, 2003; Mello et al, 2003). The adrenal glands are involved in the stress response, sugar metabolism, electrolyte balance, peripheral epinephrine synthesis, blood pressure regulation, and sex hormone metabolism. Many schizophrenics who are heavy coffee drinkers have low adrenal function. Low adrenal symptoms include sluggishness on waking, stress intolerance, lack of enjoyment, post-traumatic stress, addiction, dizziness, low blood pressure, fluctuant body temperature, insomnia at 4am, immune compromise, hypoglycemia, dermatitis, PMS, phobia, and poor libido. Schizophrenics can be warm at times and at other times cold and they may have trouble adapting to daily temperature changes. Fluctuant body temperatures and decreased heat tolerance are a sign of low adrenal function which often accompanies low thyroid function (Michel et al, 2007). Adrenal symptoms are a good indicator of adrenal status. In some cases, saliva testing is useful to assess the adrenal hormones DHEA and cortisol. Cortisol is part of the stress response but elevated cortisol disturbs mental function. Cortisol levels are commonly elevated in schizophrenics and depressives (Ritsner et al, 2004; Swigar et al, 1979). Adaptogens and supplements can be used effectively to support adrenal function without elevating cortisol.

Active thyroid hormone is responsible for enabling cells, at the DNA level, to maintain their metabolic rate. Thyroid hormone also maintains oxygen availability in the brain and elsewhere. With healthy thyroid hormone functioning, our cells produce energy and complete their tasks efficiently. When tissue cells including neurons have energy, they work efficiently. When thyroid function is low, cells remain in a state of hypofunction.

Hypofunctioning cells work slowly and produce minimal energy. Consequently, fewer enzymatic reactions occur and cells don't give off much heat and core body temperature decreases. Intolerance to cold is a typical complaint in low thyroid function (Heinrich & Grahm, 2003). When the body temperature is inadequate, enzymatic reactions do not occur as readily. Enzymatic reactions are needed throughout the body for among other things, neurotransmitter synthesis. It is not uncommon to have schizophrenics reporting that they feel warm when their body temperature, on average, is low.

Low thyroid symptoms are seen often in psychosis (Contreras et al, 2007; Bauer et al, 2003; Heinrich & Grahm, 2003; McGaffee et al, 1981). Thyroid support is becoming accepted as an integral part of the assessment and treatment of refractory depression (Jackson, 1998; Oppenheimer et al, 1995). The most obvious low thyroid symptoms include impaired cognition, easy weight gain, fatigue, pain, headache, irritability, anxiety, panic, PMS, depression, poor memory, poor concentration, insomnia, constipation, indigestion, hair loss, high cholesterol, and frequent infection (Heinrich & Grahm, 2003; Westphal, 1997; Heitman & Irizarry, 1995; Jackson, 1998). Many patients with varied non-specific complaints have low thyroid function.

The brain is highly dependent on thyroid hormone for the regulation of dopamine, norepinephrine, and serotonin pathways (Bauer et al, 2003; Haddow et al, 1999; Brouwer et al, 1998). "Brain hypothyroidism" has been described by Hatterer et al as a state that occurs when systemic T4 does not readily cross into the brain (Hatterer et al, 1993). Active thyroid hormone T3 is synthesized in the brain by brain type II 5'-deiodinase conversion of T4 to T3 (Schreiber, 2002; Oppenheimer et al, 1995). Brain neurons therefore depend on a ready supply of T4 in the brain. The choroid plexus of the brain produces transthyretin (TTR), a transport protein that binds T4 and transports it across the blood-cerebral spinal fluid barrier to the brain (Schreiber, 2002). Transthyretin is significantly downregulated in the cerebral spinal fluid (CSF) of schizophrenics versus healthy controls (Wan et al, 2006). This suggests that the schizophrenic brain lacks adequate amounts of T4 which can cause brain hypo-metabolism. This would surely diminish neurotransmitter synthesis.

Huang et al suggested that low CSF transthyretin could prove useful as a biomarker for early diagnosis of schizophrenia (Huang et al, 2006). Also of interest is the fact that lead has also been linked to the reduction of CSF transthyretin in humans (Zheng et al, 2001; Zheng et al, 1999). Reduced CSF transthyretin is also a trend seen in depression and suicidal propensity (Sullivan et al, 2006; Sullivan et al, 1999). Interestingly, many schizophrenics and depressives relapse when thyroid function drops (Heinrich & Grahm, 2003).

Peripheral blood thyroid levels could be normal in the context of brain hypothyroidism. T4 to T3 conversion by brain typeII 5'-deiodinase can be inhibited by cortisol (Hidal & Kaplan, 1988; Visser et al, 1982). This is important because cortisol levels are commonly elevated in schizophrenics especially during stress. Cortisol is a stress hormone and, during stressful periods we tend to conserve energy by shutting down thyroid hormone production.

The digestive system of a low thyroid patient will have poor motility and slow stool transit which can cause constipation and inefficient nutrient absorption (Shafer et al, 1984). In low thyroid patients, core body temperatures are often too low to allow digestive enzyme reactions to occur efficiently enough to properly break down food. After optimal CAM thyroid treatment, schizophrenics do not require as high a dose of nutrients because absorption improves. Magnesium can be used to help to improve peristaltic movement, draw water into the lower bowel, and avert tenesmus. Muscle pain syndromes (such as fibromyalgia) are also often associated with low thyroid function because muscle cells require ATP (the energy molecule provided indirectly by peripheral thyroid hormone metabolism) to relax. Chronic fatigue symptoms, at least in part, are often explained by low thyroid function.

Note that 'hypothyroidism' is a problem with the gland itself and more specifically, with its inability to produce adequate thyroid hormone. In classic hypothyroidism, blood tests reveal that there is low output of thyroid hormone (T4 or T3) and/or elevated thyroid stimulating hormone (TSH) levels. However, low thyroid cases may have normal blood test measures, low body temperature, and obvious low thyroid symptomology. It is not uncommon to see hypothyroid patients on thyroid hormone treatment with normal test measures and low thyroid symptoms. This can happen if adequate levels of circulating thyroid hormone (T4) is not readily converted peripherally into active thyroid hormone (T3) (Jackson, 1998; Oppenheimer et al, 1995; Lum et al, 1984). Currently, there is no conventionally accepted diagnostic agreement on a physiological state that accounts for normal test measures and poor peripheral conversion. Wilson's Temperature Syndrome however has emerged as a syndrome that fits that criteria. CAM interventions can help support the thyroid gland directly and also help support peripheral conversion. CAM thyroid treatment can be done safely as an adjunct to thyroid hormone medication. Blood assessments can rule out immune involvement which is typical in Hashimoto's thyroiditis. Hashimoto's is seen in 80% of hypothyroid cases and it responds well to low thyroid treatment. Blood assessments can rule out thyroid hyperfunctioning which is typical in Grave's Disease. Grave's, in its active phase, is a state of thyroid hyperfunction that requires a CAM treatment to calm thyroid function. In schizophrenia, thyroid support has global benefits because it improves the cellular physiology of the brain and other organs and body systems such as the liver, gastrointestinal tract, kidney, immune system, and musculoskeletal system.

## **Overview**

The cause of schizophrenia is unknown given its multi-factorial etiology. In the vast tomb of research on schizophrenia, investigators have described pathophysiological mechanisms that can be treated with complementary alternative protocols. The list of assessments and treatments described herein are not exhaustive but they represent the core considerations of an optimal complementary alternative treatment. These treatments can be used safely as an adjunct to conventional psychiatric treatment. Schizophrenics treated with CAM experience positive changes.

Response is based on the degree of severity and the duration of illness. We see schizophrenics who have been sick for a year or two who start responding within weeks. Schizophrenic's sick over 5 years are less responsive initially but improve with long term care. The pathological deterioration of brain tissue in schizophrenia impels us to utilize CAM treatments that keep oxidative stress at bay. The necessity of early screening and early intervention is important for both complementary alternative treatment and conventional psychiatric treatment.

Complementary treatments for schizophrenia have been developed since the early 1950's. A large outcome study is needed to compare the efficacy of nutritional adjunct treatments versus psychiatric medication alone. I foresee a time when CAM will have a key role in mainstream mental health care. Schizophrenic patients and families are constantly expressing their desire to see this happen. CAM protocols can easily be implemented and are cost effective when you consider the current costs of mental health care for each schizophrenic over his/her lifetime (Rössler et al, 2005). Improved quality of life is important to see. Schizophrenics need to return to a level of functioning where they are paying taxes and getting along well with family, friends, and society. I hope that this review has shone some light on the potential of complementary alternative treatment and its role as an adjunct to psychiatric care.

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