

# Chromium, Selenium, Copper and other Trace Minerals in Health and Reproduction

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## Introduction

Many mineral elements occur in plant and animal tissues in such minute amounts that early workers were unable to measure their precise concentrations with analytical methods then available. They were therefore described as occurring in traces, hence the term "trace element." This is still in use despite the development of modern analytical laboratory techniques such as atomic absorption spectrometry and neutron activation analysis which have an ability to measure all trace elements in the smallest of biological samples with great precision and accuracy. In fact, it could be argued that since the development of these highly sophisticated techniques, the term 'trace' has become scientifically obsolete.<sup>1,2</sup>

A trace element is considered as essential for both man and animals if it meets the following criteria: a) It is present in all healthy tissues. b) Its concentration from one species to the next is fairly constant. c) Depending on the species studied, the amount of each element has to be maintained within its required limit if the functional and structural integrity of the tissues is to be safeguarded, and the growth, health, and fertility to remain unimpaired. d) Its withdrawal induces reproducibly the same physiological and/or structural abnormalities. e) Its addition to the diet either prevents, or reverses, the abnormalities.<sup>3</sup>

Several trace elements are known to fulfill this criteria, of which the most well known are: iron, zinc, manganese, selenium, chromium, copper, cobalt, nickel, molybdenum and iodine. The majority act as catalysts in a variety of enzyme system functions. In this respect their roles range from weak ionic enzymatic cofactors to

highly specific substances known as metalloenzymes.<sup>4a</sup>

The action of each element could be further divided into the following: a) Biological action required to sustain optimum health. b) Pharmacological action where supplements are used in treating specific deficiency conditions. c) Toxicological action where a dose exceeds the biochemical need.<sup>5</sup> We will be discussing in this paper the role of chromium, selenium and copper in both animal and human metabolism.

## Chromium (Cr)

### *Chromium in glucose metabolism*

Chromium, in the form of naturally occurring dinicotinic acid -glutathione complex, also known as glucose tolerance factor (GTF), is vital for carbohydrate metabolism as it potentiates the action of insulin.<sup>4b-8</sup> Isolated from brewer's yeast, the active component of GTF was subsequently found to contain trivalent chromium, nicotinic acid, glycine, glutamic acid and cysteine.<sup>4b</sup> As such, it normalizes blood sugar levels in subjects with tendencies toward blood -sugar fluctuations associated with diabetes (hyperglycemia) and 'Low blood sugar (hypoglycemia).'<sup>9</sup>

Both animal experiments and human studies have demonstrated the first phase of marginal chromium deficiency manifests itself by slightly elevated circulating insulin levels in response to glucose loading. Largely due to an increased hormone production, in this phase most insulin dependent physiological functions tend to remain intact. The second phase, well characterized in both animal experiments and human studies, begins to show signs of the metabolic disorders associated with low chromium intake which include significantly abnormal glucose fluctuations and disturbances in lipid metabolism.<sup>10</sup>

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The final phase of inadequate chromium intake manifests itself by a marked insulin resistance to glucose loading, resembling a diabetes-like syndrome, which eventually leads to an exhaustion of pancreatic insulin production and ultimately to the development of insulin-dependent diabetes.<sup>6,11</sup>

Research has already established that insulin-dependent diabetic children exhibit a significantly lower hair chromium concentration compared to controls.<sup>12</sup> Other studies have found that chromium absorption and excretion in diabetics is two to four times greater than in healthy individuals,<sup>13</sup> and that subjects who died with diabetes had significantly lower hepatic chromium concentration compared to nondiabetics.<sup>14</sup>

#### *Chromium in lipid metabolism and ischemic heart disease*

Ever increasing research evidence has linked low dietary chromium with disturbances in lipid metabolism and hence in the development of arteriosclerosis. For example, when rats were placed on low chromium diet, not only their glucose tolerance became impaired but also their serum cholesterol levels increased. Further investigations revealed that these animals suffered a far greater number of aortic plaques compared to those fed with sufficient chromium.<sup>15,16</sup> Similar results have been observed when experimenting with rabbits.<sup>17,18</sup>

Studies among the human population-made similar findings.<sup>19-25</sup> For example, one large epidemiological survey found significantly lower chromium values in individuals with cardiovascular morbidity and mortality compared to controls.<sup>22</sup> Another found a far greater incidence of low hair chromium concentration in subjects with arteriosclerotic heart disease compared to healthy individuals of the same age.<sup>23</sup> Yet another reported that subjects who had died from coronary artery disease had much lower chromium levels in their aortic tissue compared to those who died from accidents.<sup>24</sup>

One study found significantly lower serum chromium levels in individuals with angiographically determined coronary artery disease compared to healthy controls.<sup>25</sup> According to the authors: "When the role of chromium was assessed in the context of selected risk factors (age, sex, race, cholesterol, triglycerides, systolic blood pressure and diastolic blood pressure) by simple regression analysis, low chromium concentrations proved to be the best predictor of coronary artery disease.<sup>25</sup> The protective effect of chromium against the development of heart disease is not yet fully understood. However, considering that chronically high insulin levels are characteristic in many subjects who either have developed, or might develop, arteriosclerosis, some researchers suggested that one reason for the high frequency of coronary artery disease seen in chromium-deficient individuals, could be their inability to maintain normal levels of insulin.<sup>26</sup>

#### *Chromium in protein synthesis*

The role of chromium in the function of nucleic acids metabolism and synthesis is indicated by the high concentrations of this trace element present in nuclear proteins relative to other transition metals.<sup>4b,7,27</sup> Animal experiments have shown that chromium is concentrated largely in the nuclear fraction of the cells, the remainder is divided between the mitochondria and the microsomes.<sup>4b</sup> Other experiments have demonstrated that chromium-deficient diets lead to an impaired capacity for incorporating amino acids, particularly glycine, serine, methionine and gamma-aminoisobutyric acid, into proteins.<sup>4b</sup>

#### *Chromium in reproduction*

As chromium deficiency has an ability to depress nucleic acid synthesis, experiments have shown that rodents fed diets low in chromium have a significantly lower sperm count and decreased fertility compared to chromium-supplemented con-

trols.<sup>28</sup> Considering that chromium is essential for maintaining the structural stability of proteins and nucleic acids, studies on animals have found that this element is also vital for healthy fetal growth and development.<sup>4b</sup>

To date, studies on humans have established that premature infants, and those with evidence of intrauterine growth retardation, have significantly lower hair chromium status compared to infants born full-term.<sup>31</sup> Others have found that multiparous women have far lower body chromium levels compared to nulliparae.<sup>32</sup> These findings indicate that chromium is indeed an essential trace element during fetal growth and development.<sup>29-31</sup>

#### *Chromium content in foods*

Dietary surveys have established that chromium content in Western diets is consistently below the Recommended Dietary Allowance (RDA). This is largely due to an ever increasing consumption of refined sugar and white flour,<sup>27,29,30,33</sup> not only because chromium is discarded in these foods during processing but also because these foods further exacerbate chromium deficiency. This is because the human body cannot metabolize and transform these highly refined foods into energy without the presence of chromium. It is therefore obvious that the more of these highly refined foods one consumes, the more chromium is depleted from already marginal body stores.<sup>27</sup>

#### *Selenium (Se)*

As with other trace elements, early researchers concentrated on the role of selenium in animal disease conditions. The role of selenium in animal physiology was first established when it was found that selenium could prevent liver necrosis in vitamin E-deficient rats.<sup>34</sup> Selenium is able to prevent exudative diathesis and pancreatic fibrosis in poultry, hepatitis dietetica in pigs and muscular dystrophy in lambs, calves and other species. Furthermore, it is

a vital element for growth and for maintaining optimum fertility status.<sup>4c</sup>

In humans, selenium increases the growth of fibroblasts in culture.<sup>35</sup> It is also a vital component of an antioxidant enzyme known as glutathione peroxidase.<sup>36</sup> Furthermore, it prevents the occurrence of Keshan disease and juvenile cardiomyopathy, found in countries where the soil is low in this essential mineral.<sup>37</sup> An ever increasing number of epidemiological surveys are linking low dietary selenium with the development of cancer and cardiovascular disorders.<sup>38,39</sup>

#### *Selenium in Glutathione Peroxidase*

Selenium is a vital component of an enzyme known as glutathione peroxidase (GSH-Px) which forms a part of the body's defence system by protecting cells against lipid peroxidation.<sup>40-45</sup> The activity of GSH-Px has been demonstrated to occur in wide range of body tissues, fluids, cells and sub-cellular fractions. The highest GSH-Px activity has been found to occur in the liver, moderately high in erythrocytes, heart muscle, lung and kidneys, and lesser in the intestinal tract and skeletal muscles.<sup>4c</sup>

When it became evident that selenium is an essential component of glutathione peroxidase, the puzzling relationship between selenium and vitamin E became better understood. It is believed that the role of vitamin E in selenium metabolism is to enhance the GSH-Px activity.<sup>45</sup> Others are more precise suggesting that selenium, in the form of GSH-Px, is of primary importance because of its ability to destroy the formation of free radicals before they have a chance to attack the cellular membranes, while vitamin E functions on the cell membrane itself as a specific lipid-soluble antioxidant.<sup>4c</sup>

#### *Selenium and cancer*

The idea that selenium has an inhibitory effect on carcinogenesis comes both from animal experiments and human stud-

ies. The epidemiological evidence of low selenium status and human cancer was first demonstrated in ten cities with a population of 40,000-70,000 by Shamberger and Frost.<sup>46</sup> The results showed a clear inverse relationship between selenium status and cancer death rates. Cancer of the stomach, esophagus and rectum were found to be particularly high in selenium-poor areas. Another survey compared selenium distribution with female breast cancer mortality. The study found that the incidence of breast cancer was significantly higher in selenium-poor areas compared to areas high in selenium.<sup>4c</sup> Other researchers have come to similar conclusions.<sup>47</sup>

Admittedly these findings do not necessarily imply a causal relationship between low selenium status and cancer. However, when epidemiological data are taken in conjunction with animal experiments, there seems to be little reason to doubt that selenium has an inhibitory effect on cancer formation. An obvious logical corollary to these findings is that human cancer incidence and mortality could be lowered by taking selenium supplements.<sup>4c,46-50</sup>

### *Selenium and Cardiovascular Disease*

Epidemiological evidence has shown a significantly increased incidence of heart disease and thrombosis in areas low in selenium compared to selenium-rich areas.<sup>33,38,39,51,52</sup> It is believed that the role of selenium in the prevention of heart disease stems from its activity to protect, via glutathione peroxidase, blood platelets and cells against oxidative injury.<sup>52-54</sup> Studies on animals have shown that during graded selenium depletion, glutathione peroxidase activity decreases stepwise with lesser dietary intake and increases when selenium is added to the diet.<sup>55,56</sup> In order to protect against the development of heart disease everyone, particularly those living in selenium-poor areas, ought to take an additional selenium supplement.<sup>51-56</sup> However, it is worthy to note that selenium can be toxic when taken in excess.

### *Selenium in Reproduction*

Selenium deficiency results in impaired reproductive performance in all species studied. In hens, selenium deficiency reduces both egg production and hatchability. In cows and ewes it leads to high embryonic mortality. Rats fed on low selenium, gave birth to pups which were almost hairless, grew slowly and failed to reproduce when mature. In all instances, selenium added to the basic diet restored both growth and reproductive capability.<sup>4c</sup>

Earlier studies of the role of selenium in fertility were largely confined to the female but research is now extended to the male. Experiments on rodents have shown that selenium is vital for maintaining the integrity of sperm mitochondria.<sup>57,58</sup> Also that selenium deficiency leads to a reduced testicular growth. Further investigations revealed degenerative changes in the epididymis which is related to sperm maturation. The epididymal changes appeared to be even more sensitive to selenium deficiency than the growth and development of the testis. In addition, the sperm was found to be immotile. This improved almost linearly with the increasing amount of selenium added to the basal diet.<sup>4c</sup>

### *Selenium Content in Foods*

Since selenium is not essential for plant growth, the level of selenium in foods of plant origin depends on the soil conditions under which they are grown. Studies have shown that the selenium content of cereal crops between different countries, even between regions, can vary as much as 1,000-fold. This has been compounded further by the extensive use of agrochemicals which, with acid rain, tends to wash any remaining traces of selenium out of the soil. As a result, even the livestock that graze on these selenium-poor pastures are invariably low in this essential trace element. This means that not only is the meat we eat low in selenium but also products such as eggs and milk.<sup>38</sup> However, since cereals tend to be the main component of most diets, studies

have found that the selenium intake in Britain has declined by about 50% since the 1970s when imports of high selenium North American wheat (200-500mcg/kg) were replaced with low-selenium UK (EU) wheat (20-50 mcg/kg). Consequently it is estimated that dietary selenium intake in Britain is less than half that which is required for optimum health.<sup>59</sup> Food processing further depletes selenium from our staple diet. For example, brown rice has fifteen times the selenium content of white rice, and whole wheat flour contains twice as much of this vital trace element compared with the white variety.<sup>60</sup>

### Copper (Co)

The earliest manifestation of copper deficiency was found to lead to anemia in rodents.<sup>61</sup> Subsequently, a host of other abnormalities were recognized in copper-deficient animals including defective wool keratinization, abnormal bone formation and arterial and cardiac aneurysm.<sup>62-64</sup> Other features among the offspring born to animals subjected to severe copper deficiency was found to include neurological problems such as ataxia, seizures and episodic apnea which were believed to be caused by a lack of myelination leading to a reduced nerve cell formation during embryonic development.<sup>4d,65,66</sup>

As the investigation of copper biochemistry has advanced, the identification of intermediary pathways of various cuproenzymes has provided an increased understanding of the pathophysiological basis for these abnormalities. Consequently, an ever increasing number of disorders associated with copper deficiency have been recognised in humans which have been noted to be strikingly similar to those observed in animal experiments<sup>4d,67,68</sup>

### *Copper deficiency in anaemia*

In humans, nutritional copper deficiency leads to hypochromic anemia and neutropenia.<sup>67-69</sup> Further studies have established that the anaemia appears to be related to defects of iron mobilization due to a com-

bined defect of both ceruloplasmin ferroxidase activity and intracellular iron utilization.<sup>70,71</sup>

### *Copper in Superoxide Dismutase (SOD)*

In human blood, equal quantities of copper is bound in red blood corpuscles and plasma. In the former, it is loosely bound to amino acids. Moreover, 60% of copper in the blood is tightly bound to a copper-zinc-dependent enzyme known as superoxide dismutase (CuZnSOD) which is a powerful antioxidant. A similar antioxidative enzyme is dependent on the trace mineral manganese (MnSOD). As with glutathione peroxidases the role of superoxide dismutases is to protect cells against free-radical injury.<sup>33</sup>

### *Copper in bone and arterial defects*

Menkes disease, caused by a genetic copper deficiency, was first described in 1962 as a syndrome seen in infants characterized by poor growth, white brittle hair with peculiar twisting, arterial defects, focal cerebral degeneration and mental retardation.<sup>72,73</sup> Some studies have also linked a severe copper deficiency in infants to pathological bone fractures similar to those seen in "battered child syndrome."<sup>74</sup> In experimental settings, these defects are believed to be related to reduced activity of a copper-dependent enzyme, lysyl oxidase, which is vital for the cross-linking of collagen.<sup>75,76</sup>

### *Copper in cardiovascular and lung disorders*

Cardiovascular disorders are evident in almost all species subjected to severe copper deficiency whether genetic or nutritional in origin.<sup>4d</sup> These appear to be caused by an impairment of cross-link formation of soluble elastin and collagen due to depression of the previously mentioned lysyl oxidase activity.<sup>76-78</sup> Similarly, the emphysema-like lung condition observed in some copper deficiency states appears to occur for the same reason.<sup>68</sup> Other factors, par-

ticularly the peroxidative damage that is frequently seen in both lung and cardiovascular pathology, is believed to be directly related to the excessive free radical formation due to a reduced superoxide dismutase (CuZnSOD) activity.<sup>67</sup>

### *Copper Poisoning and Toxicity*

Although copper is an essential element, an excessive amount is toxic. The symptoms of copper poisoning, which is frequently associated with suicidal intent, are clearly documented including: nausea, vomiting, diarrhea, hypotension, jaundice, hematuria, anuria, coma and death.<sup>80</sup> Unfortunately however, a low-level copper toxicity seems to affect most of us. One of the most prominent sources of copper comes from our drinking water supplies running through copper piping, particularly in areas where the water is soft and acidic, as this literally corrodes layers of copper from the pipes. This action also occurs when acidic foods are cooked in copper pans.<sup>29,30</sup> Cigarette smoking is another prominent source of excessive copper accumulation.<sup>81</sup> Similarly oral contraceptives are notorious in raising the body's copper burden.<sup>29,30,82,83</sup>

The late Dr. Carl Pfeiffer of the Brain Biocentre in Princeton, New Jersey, conducted extensive research on copper metabolism and human health. His findings indicate that a high body copper burden can be responsible for such diverse disorders as hypotension, heart disease, premenstrual tension, postpartum depression, paranoid and hallucinatory schizophrenias, childhood hyperactivity and autism.<sup>60</sup>

### *Toxic Trace Elements*

The classification of trace elements includes a group of non-essential or toxic trace elements because their biological significance is confined to their toxic properties only. These include (besides an excess of copper) lead, cadmium, mercury and aluminium, all of which we acquire mainly

through environmental contamination including air pollution, modern agriculture and industrial practices and contaminated food/water supplies.<sup>29,30</sup>

An excessive lead accumulation in children is known to cause hyperactivity, a reduced intelligence and anti-social behaviour. In adults, it is associated with heart disease, cancer and infertility, and with criminality.<sup>84</sup> In addition, a high maternal lead is known to lead to miscarriage, a reduced birth weight and a number of fetal malformations.<sup>29,30,85</sup> High aluminium, mercury and cadmium are linked with similar problems to those associated with high lead and copper. Evidence has shown that all heavy metals, even at relatively low concentrations, have a significantly negative effect on fertility and pregnancy outcome.<sup>29,30</sup>

### *Hair-Mineral Analysis*

Until recently, the recognition and consequent treatment of heavy metal excesses, including trace and macro-mineral deficiencies, has been hindered by a lack of reliable diagnostic techniques. Although blood, sweat and urine have been used, unfortunately these have been found to be ineffective in detecting long-term exposure due to the fact that body fluids are in a constant state of flux, thereby reflecting only a very recent exposure of some hours or days.<sup>87-89</sup>

However, since the development of modern laboratory techniques such as atomic absorption spectrometry and neutron activation analysis, trace element concentrations can now be measured from the smallest of samples with great precision and accuracy. Particularly, since the introduction of the inductively coupled plasma mass spectrometry (ICP-MS) system which has a multi-detection capacity, hair tissue analysis has become the diagnostic tool of choice because it has an ability to measure simultaneously the presence of the following trace elements: zinc,<sup>1,2,90</sup> copper,<sup>1,2,90</sup> manganese,<sup>1,2,90,91</sup> selenium, molybdenum,<sup>1,2,94</sup> vanadium,<sup>1,2,95,96</sup> cadmium<sup>1,2,97,98</sup> lead<sup>1,2,99,100</sup> and mercury.<sup>1,2,101,102</sup>

The advantages of hair tissue analysis over other diagnostic samples are as follows: a) Mineral concentrations are not subject to rapid fluctuations due to diet or other variabilities and therefore reflect a long-term nutritional status. b) Sample collection is non-invasive. c) Samples are stable at room temperature. d) Analytical methods are simple because mineral concentrations in hair are relatively high compared to other measurements.<sup>27</sup>

In the past, hair analysis had a rather doubtful reputation because laboratories tended to use different sample preparations which affected the outcome. However, since most laboratories are currently using similar preparation and digestion processes, the results are becoming more identical. However, it is unlikely that the results between different laboratories will ever be exactly alike as each machine tends to have its own particular level of sensitivity. To avoid these fluctuations in comparing results, it is recommended to use the same laboratory instrument.

### Trace Element Interactions

With the progress made in measuring and understanding the specific functions of macro, trace and toxic minerals in human physiology, it has become evident that the action of each element can either be potentiated, or reduced, by the presence of another. This is also why the ratio between the concentration of any given mineral found in body chemistry affects whether or not deficiencies or toxicities may occur. The requirement and hence the nutritional adequacy of a particular mineral depends on other minerals already present in the body chemistry. To appreciate this concept it is necessary to delineate a basic definition.<sup>103</sup>

Interactions between minerals can be either positive or negative. A positive (synergistic) action takes place where an element requires the presence of at least one other element for its metabolic efficacy. An example of synergy is between copper

and iron as both are required for the promotion of hematopoiesis. A negative (antagonistic) interaction occurs whenever a normal metabolic function of an element is impaired by the relative excess of another. A good example is between copper and iron because an excess of one reduces/affects the presence of the other. This phenomenon invariably takes place when competing ions possess the same, or very similar, electron configuration.<sup>104</sup>

The synergistic or antagonistic classifications say nothing about the exact site of their occurrence, however, most occur either at the site of absorption, metabolism or excretion.<sup>103</sup> Antagonistic interactions are particularly evident between selenium:cadmium and selenium:mercury,<sup>103,105</sup> and between manganese:iron, zinc:cadmium, zinc:iron and zinc:copper.<sup>103,106,107</sup> This means that high cadmium and/or mercury levels can be lowered by taking additional selenium. Likewise, zinc can be used for reducing a high copper, iron and/or cadmium burden.

The antagonism between copper and zinc warrants special concern because zinc is centrally involved in over 80 different enzyme system functions, including most events relating to cell division and nuclear acid synthesis.<sup>108</sup> Considering the importance of zinc in human physiology, it is not surprising that zinc deficiency is associated with numerous mental, physical and reproductive disorders.<sup>108</sup>

In infants, sub-clinical zinc deficiency is known to lead to poor growth, hypogonadism and reduced immunity. In children, it is associated with autism, dyslexia, apathy, lethargy, irritability and childhood hyperactivity. In adults zinc deficiency has been linked with the development of both senility and Alzheimer's disease.<sup>108</sup>

Considering that most enzymes relating to cell division and replication are zinc-dependent the time of conception and pregnancy, represent the most vital period for ensuring an optimum zinc status. Both animal experiments and human studies

have found that low maternal zinc leads to the following reproductive failures: infertility, miscarriage, intrauterine growth retardation, small head circumference and an increased number of congenital malformations. In males, a low zinc nutriture has been found to be responsible for a low sperm count, slow sperm motility, malformed sperm and infertility.<sup>29,30,108</sup>

### The Foresight Approach

Realizing that both toxic metal excesses and trace mineral deficiencies are associated with all forms of reproductive failures, Foresight (The Association for Promotion of Preconceptual Care) has, since it was formed over 20 years ago, advocated hair tissue analysis before conception takes place.<sup>29,30</sup> If the results show that metals are above the threshold, Foresight advises an individually tailored cleansing program which may include, besides appropriate minerals, vitamin C and/or garlic which are known for their ability to eliminate heavy metals. If the toxic metal burden is severe, a combination of minerals may be suggested.<sup>30</sup> In addition, if hair-tissue analysis shows either trace- or macro-mineral deficiencies, Foresight recommends appropriate supplementation. This program is given for a stated period after which the hair is re-tested. In cases where the results have not yet reached the levels required for a healthy fetal development, supplements will either be repeated or adjusted, until hair-tissue analysis is compatible with the optimum health and development of the future infant.<sup>29,30</sup>

Foresight's Preconception Care Program is highly effective, This was confirmed by an audit conducted by Dr Neil Ward and his team at the University of Surrey Chemistry Department, after following a cohort of 367 Foresight couples. Of these, 136 couples had previous infertility problems and 139 had suffered from one to five previous miscarriages. The cohorts also included 11 couples who had delivered a stillborn child,

seven whose children were malformed and 45 couples who had infants born with a low birth weight. A total of 86 couples reported more than one of these problems.

After implementation of Foresights' recommendations and within the timescale of the study, 327 babies were born. The average gestation age was 38.5 weeks and the average birthweight 3.3 kg. Each child was born perfectly healthy and no baby had to be admitted to Special Baby Care Unit. There were no miscarriages or stillbirths.<sup>109</sup>

In January, 1996 Earl Baldwin of Bewley discussed in the House of Lords the effectiveness of Foresight's Preconception Care Programme. He states: "In the realm of reproductive health, Professor Barker in Southampton has been showing that malnutrition in the womb can affect health in later life. But few people know of the pioneering work of a small organization called Foresight, which for years has been targeting the health of couples before conception, In this country a quarter of all pregnancies ends in miscarriage. One baby in 11 is born prematurely one in 17 is malformed, to say nothing of those couples who are unable to conceive at all. Foresight's doctors attend to the parent's diets, especially their micronutrient levels, and to the possibility of a toxic overload with lead and other substances. When you consider all that is involved in *in vitro* fertilization you would think that some encouragement might be given to the low-cost alternative, instead of the demand that Foresight should fund and conduct a double-blind trial which by the nature of the treatment is an impossibility. Here we have a classic example of the mismatch between orthodox research tools and non-conventional approaches which invariably blocks the progress in promising fields..."<sup>110</sup> Foresight's Preconception Care Programme helps to assure a healthy birth based on consideration of the important role played by trace minerals in reproduction.



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# Correspondence

## Treating ALS

In a recent edition of the *Journal of Orthomolecular Medicine*<sup>1</sup> I argued that Parkinson's disease, multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) all occurred as a consequence of an excess of glutamate. In subsequent correspondence,<sup>2</sup> I suggested that nicotine, a glutamate antagonist, would prove to be protective against Parkinson's disease, in part, because it augments dopaminergic neurotransmission.<sup>3</sup> I am happy to report that Dr. Paul Newhouse of the University of Vermont has since shown that 15 Parkinson's patients made substantial physical and mental improvement whilst wearing the nicotine patch.<sup>4</sup> If my iodine-dopachrome-glutamate hypothesis is correct, I expect nicotine will also be helpful in the treatment of both MS and ALS.

In the original paper,<sup>1</sup> I further argued that levodopa should prove to be of benefit in the treatment of all three disorders, but could provide only evidence of its value in Parkinsonism and MS. Subsequently I have discovered a very stimulating thirty-year-old paper, authored by Dr. André Barbeau, the then Director of the Department of Neurobiology at the Clinical Research Institute of Montreal.<sup>5</sup> This paper describes an attempt to explore the value of additional dopamine in the treatment of a wide range of disorders, including Parkinson's disease, ALS, Steele-Richardson-Olszewski syndrome, Torsin dystonias, Wilson's disease, Pick's and Jakob-Creutzfeldt diseases, renal function, mania and depression. Of particular interest here are Barbeau's comments on levodopa's impact on amyotrophic lateral sclerosis.<sup>5</sup>

"The knowledge that symptoms of this disease (ALS) were often present in patients afflicted with Parkinson-dementia complex led us, as a last measure, to try L-dopa in a few advanced cases. The preliminary results are surprising, and although we do not understand them, they are of such a nature as to warrant further con-

trolled studies."

I have searched, without success, for any additional literature published by Dr. Barbeau and/or his colleagues, describing the impact of levodopa on advanced ALS. However, the quotation just provided suggests to me that his initial use of levodopa produced improvement in the well being of advanced ALS patients. If this interpretation of his comments is correct, it provides further evidence to support the iodine-dopachrome-glutamate hypothesis.<sup>1</sup>

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